International Peer Review Journal
p-ISSN 1817-5562
e-ISSN 1998-037X (Online)
CD-ROM ISSN 1998-0361

The New Iraqi Journal Of Medicine
The Official Journal Of The Iraqi Ministry Of Health and Iraq Headquarter of Copernicus Scientists International Panel

Volume 7 Number 3 December 2011

The New Iraqi Journal of Medicine has agreed the use of the uniform requirements of manuscripts submitted to biomedical journals published by the INTERNATIONAL COMMITTEE OF MEDICAL JOURNAL EDITORS (ICMJE) and it's the first Iraqi peer-review medical journal listed by the ICMJE journal list. The first two issues of this journal appeared under the title of Al Karkh journal of Medicine

www.newiraqijm.4t.com
Indexed by Copernicus Index Journal Master List and EMR index medicus

The New Iraqi Journal of Medicine 2011 7(3):3-4

Instructions for Contributors: Online submission

http://newiraqijm.blogspot.com/

Aamir Jalal Al Mosawi
Editor -in - chief
Training and development center
Iraqi Ministry of Health
E-mail: new_iraqijm@yahoo.com

The New Iraqi Journal of Medicine www.new_iraqijm.4t.com is a peer-reviewed scientific journal that publishes original articles in all fields of experimental and clinical medicine and related disciplines. The New Iraqi Journal of Medicine is currently issued 3 times per year. Acceptance depends on receiving positive reviewer's opinion from two different countries.

ONLINE SUBMISSION OF MANUSCRIPT:
During the year 2011 of manuscript should be submitted online through the online submission system at www.newiraqijm.4t.com

The editors endorse the principles embodied in the **Declaration of Helsinki RECOMMENDATION FOR CONDUCT OF CLINICAL RESEARCH** and expect that all investigations involving humans will have been performed in accordance with these principles.

REVIEW PROCESS: Manuscripts are evaluated on the basis that they present new insights to the investigated topic, are likely to contribute to a research progress or change in clinical practice or in thinking about a disease. It is understood that all authors listed on manuscript have agreed to its submission. The signature of the corresponding author on the letter of submission signifies that these conditions have been fulfilled

Received manuscripts are first examined by the editor. Manuscripts with insufficient priority for publication are rejected promptly. Incomplete packages or manuscripts not prepared in the advised style will be sent back to authors without scientific review. The manuscripts are sent to experts for scientific evaluation. The evaluation process usually takes 1–4 weeks. Submitted papers are accepted for publication after a positive opinion of the two reviewers.

COPYRIGHT TRANSFER: Upon acceptance, authors transfer copyright to The N Iraqi J Med. Upon acceptance all published manuscripts become the permanent property of The New Iraqi J Med, and may not be published elsewhere without written permission from the editor sponsor.

ARTICLE STRUCTURE: Original research articles, clinical studies, and case reports should be organized as follows: Text should be one spaced with 12 points typeface. Margins: 2.5 cm (1 inch) at top, bottom, right, and left. Illustrations are very helpful and for case reports are mandatory. The Editor reserves the privilege of adjusting the format of the article.

THE MANUSCRIPT SHOULD INCLUDE:

Title page should include

- Full names of all authors
- Name of the department and institution

in which the work was done

- Affiliations of the authors
- Manuscript full title
- Full name, address, telephone and/or
- E-mail

Abstract Page: Abstract (300 words) should consist of four paragraphs labeled: Background, Material (Patient and Methods), Results, Conclusion.

Key words (3 to 6) or short phrases should be written at the bottom of the page.
Text: The text of the article should be divided to seven paragraphs labeled: Introduction, Material (Patient) and Methods, Results, Discussion, Conclusions, Acknowledgements, References.

Introduction should contain scientific rationale and the aim of the study or (in the case of a review) purpose of the article.

Material (Patient) and methods should describe clearly the selection of observational or experimental subjects (Patients or laboratory animals) including controls, such as age, gender, inclusion and exclusion criteria, (the circumstances for rejection from the study should be clearly defined), randomization and masking (blinding) method. The protocol of data acquisition, procedures, investigated parameters, methods of measurements and apparatus should be described in sufficient detail to allow other scientists to reproduce the results. Name and references to the established methods should be given. References and brief description should be provided for methods that have been published but are not well known, whereas new or substantially modified methods should be described in detail. The reasons for using them should be provided along with the evaluation of their limitations.

The drugs and other chemicals should be precisely identified including generic name, dose and route of administration. The statistical methods should be described in detail to enable verification of the reported results.

Results should concisely and reasonably summarize the findings. Do not duplicate data in graphs and tables. Give numbers of observation and report exclusions or losses to observation such as drop outs from a clinical trial. Report treatment complications. The results should be presented in a logical sequence in the text, tables and illustrations. Do not repeat in the text all the data from the tables or graphs. Emphasize only important observations.

Discussion should deal only with new and/or important aspects of the study. Do not repeat in detail data or other material from the Background or the Results section. Include in the Discussion the implications of the findings and their limitations, including implications for future research.

Conclusions should be linked with the goals of the study. State new hypotheses when warranted. Include recommendations when appropriate. Unqualified statements and conclusions not completely supported by the obtained data should be avoided.

References must be numbered consecutively as they are cited. References should be denoted numerically and in sequence in the text, using Arabic numerals placed in square brackets, i.e., [12]. List references in numerical order in the Reference list. References selected for publication should be chosen for their importance, accessibility. References first cited in tables or figure legends must be numbered so that they will be in sequence with references cited in the text. The style of references is that of Index Medicus. List all authors when there are six or fewer; when there are seven or more, list the first three, then et al.

The following is a sample reference: Standard journal article

*Lahita R, Kluger J, Drayer DE, Koffler D, Reidenberg MM. Antibodies to nuclear antigens in patients treated with procainamide or acetylprocainamide. N Engl J Med 1979; 301:1382-5.

Book, personal author(s)

Ringsven MK, Bond D. Gerontology and leadership skills for nurses. 2nd ed. Albany (NY): Delmar Publishers; 1996, pp 30-45. Book, editor(s) as author Norman IJ, Redfern SJ, editors. Mental health care for elderly people. New York: Churchill Livingstone; 1996, pp.

Tables: Do not submit tables as photographs. Number tables consecutively in the order of their first citation in the text, and supply a brief title for each. All non standard abbreviations that are used in each table.

Figures should be numbered consecutively according to the order in which they have been first cited in the text. Define in the legend all abbreviations that are used in the figure.

Review articles Each review article should concentrate on the most recent developments in the field. These articles aim to summarize and highlight recent significant advances in and ongoing challenges in the field. Authors should strive for brevity and clarity. The final structure of the review will, of course, depend on the title/focus but wherever possible, the following sections should be included.

The New Iraqi Journal of Medicine

Original Article

Endocrinology

Obesity and rheumatoid arthritis: results from a case-control study

*Mohammad Mahdi Eftekharian *, Zahra Basiri **, Khosro Mani Kashani****

Abstract

Background: Rheumatoid arthritis (RA), the chronic autoimmune disease with several opinions about its etiology, has affected more than 50 million people in the world. The aim of this 2009 study was to investigate the association between obesity and RA in Hamedan, a western city of Iran.
Methods: As a case-control study, obesity was assessed using BMI (Body Mass Index) from 128 cases and 129 controls, matched for age and sex and analyzed by SPSS (chi-square tests).
Results: In case and control groups, females were 116 and 117 persons respectively and the rest were males. Statistical analysis showed that there is no significant association between obesity and RA ($p > .05$).
Conclusions: Considering previous global investigations on this topic with different results and the results of our study, it seems that more studies will be needed to describe the association between obesity and RA.

The N Iraqi J Med, December 2011; 7(3):5-9

Keywords: *Rheumatoid arthritis, Obesity, Body Mass Index, Risk factors*

INTRODUCTION[1]

Rheumatoid arthritis (RA) with its unknown etiology is one of the most important autoimmune diseases that affects more than 50 million individuals in the world. RA is a form of recurrent chronic arthritis that usually involves several joints symmetrically and similar to other multi-factorial diseases, is believed to occur as a result of the interaction between genetic constitution and environmental triggers [1-4]. However, as in most other complex diseases, few such interactions have been described and it has been assumed that more studies will be needed to describe significant gene–environment interactions in these diseases. The main genetic risk factor is the shared epitope (SE) of HLA-DR, but several proposals have been presented about environmental risk factors [1-4]. One of the most important of these proposals should be the history of particular infections such as Epstein-Barr virus (EBV) [2, 5-10]. After entering the B lymphocyte, this virus causes the polyclonal activation of these cells and in turn production of rheumatoid factor (RF). RF is a kind of IgM-class auto antibody that reacts with auto-IgG then precipitates in joints. Some scientists believe that targeted IgG is a particular gamma globulin with an abnormal structure that is produced by synovial lymphocytes. In connection with RA etiology there are also other microorganisms (mycoplasma, cytomegalovirus and rubella) that probably have a hand in the appearance of RA following a history of infection by them [2]. In this case, some agents such as cross-reaction between microbial antigens and joint proteins or super antigen presentation should be noted. The incidence rate of RA in the world is about 1% (range 0.3% to 2.1%) and, based on previous studies, women are more susceptible than men [1-4]. Familial studies have also shown that genetic susceptibility is important in this connection and, as mentioned previously, the role of shared epitope of HLA has been proved [1-4]. Several other areas of research about other risk factors have identified coffee consumption [11-13], blood transfusion history [14,

* *Faculty of Para medicine, Hamedan University of Medical Sciences, Hamedan, Iran*
Email: eftekharian@umsha.ac.ir
***Faculty of medicine, Hamedan University of Medical Sciences, Hamedan, Iran*
Email: basiri@umsha.ac.ir
****Faculty of Medicine, Hamedan University of Medical Sciences, Hamedan, Iran*
Email: mani@umsha.ac.ir

15], kind of sex [1-4, 16], sex hormones [2, 17], diet [2, 18-20], weather [2, 21, 22] and smoking [2-4, 23-36]. Since in obesity as one of the most complex health problems in the world, the balance between biochemical reactions and endocrine system is targeted, this is an area of study that merits more research. As mentioned in other reports, 80% of RA cases begin in the fourth and fifth decades of life, and information about relative risk factors and useful instruction should assist in preventive methods and decrease the incidence of RA. Other scientists have studied the association of obesity and RA previously [14, 15, 27, 35], but different results related to different areas of the world demonstrate that geographically limited studies cannot be generalized to other parts of world because some known and unknown area-dependent factors should have an effect. Thus in 2009 we start to study the relation of some risk factors (such as obesity) with RA in Hamedan, a city located in the west of the Iran.

METHODS

Design of Study

This research was designed as a case-control study involving incident cases of RA that were derived from the population ages 20–55 years in a geographically defined city in the western parts of Iran, Hamedan. The recruitment period for the cases and controls was 2009.

Selection of the Cases and Controls

All referring potential cases were examined and diagnosed by a rheumatologist in Mobasher hospital, the centre of rheumatology care in this aforementioned city. Definite RA diagnosis was completed on 128 individuals after RA latex examination on blood samples, physical exam, clinical symptoms and study of personal history. Primary statistical analysis was then conducted in order to calculate the average of sex and age in the case group.

A total of 129 control populations were selected by physicians among healthy persons matched for age and sex with the case group after examination.

Assessment for obesity

Obesity has been assessed using BMI (Body Mass Index) (weight divided by height squared) as a most common anthropometric assessment for obesity, according to World Health Organization (WHO) guidelines with the consent of both patients and controls in the presence of physician. Individuals with a BMI of >30 kg/m^2 and 25–30 kg/m^2 are classified as obese and overweight respectively. (As a distinct category)

Statistical Analysis:

Statistical analysis was performed by SPSS version 16 with Pearson's chi-square tests. P value lower than 0.05 was considered a significant result. Results were analyzed and studied by cross-tabulation.

RESULTS

Results after filling out the questionnaire were cross-tabulated including sex distribution in two groups, case and control and are shown in Table 1. The study of relation between obesity and R.A. was analyzed using Pearson's chi square test and p value was 0.66, meaning that there is not significant relation between the obesity and RA (Table 2).

Studied groups	Male		Female		Total	
	Number	Percent	Number	Percent	Number	Percent
Case	12	9.38	116	90.62	128	100
Control	12	9.31	117	90.69	129	100
Total	24	9.35	233	90.65	257	100

Table 1: Cross-Tabulation for sex distribution in case and control groups

Studied groups	obese		Non-obese		Total		P.value
	Number	Percent	Number	Percent	Number	Percent	0.66
Case	45	35.2	83	64.8	128	100	Not-significant
Control	42	32.6	87	67.4	129	100	
Total	87	33.9	170	66.1	257	100	

Table 2: Cross-Tabulation between obesity and RA

DISCUSSION

The measurement of body weight is routinely performed in most rheumatology clinics and reported in RA research as a demographical characteristic of the studied population. So it is usually disregarded from further analyses [37]. We know RA also has a relation with altered body composition. The chronic inflammation of the disease, particularly activation of the nuclear factor kappa-beta (NF-κβ) pathway, triggers metabolic alterations leading to the degradation of lean tissue, especially muscle mass. In the absence of physically active lifestyle, this event often leads to muscle mass reduction and accumulation of body fat (BF) followed by stable or slightly increased body weight, a condition known as rheumatoid cachexia [37].

As mentioned previously, Scientists have studied the association of obesity and RA previously. Some of them are here: In 1997 and 2002, Symmons et al. [15, 35] through a population-based case-control study in Norfolk located in England, involving adult patients, ages 18-70 and controls matched for age and sex, showed that there is a significant association between obesity (having BMI>30) and RA in both gender groups. In 2002, Cerhan et al. [14] in the United States reported that there is not any significant association between anthropometric factors (height, weight, BMI and body fat distribution) and RA. Their study was performed in a prospective cohort study and included 31336 women aged 55-69 years without history of RA. In 1990 in the United States, Hernandez Avila et al. [27] through a cohort study including 121700 female nurses aged 30-55, reported that there is no significant association between obesity and RA incidence. In 1994, Voigt et al. [38] in the United States, demonstrate that obesity firstly, causes decrease the level of estrogen in blood and secondly has a significant direct association with RA. In other years and other parts of the world, similar researches have been performed by other scientists. Dao et al. [39] in 2010 investigated the frequency of metabolic syndrome (MetS) among Vietnamese women with early rheumatoid arthritis by a cross-sectional study. They showed that Women with early RA already had higher prevalence of MetS compared with healthy controls.

As we see, despite the multiplicity of studies about the relation between obesity and RA, particularly in the European and Scandinavian countries and the United States, the gained results remain controversial and seem that they do not suffice for exact deduction. We think that There are two major causes to justify these contradictions: Firstly, The selection of suitable method for body composition assessment and secondly, geographically limitation. There are two major methods for body composition assessment that their selection depends on the balance between validity, time and money availability. Usually, methods that assess detailed body composition [such as 40K, dual-energy X-ray absorptiometry (DEXA) and MRI] are expensive and time consuming, so they are used for research in small groups. Contrarily, the methods based on anthropometric indexes—such as weight, height, BMI and different circumferences—are cheap, quick and easy to perform, since they are frequently used in the clinical researches (e.g. this study) [37]. BMI is an index for obesity assessment at the whole-body level and considers total weight. Then it does not distinguish between different tissues that comprise it. Total weight consists of two types of tissues; Fat mass and fat-free mass (e.g. skeletal muscle, bone and organs). Mentioned tissues can vary enormously between individuals [37]. It means that, in populations with altered body composition, BMI may not be a valid predictor of body fat. So, for this purpose anthropometric measures of central adiposity such as waist circumference and waist to hip ratio should be better. But it seems that, more research is necessary to find the best definition of obesity as a predictor for cardiovascular disease and specific subgroups of population such as the RA patients [37].

As mentioned previously, these studies are geographically limited and have been affected by several other factors (e.g. weather) which most of them may be disregarded in studies. In other words, different results related to different areas of the world may be results of some known and unknown area-dependent factors and this causes that geographically limited studies cannot be generalized to other parts of world.

As conclusion, obesity affects several aspects of the life of RA patients. We showed that there is no significant association between obesity and RA incidence in Hamedan. The controversy in the findings may come from unsuitable or different methodology or geographically limited factors rather than a true discrepancy in the effects of obesity. So, development the disease-specific measures of adiposity and correction the fat assessment, particularly visceral fat and fat-free mass should be noted.

REFERRENCES

1- Kallbeg H, Padyukov L, Plenge RM, Ronnelid J, Gregersen K, Van der Helm-van Mil AH, Toes RE, Huizinga TW, Klareskog L , Alfredsson L. Gene–gene and gene–environment interactions involving HLA-DRB1, PTPN22, and smoking in two subsets of rheumatoid arthritis. American Journal of Human Genetics 2007; 80(5): 867–875.

2- Kobayashi S, Momohara S, Kamatani N , Okamoto H: Molecular aspects of rheumatoid arthritis: Role of environmental factors. The FEBS Journal 2008; 275(18): 4456–4462.

3- Padyukov L, Silva C, Stolt P, Alfredsson L , Klareskog L. A gene–environment interaction between smoking and shared epitope genes in HLA-DR provides a high risk of seropositive rheumatoid arthritis. Arthritis and Rheumatism 2004; 50(10): 3085–3092.

4- Stolt P, Bengtsson C, Nordmark B, Lindblad S, Lundberg I, Klareskog L, Alfredsson L. Quantification of the influence of cigarette smoking on rheumatoid arthritis: Results from a population based case-control study, using incident cases. Annals of the Rheumatic Diseases 2003; 62(9): 835–841.

5- Alspaugh MA, Henle G, Lennette ET, Henle W: Elevated levels of antibodies to Epstein-Barr virus antigens in sera and synovial fluids of patients with rheumatoid arthritis. The Journal of Clinical Investigation 1981; 67(4): 1134–1140.

6- Alspaugh MA, Talal N, Tan EM. Differentiation and characterization of autoantibodies and their antigens in Sjögren's syndrome. Arthritis and Rheumatism 1976; 19(2): 216–222. Annals of the Rheumatic Diseases 67(4): 466–470.

7- Balandraud N, Meynard, JB, Auger I, Sovran H, Mugnier B, Reviron D, Roudier J, Roudier C: Epstein-Barr virus load in the peripheral blood of patients with rheumatoid arthritis: Accurate quantification using real-time polymerase chain reaction. Arthritis and Rheumatism 2003; 48(5): 1223–1228.

8- Balandraud N, Roudier J, Roudier C: Epstein-Barr virus and rheumatoid arthritis. Autoimmunity Reviews 2004; 3(5): 362–367.

9- Posnett DN. Herpes viruses and autoimmunity. Current Opinion in Investigational Drugs 2008; 9(5): 505–514.

10- Roudier J, Petersen J, Rhodes GH, Luka J, Carson DA. Susceptibility to rheumatoid arthritis maps to a Tcell epitope shared by the HLA-Dw4 DR beta-1 chain and the Epstein-Barr virus glycoprotein gp110. Proceedings of the National Academy of Sciences USA 1989; 86(13): 5104–5108.

11- Heliovaara M, Aho K, Knekt P, Impivaara O, Reunanen A , Aromaa A. Coffee consumption, rheumatoid factor, and the risk of rheumatoid arthritis. Annals of the Rheumatic Diseases 2000; 59(8): 631–635.

12- Karlson EW, Mandl LA, Aweh GN , Grodstein F. Coffee consumption and risk of rheumatoid arthritis. Arthritis and Rheumatism 2003; 48(11): 3055.

13- Mikuls TR, Cerhan JR, Criswell LA, Merlino L, Mudano AS, Burma M, Folsom AR , Saag KG. Coffee, tea, and caffeine consumption and risk of rheumatoid arthritis: Results from the Iowa Women's Health Study. Arthritis and Rheumatism 2002; 46(1): 83–91.

14- Cerhan JR, Saag KG, Criswell LA, Merlino LA , Mikuls TR. Blood transfusion, alcohol use, and anthropometric risk factors for rheumatoid arthritis in older women. Journal of Rheumatology 2002; 29(2): 246–254.

15- Symmons DP, Bankhead CR, Harrison BJ, Brennan P, Barrett EM, Scott DG, Silman AJ. Blood transfusion, smoking, and obesity as risk factors for the development of rheumatoid arthritis. Results from a primary care-based incident case-control study in Norfolk, England. Arthritis and Rheumatism 1997; 40(11): 1955–1961.

16- Jawaheer D, Lum RF, Gregersen PK, Criswell LA: Influence of male sex on disease phenotype in familial rheumatoid arthritis. Arthritis and Rheumatism 2006; 54(10): 3087–3094.

17- Heikkilä R, Aho K, Heliövaara M, Knekt P, Reunanen A, Aromaa A, Leino A , Palosuo T: Serum androgen-anabolic hormones and the risk of rheumatoid arthritis. Annals of the Rheumatic Diseases 1996; 57(5): 281–285.

18- Ariza-Ariza R, Mestanza-Peralta M, Cardiel MH. Omega-3 fatty acids in rheumatoid arthritis: an overview. Seminars in Arthritis and Rheumatism 1998; 27(6): 366–370.

19- Cutolo M, Otsa K, Uprus M, Paolino S , Seriolo B. Vitamin D in rheumatoid arthritis. Autoimmunity Reviews 2007; 7(1): 59–64. Epub August 14, 2007.

20- Okamoto H, Shidara K, Hoshi D , Kamatani N. Anti-arthritis effects of vitamin K(2) (menaquinone-4): A new potential therapeutic strategy for rheumatoid arthritis. The FEBS Journal 2007; 274(17): 4588–4594.

21- Strusberg I, Mendelberg RC, Serra HA, Strusberg AM. Influence of weather conditions on rheumatic pain. Journal of Rheumatology 2002; 29(2): 335–338.

22- Vergés J, Montell E, Tomàs E, Cumelles G, Castañeda G, Marti N , Moller L. Weather conditions can influence rheumatic diseases. Proceedings of the Western Pharmacology Society 2004; 47: 134–136.

23- Eftekharian M M, Basiri Z, Mani kashani Kh: A Study of the Association between Smoking and Rheumatoid Arthritis. The Journal of Smoking Cessation 2010; 5(1): 1-6 https://www.australianacademicpress.com.au/journals/details/6/Journal_of_Smoking_Cessation

24- Criswell LA, Merlino LA, Cerhan JR, Mikuls TR, Mudano AS, Burma M, Folsom AR , Saag KG: Cigarette smoking and the risk of rheumatoid arthritis among postmenopausal women: Results from the Iowa Women's Health Study. The American Journal of Medicine 2002; 112(6): 465–471.

25- Hazes JM, Dijkmans BA, Vandenbroucke JP, de Vries RR, Cats A. Lifestyle and the risk of rheumatoid arthritis: Cigarette smoking and alcohol consumption. Annals of the Rheumatic Diseases 1990; 49(12): 980–982.

26- Heliövaara M, Aho K, Aromaa A, Knekt P , Reunanen A. Smoking and risk of rheumatoid arthritis. Journal of Rheumatology 1993; 20(11): 1830–1835.

27- Hernández Avila M, Liang MH, Willett WC, Stampfer MJ, Colditz GA, Rosner B, Roberts WN, Hennekens CH , Speizer FE. Reproductive factors, smoking, and the risk for rheumatoid arthritis. Epidemiology 1990; 1(4): 285–291.

28- Hutchinson D, Shepstone L, Moots R, Lear JT, Lynch MP. Heavy cigarette smoking is strongly associated with rheumatoid arthritis (RA), particularly in patients without a family history of

RA. Annals of the Rheumatic Diseases 2001; 60(3): 223–227.
29- Karlsson EW, Lee IM, Cook NR, Manson JE, Buring JE , Hennekens CH. A retrospective cohort study of cigarette smoking and risk of rheumatoid arthritis in female health professionals. Arthritis and Rheumatism 1999; 42: 910–917.
30- Klareskog L, Stolt P, Lundberg K, Källberg H, Bengtsson C, Grunewald J, Ronnelid J, Harris HE, Ulfgren AK, Rantapaa-Dahlqvist S, Eklund A, Padyukov L , Alfredsson L. A new model for an etiology of rheumatoid arthritis: Smoking may trigger HLA-DR (shared epitope)-restricted immune reactions to autoantigens modified by citrullination. Arthritis and Rheumatism 2006; 54(1): 38–46.
31- Krishnan E, Sokka T, Hannonen P: Smoking-gender interaction and risk for rheumatoid arthritis. Arthritis research, therapy 2003; 5(3): R158–62.
32- Mattey DL, Hutchinson D, Dawes PT, Nixon NB, Clarke S, Fisher J, Brownfield A, Alldersea J, Fryer AA , Strange RC. Smoking and disease severity in rheumatoid arthritis. Association with polymorphism at the glutathione S-transferase M1 locus. Arthritis and Rheumatism 2002; 46(3): 640–646.
33- Papadopoulos NG, AlamanosY, Voulgari PV, Epagelis EK, Tsifetaki N , Drosos AA. Does cigarette smoking influence disease expression, activity and severity in early rheumatoid arthritis patients? Clinical and Experimental Rheumatology 2005; 23(6): 861–866.
34- Reckner Olsson A, Skogh T, Wingren G. Comorbidity and lifestyle, reproductive factors, and environmental exposures associated with rheumatoid arthritis. Annals of the Rheumatic Diseases 2001; 60(10); 934–939.
35- Symmons DP: Epidemiology of rheumatoid arthritis: Determinants of onset, persistence and outcome. Best Practice, Research. Clinical Rheumatology 2002; 16(5): 707–722.
36- Symmons DP. Environmental factors and the outcome of rheumatoid arthritis. Best Practice, Research. Clinical Rheumatology 2003; 17(5): 717–727.
37- Stavropoulos-Kalinoglou A, Metsios GS, Koutedakis Y , Kitas GD. Obesity in rheumatoid arthritis. Rheumatology (Oxford) 2010; Oct 19.
38- Voigt LF, Koepsell TD, Nelson JL, Dugowson CE , Daling JR: Smoking, obesity, alcohol consumption, and the risk of rheumatoid arthritis. Epidemiology 1994; 5(5): 525–532.
39- Dao HH, Do QT , Sakamoto J. Increased frequency of metabolic syndrome among Vietnamese women with early rheumatoid arthritis. a cross-sectional study. Arthritis Res Ther. 2010; Dec 23; 12(6):R218

The New Iraqi Journal of Medicine

Original Article

Oncology

Diagnosis and management of neuropathic pain among cancer patient in UKMMC

Y C Choy , AG. Muhammad Hazim, BS. Yap, CH. Yap, R. Hannah, CH. Chan, N. Nurul Hakimi

Abstract

Background: Pain is a common problem affecting patients suffering from cancer. Majority of the pain is nociceptive in nature, however, a small percentage of these patients have neuropathic pain which is frequently undiagnosed and not properly managed.

Patient and method*:* This was an observational, cross sectional study to evaluate the prevalence of neuropathic pain among cancer patients and its management in Universiti Kebangsaan Malaysia Medical Centre (UKMMC). The nature of neuropathic pain was studied, a pain assessment tool, (ID Pain) was used to identify the presence of neuropathic pain, drug therapy was investigated and patient satisfaction was also assessed.

Results: One hundred cancer patients with significant complain of pain participated in a 4-weeks study. The mean age was 53.1 years, 40 males and 60 females. In the study sample, 43 patients (43%) were identified to have neuropathic pain. Neuropathic pain caused significant impairment of sleep and daily activity ($\chi 2$ test, p=0.003 and p=0.013) respectively. Out of these 43 patients, 31 (72.1%) were managed according to WHO analgesic ladder guidelines, using analgesics only without adjuvant, whereas, 7 (16.3%) received analgesics plus adjuvant therapy which is an essential component in the management of neuropathic pain. Patients treated according to WHO guideline resulted in significant improvement in satisfaction (Fisher Exact test, p=0.03). There was also significant improvement of pain score (visual analogue score) among these patients after receiving treatment (Paired t-test, p=0.00).

Conclusions: the prevalence of neuropathic pain in cancer patients was comparable to that reported in the literature, symptom burden was significant and treatment with adjuvant analgesics were lacking. However patient satisfaction was acceptable, but could be improved if awareness among health care providers in recognising neuropathic pain and the importance of applying proper treatment regimens were emphasised.

The N Iraqi J Med, December 2011; 7(3):10-16

Keywords: *Neuropathic pain, cancer, adjuvant analgesic, opioids, WHO analgesic ladder*

INTRODUCTION

Cancer pain remains a major problem afflicting many patients across a wide spectrum of clinical environment. The scope of pain management in particular chronic pain has expanded tremendously over the last decades [1]. Knowledge of pain etiologies and clinical characteristics has brought about the recognition of neuropathic pain, which currently remain a challenge to clinician dealing with cancer pain. The International Association for Study of Pain defines neuropathic pain as 'pain initiated or caused by a primary lesion or dysfunction in the nervous system'. It is a heterogeneous group of conditions that differs in aetiology, location and symptoms do neither respect cause nor anatomical site.

* *Department of Anaesthesiology, Faculty of Medicine Universiti Kebangsaan Malaysia Medical Centre, J alan Yaacob Latif, Bandar Tun Razak, 56000 Cheras, Kuala Lumpur*
E-mail: choy@ppukm.ukm.my / choyyinchoy@ymail.com

The occurrence of neuropathic pain in cancer patients ranged from approximately 30 to 55% [1, 2, 3, 4]. However the pathophysiology of such pain in cancer has not been fully understood, further more chemotherapy, radiotherapy, post surgical and/or the tumor itself could cause this pain. This often leads to poor management and needless suffering. Neuropathic pain is different from a nociceptive pain in that it is notoriously difficult to treat and tends to be refractory to the analgesics commonly employed for treating nociceptive pain, such as paracetamol, non-steroidal anti-inflammatory drugs (NSAIDs) and other non-opioid drugs. It is often associated with co-morbid symptoms such as poor sleep, disturbed daily activity, depression, mood disturbances, and a lowered quality of life. Drugs that have efficacy for neuropathic pain include some opioids and adjuvant analgesics such as anticonvulsants, antidepressants, and corticosteroids. Therefore it is important to make an early and accurate diagnosis of neuropathic pain in order to provide appropriate management.

The World Health Organization (WHO) published guidelines which aimed to improve the treatment of cancer pain worldwide. Although often described by terms such as, 'treatment refractory' and 'opioid resistant'. Grond S. *et al.* concluded that neuropathic cancer pain is not intractable and can be relieved in majority of patients following the WHO guidelines [4]. The efficacy of cancer pain treatment following the WHO guidelines has been proven for patients with neuropathic, nociceptive as well as mixed pain profiles.

This study was designed aiming to determine the prevalence of neuropathic pain among cancer patients and to evaluate its management in UKMMC. The impact of neuropathic pain on these patients' sleep and daily activities, pharmacological treatment, objective improvement in pain score and patient satisfaction were assessed.

PATIENTS AND METHODS

This was a cross-sectional study done over 4 weeks duration on cancer patients admitted to the wards or visited clinics of the oncology department in Universiti Kebangsaan Malaysia Medical Centre (UKMMC) with approval of the ethics committee. A convenient sample consisting of 100 patients were recruited in this study. The inclusion criteria were, known cancer diagnoses, over the age of 12 years and presented with pain. Patients with subnormal mentality and those not able to participate in the interview due to severe illness were excluded. After obtaining informed consent, interview was done by using a standardized questionnaire with sections on various aspects of diagnosis, pain assessment (visual analogue score), drug therapy, effects on patient's quality of life and included the use of "ID Pain Screening Tool" to identify neuropathic pain Portenoy [5]. "ID pain" is a patient self-administrated screening tool that consisted of 6 very simple questions (Figure 1). Diagnosis of neuropathic pain was based on the total score of the ID pain tool.

Demographic and clinical data were collected from each participant and the relevant medical record. Pharmacological treatment following WHO guidelines and non-pharmacological treatment that the patients received was identified and recorded. Patients' satisfaction towards their treatment was also evaluated with a graded scale. Patients identified to have neuropathic pain were assessed particular as to whether they were given adjuvant therapy in addition to opioids. Improvement of the pain score was assessed based on the Visual Analogue Scale (VAS) before and after patients received medication for pain. Patients with neuropathic pain were also asked about the effect of pain on their daily activities and sleep pattern.

Data were analysed using the Statistical Package for Social Science (SPSS) version 19. Descriptive statistics on prevalence of neuropathic pain, gender, race, age, types of cancer, site of pain, clinical manifestation, patient satisfaction, improvement of pain score before & after treatment and affected daily activity and sleep were presented using percentage, mean, median and standard deviation. Patients identified with neuropathic pain were analysed as a sub-group to show any relation between proper cancer pain management and their satisfactory level using the Fisher's exact test. Chi square test was employed for assessing any association between neuropathic pain and how it affected daily activities and sleep. Paired t-test was used to evaluate the improvement of pain scores before and after receiving the treatment based on Visual Analogue Scale. All statistical tests were interpreted at 5% significant level (two-tailed).

	Answer / Score			
(1) Did the pain feel like pins and (2) needles?	Yes	1	No	0
(2) Did the pain feel hot/burning?	Yes	1	No	0
(3) Did the pain feel numb?	Yes	1	No	0
(4) Did the pain feel like electrical shocks?	Yes	1	No	0
(5) Is the pain made worse with the touch	Yes	1	No	0

of clothing or bed sheets?	
(6) Is the pain limited to your joints?	Yes -1 No 0

Figure 1: ID Pain screening tool.

Interpretation of total score:

a. Neuropathic pain not likely -1
b. Neuropathic pain less likely 0-1
c. Consider neuropathic pain 2-3
d. Strongly confirm neuropathic pain4-5

RESULTS

One hundred cancer patients, 40 males and 60 females participated in the study. Demographic data and clinical findings are shown in Table I. Symptom characteristics and regional distributions of cancer are shown in Figure 1 & 2. Using the "ID pain screening tool", 43 cancer patients (43%) were identified to have neuropathic pain. Pharmacological treatment of these patients is shown in Figure 3. Overall response of patients towards management in hospital were: 83% satisfied, 10% very satisfied, 4% unsatisfied and 3% very unsatisfied.

Age (yr)	
20 – 39	14
40 – 59	54
60 – 79	30
80 and above	2
Race:	
Malay	63
Chinese	30
Indian	7
Gender: male / female	40 / 60
ID Pain score	
NeP not likely	9
NeP less likely	48
Consider NeP	39
Strongly NeP	4
Cancer diagnosis	
Breast cancer	36
Lung cancer	12
Colorectal cancer	20
Bone cancer	1
Renal cancer	2
Head and neck cancer	8
Miscellaneous	7

Table I: Demographic and clinical characteristic (n=100)

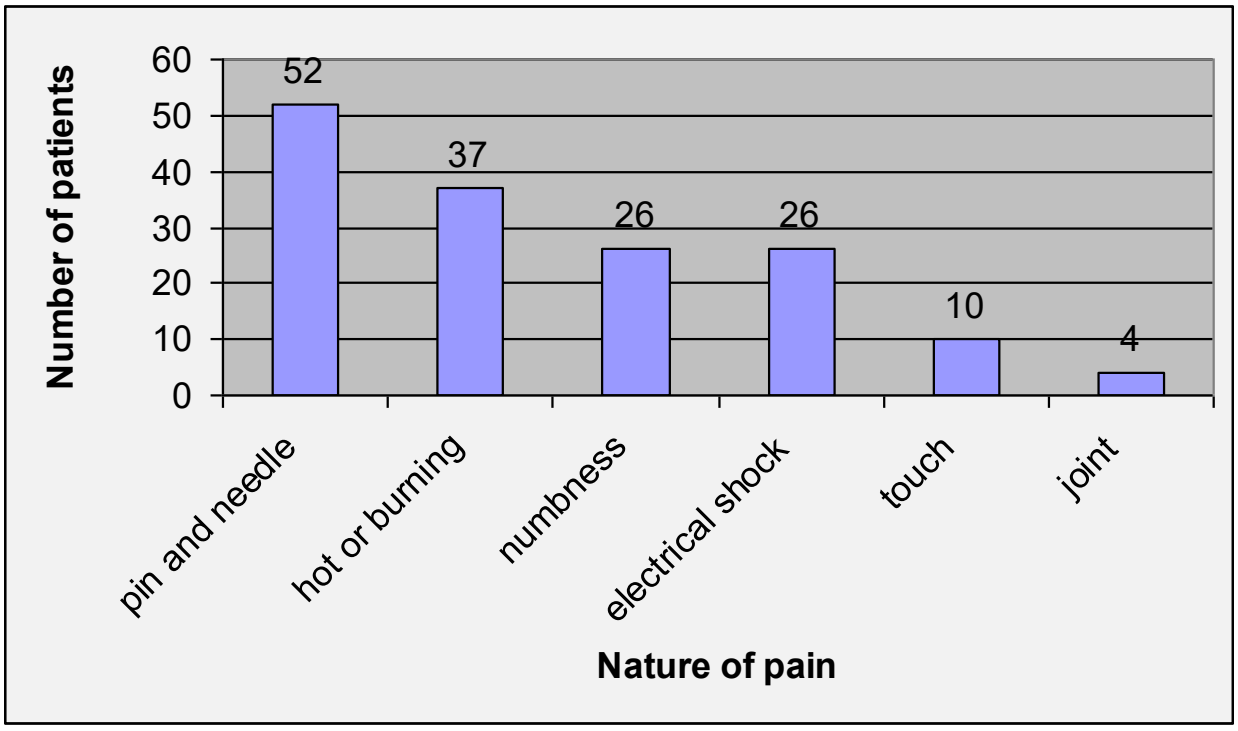


Figure 1: Symptom characteristics of cancer patients

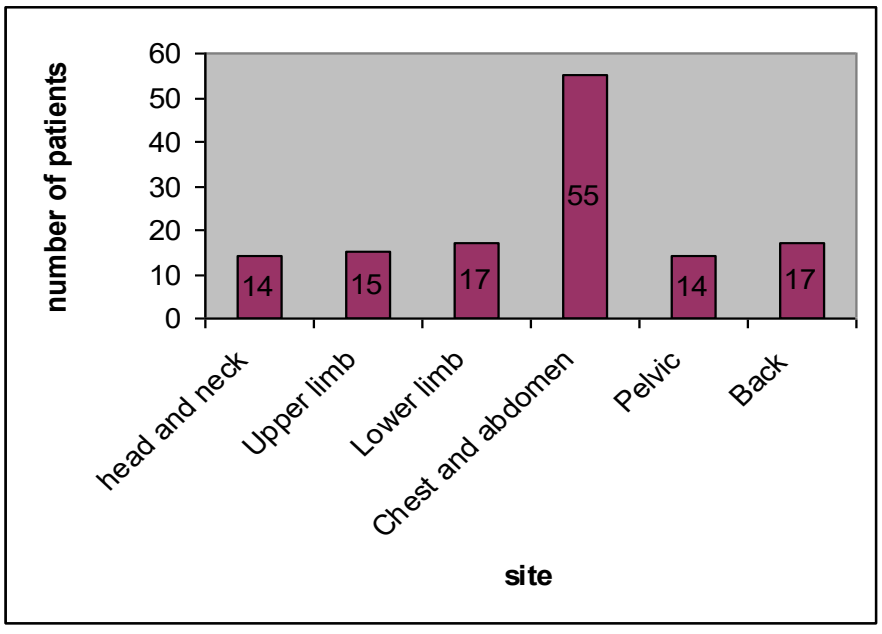


Figure 2: Regional distribution of pain among cancer patients

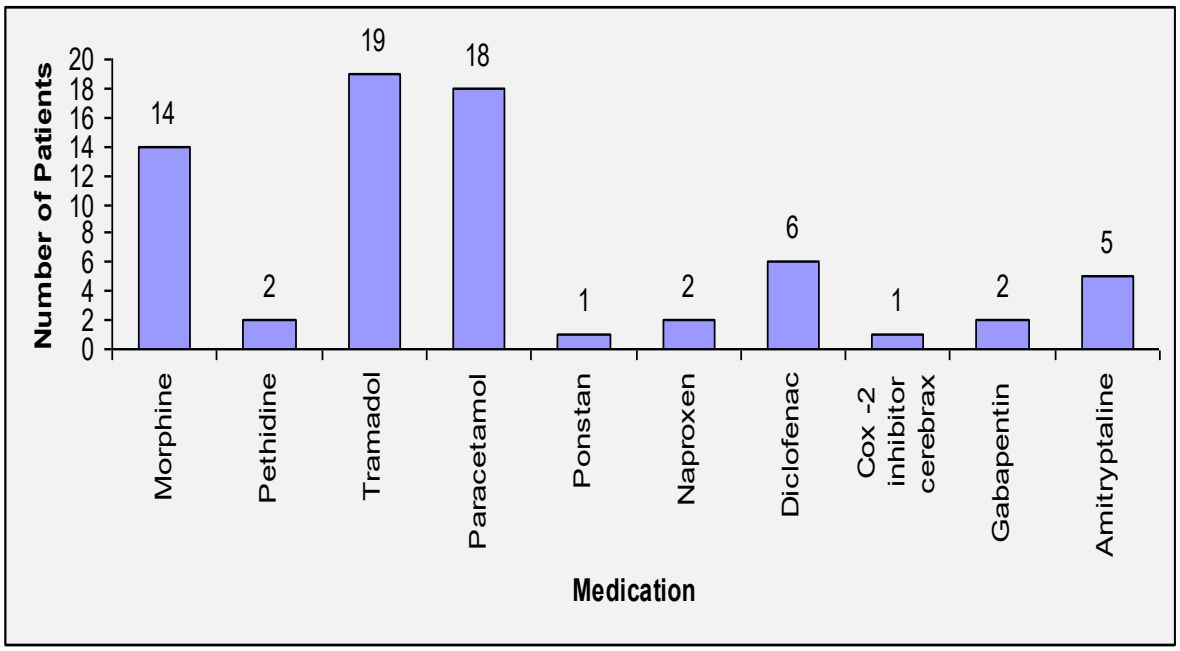


Figure 3: Medications received by patients with neuropathic pain

Pain intensity based on visual analogue scale (VAS) before (7.44 ± 1.71) and after the combination of analgesic including opioids with or without adjuvant (3.58 ± 1.92) showed a statistically significant difference ($p < 0.05$).

Thirty one out of total 43 neuropathic pain cancer patients (72.1%) complained of disturbed daily activities (p=0.013). Thirty one neuropathic cancer patients (72.1%) have disturbed sleep (p=0.003).

Out of a total 43 neuropathic pain cancer patients, 38 of them (88.4%) were given basic pain management using combination of analgesics including opioids with or without adjuvant drugs. Five patients (11.6%) did not receive any pharmacological management for their pain. Thirty five patients (81.4%) were satisfied with the outcome while 8 patients (18.6%) were not satisfied.

DISCUSSION

The occurrence of neuropathic pain in cancer patients ranged from approximately 30 to 55% [1, 2, 3, 4]. Portenoy R. applied the "ID pain tool" as a patient self-administered instrument [5]. Hans G. *et al.,* in 2007, also concluded that "ID Pain tool" is a reliable tool in identifying neuropathic pain with sensitivity of 73% and specificity of 55% [6].

Amongst the cancer patients we studied, 43% were identified to have neuropathic pain (NeP), which was consistent with current reports. Most of our patients were not proficient in English, thus, the investigator had to facilitate the process by helping in translating the questions. This could have been hampered by the difficulty encountered trying to communicate with the patients. Thus, the accuracy of ID Pain score could be minimally compromised. Investigator's interpretation of descriptions given by patients regarding their pain during the interview could also have led to inaccurate assessment. Being designed as a simple screening tool the "ID pain" instrument does not include physical examination as one of the component in identifying neuropathic pain compared to two other neuropathic pain screening tools: Leeds Assessment of Neuropathic Symptoms and Signs pain scale (LANSS, Bennett); Douleur Neuropathique en 4 questions (DN4)[7,8].

The presence of neuropathic pain caused significant disturbance to the daily activity and sleep of the patients. These findings were also in line with the research conducted by Hans G et al, who found that there were 91.2% of cancer patients had sleep disturbances [6]. These disturbances included: difficult falling asleep; interruption of sleep; premature awakening and non-restorative sleep. Chronic pain often results in mood disturbances, anxiety and depression, disorders that in turn negatively impact on sleep. Patients' suffering is compounded as lack of sleep decreases pain thresholds and leads to increased pain perception, and/or diminishes the patient's ability to cope with pain. In addition, Hans G et al also reported a negative impact of pain on patients' activities of daily

living in 93.6% of the studied patients.

There was statistical significant association with proper pain management and patient satisfaction. Sterman E. showed that effective pain management plan can lead to an increase in patient satisfaction [9]. Grond S et al also concluded that neuropathic pain can be relieved in most patients [4]. The WHO guidelines provided well for cancer pain treatment both for nociceptive as well as neuropathic pain. However, Bowsher D (1991) showed pharmacological therapy and subsequent pain relief is not the only factor affecting patient's satisfaction level [10]. Patient's satisfaction in hospital was also related to the fact that doctors and nurses communicated well with the patients and that pain management was given a high priority. Communicating with patients about their comfort goals, tailoring pain management to reach these goals, and educating patients regarding treatment plans enhance patient satisfaction. Communication rather than effective pain relief is the key to determine patient's satisfaction level. Furthermore, knowledge and clinical hand on experiences of clinical practitioner will affect cancer pain management satisfaction level.

Patient's pain severity based on visual analogue scale (VAS) before and after the combination of analgesic which include of opioids with or without adjuvant showed there was significant improvement of pain score after treatment. Most patients received multimodal treatment, including analgesics, adjuvants, palliative anti-neoplastic treatment and other measures; we did not explore this aspect in detail. In a study by Gond S et al, analgesic including adjuvant treatment resulted in significant pain relief in patients with nociceptive or neuropathic or mixed pain groups[4]. However, Harden N et al noted that the assessment done with scales that measure pain intensity and pain relief of peripheral neuropathic pain do not reflect the patient's suffering or therapeutic ratio of treatment [11]. The subjective nature of pain, problem of poor patient recall and the problems associated with the diagnosis, assessment and treatments of neuropathic pain can complicate the measurement of outcomes. Patients may find difficulties in relation to the measure of pain relief on VAS when they cannot adequately recall what the 'baseline' level of pain felt like. Moreover, patients may think that return to normal baseline daily activities is the indicator of pain relief. Thus, accurate meaning of pain relief should be viewed at the bio-psycho- social aspect of the patients which include their pain intensity, reduced work status, interference with home and leisure activities, side effect of drug treatment and co morbid symptoms.

Out of 43 patients identified to have neuropathic pain, 31 patients received combination of analgesics without adjuvant drug, whereas, only 7 patients received combination of analgesics with adjuvant drug. In patients affected by neuropathic pain, addition of adjuvant drugs i.e. anticonvulsants, corticosteroids was advised to be added at each step of the WHO ladder because it is widely accepted to be effective in neuropathic pain. Only a small percentage of patients identified to have neuropathic pain received adjuvant drugs suggesting the need to enhance knowledge in the use of adjuvants for the management of this type of pain. This could be due to inadequate knowledge of pain management especially neuropathic pain. These initial findings need to be confirmed by a larger, high-quality, prospective follow-up study.

Conclusion

The prevalence of neuropathic pain in cancer patients was comparable to that reported in the literature, symptom burden was significant and treatment with adjuvant analgesics were lacking. However patient satisfaction was acceptable, but could be improved if awareness among health care providers in recognising neuropathic pain and the importance of applying proper treatment regimens were emphasised.

Acknowledgements

The authors wish to thank all the medical and nursing staff for their help in this study.

REFERRENCES

1. Lesage P, Portenoy R K. Trends in cancer pain management. Cancer Control 1999; 6:136-45.
2. Manfredi PL, Gonzales GR, Sady R, et al. Neuropathic pain in patients with cancer J Palliat Care 2003; 19:115-8.
3. George RM, Ahmedzai SH. The management of neuropathic pain in cancer: clinical guidelines for the use of adjuvant analgesics. Indian J Cancer 2000; 37:4-9.
4. Grond S, Radbruch L, Meuser T,Sabatowski R, Loick G, Lehmann K A. Assessment and treatment of neuropathic cancer pain following WHO guidelines. Department of Anaesthesiology. Pain 1999; 79. 15-20
5. Portenoy R. Development and Testing of a Neuropathic Pain Screening Questionnaire: ID Pain. Current Medical Research Opinion 2006;22: 1555-1565
6. Hans G, Etienne M, Patricia D. C. The Diagnosis and Management of Neuropathic pain in Daily Practice in Belgium. Medical Department Pfizer Belgium. 2007. BMC Public Health 2007; 7:170.
7. Bennett M. 2000. The LANNS Pain Scale: Leeds Assessment of Neuropathic Pain Symptoms and signs. Pain 92 (2001). 147-157
8. Bouhassira D, Attal N, Alchaar H, et al. Comparison of pain syndromes associated with nervous or somatic lesions and development of a new neuropathic pain diagnostic questionnaire (DN4). Pain 114 (2005):29-36
9. Sterman E, Gauker S, Krieger JA Comprehensive Approach to Improving Cancer Pain Management and Patient Satisfaction. Oncology Nursing Forum. 2003;VOL 30, NO 5 : 857-962
10. Bowsher D. Neurogenic Pain Syndromes and their Management. Br Med Bull 1991;47:644-666
11. Harden N, Cohen M. Unmeet Needs in the Management of Neuropathic pain 2003; VOL 25 (5) S12-S17

The New Iraqi Journal of Medicine

Original Article

Neurology

Validation of a new coma scale, the FOUR Score, in the emergency department

*Nasrin Sarabi *, shahrokh alinia***

Abstract

Objective: In this study, we sought to validate the use of FOUR score in the emergency department (ED) using non-neurology staff. We also compared its performance to the Glasgow Coma Scale (GCS) and correlated it to functional outcome at hospital discharge and overall survival.

Patient and method*:* We prospectively rated 85 patients with initial neurologic symptoms presenting to the ED. Two types of examiners performed the FOUR score: ED physician and ED nurse. Patients were followed through hospital discharge; functional outcome was measured using modified Rankin Score (mRS).

Results: We found that the inter-rater reliability was excellent with the FOUR score (_w _ 0.82) and good to excellent for physician rater pairs. The agreement among raters was similar with the GCS (_w _ 0.82). Patients with the lowest GCS score could be further distinguished
using the FOUR score.

Conclusions: the neurologic detail incorporated in the FOUR score makes it more useful in management and triage of patients.

The N Iraqi J Med, December 2011; 7(3): 17-23

Keywords: *FOUR score, Inter-rater agreement, Glasgow Coma Scale*

INTRODUCTION

Coma scales have been created to improve communication between providers and have been used to triage patients with impaired consciousness in and out of the Emergency Department (ED). The Glasgow Coma Scale (GCS) was originated in a Neurosurgical Intensive Care Unit, but found its way elsewhere, and became a standard scale used in the field by first responders, emergency physicians, and neuroscience specialists [1]. Over the years, considerable limitations have been identified on this scale: crucial parts of the neurologic examination of a patient with impaired consciousness were not included (e.g., brainstem reflexes and eye movements) and language evaluation—largely an assessment of orientation rather than consciousness— became useless in intubated patients. More concerning, the performance of the GCS in the ED has mixed results.

Recently, pre-hospital GCS scores were compared with its assessment in the ED, and poor agreement was found in patients with traumatic head injury and GCS sum scores <13 points [2]. This disagreement between emergency medical service and emergency physicians confirmed a number of earlier studies that found only good agreement in alert or near alert (GCS 13–15) patients [3,4]. Other observational studies found concerning disagreements between ED physicians and nurses when rating consciousness using the GCS [5, 6], and marked differences between level I trauma centers in calculations of the GCS were found [7]. Attempts have been made to modify the GCS; however, most of these scales were more complicated, and were seldom used outside the country of origin. [8,9] Others have suggested simplification of the GCS score after documenting poor inter-observer reliability in traumatic brain injury.[10] These concerns and prior

Nasrin Sarabi, shahrokh alinia
Sender Author: NASRIN SARABI
ISLAMIC-AZAD UNIVERSITY; University of Social Welfare and Rehabilitation Science, Tehran, Iran
E-mail:nasinsaraby06@gmail.com

attempts to design new scales strongly suggest a new scale is needed that could provide further neurological detail in coma that is easy to use and that could predict outcome. The Full Outline of Unresponsiveness (FOUR) score is a recently developed and validated [11, 12] in the Neuro-intensive Care Unit and can supplement the GCS. The FOUR score consists of 4 components—eye, motor, brainstem, and respiration—and each component has a maximal score of 4. A low FOUR score is associated with in-hospital mortality and disability in patients with acute brain injury [13].

As use of the FOUR score becomes more widespread, we sought to test its validity in the ED setting and compare its performance to the GCS and correlate it to functional outcome at hospital discharge.

PATIENTS AND METHODS

The new coma scale was named the FOUR score (Figure-1). The FOUR score has four testable components, in contrast with the GCS (Table 1). The number of components and the maximal grade in each of the categories is four (E4, M4, B4, R4). (It is easier to remember than the GCS with its varying number of scores [E4, M6, V5] and is reinforced by the acronym.) The FOUR score detects a locked-in syndrome, as well as the presence of a vegetative state where the eyes can spontaneously open but do not track the examiner's finger. The motor response is obtained preferably at the up-Stokes respiration and irregular breathing can represent bi-hemispheric or lower brainstem dysfunction of respiratory control. In intubated patients, overbreathing the mechanical ventilator represents functioning respiratory centers. With all categories graded 0, the examiner is alerted to consider brain death evaluation. The FOUR score can be graded in a few minutes (Figure-1).

This is an observational study in adult patients presenting with acute neurologic disease to an ED from 1 October 2009 to 1 October 2010.

The study was designed to enroll 85 patients sampled from all four alertness group categories: 40 alert patients, 25 comatose and 20 drowsy/stuporous patients. Patients aged 18 years and older who were admitted to the ED were included in the study. Patients taking sedative agents that could not be temporarily discontinued and those who deemed too medically unstable to allow for repeat GCS scoring were excluded. The raters were selected from two different training type groups (ED physicians and ED nurses).

With the use of video examples, one-page handout, instruction cards, describing both the FOUR score and the GCS, and shown a patient example each participant was trained for 20 to 30 minutes. Each participant was allowed to practice on 1 to 2 patients while being supervised by one of the authors.

Once a patient was deemed suitable for inclusion in the study, was assessed on both scales (FOUR score and Glasgow Coma Scale) by two different raters, who performed their examination within 10 min of each other without knowledge of the other's scores. The order of the evaluations was randomized to reduce bias. (For instance, of the 20 subjects rated by both a nurse and a physician, 10 were rated by the nurse first followed by physician, and 10 rated by the physician first).

We recorded in-hospital mortality and clinical diagnosis of brain death. Morbidity was assessed at 3 months using the modified Rankin Scale.13 In brief, 0 _ no symptoms; 1 _ no significant disability despite symptoms; 2 _ slight disability, unable to carry out all previous activities, able to take after own affairs; 3 _ moderate disability, requiring some help, but able to walk without assistance; 4 _ moderately severe disability, unable to walk without assistance, and unable to attend to own bodily needs without assistance; 5 _ severe disability, bedridden, incontinent, and requiring constant nursing care; 6 _ dead.

This study was approved by the Islamic Azad university- Sanandaj Branch. As repeated LOC measurement in patients with an altered LOC is a routine part of clinical practice, patient consent was deemed not necessary.

For both the FOUR score and the GCS overall average, weighted Kappa scores were calculated to determine the degree of agreement between pairs.

Kw (weighted Kappa) of 0.4 or less is considered poor. Values between 0.4 and 0.6 are considered fair to moderate; values between 0.6 and 0.8 suggest good observer agreement, and values greater than 0.8 suggest excellent agreement.

FOUR Score	Glasgow Coma Scale
Eye response	**Eye response**
4 _ eyelids open or opened, tracking, or blinking to command	4 _ eyes open spontaneously
3 _ eyelids open but not tracking	3 _ eye opening to verbal command
2 _ eyelids closed but open to loud voice	2 _ eye opening to pain
1 _ eyelids closed but open to pain	1 _ no eye opening
0 _ eyelids remain closed with pain	
Motor response	**Motor response**
4 _ thumbs-up, fist, or peace sign	6 _ obeys commands
3 _ localizing to pain	5 _ localizing pain
2 _ flexion response to pain	4 _ withdrawal from pain
1 _ extension response to pain	3 _ flexion response to pain
0 _ no response to pain or generalized myoclonus status	2 _ extension response to pain
	1 _ no motor response
Brainstem reflexes	**Verbal response**
4 _ pupil and corneal reflexes present	5 _ oriented
3 _ one pupil wide and fixed	4 _ confused
2 _ pupil or corneal reflexes absent	3 _ inappropriate words
1 _ pupil and corneal reflexes absent	2 _ incomprehensible sounds
0 _ absent pupil, corneal, and cough reflex	1 _ no verbal response
Respiration	
4 _ not intubated, regular breathing pattern	
3 _ not intubated, Cheyne–Stokes breathing pattern	
2 _ not intubated, irregular breathing	
1 _ breathes above ventilator rate	
0 _ breathes at ventilator rate or apnea	

Table 1. Comparison of the FOUR Score with the Glasgow Coma Scale

FOUR _ Full Outline of Unresponsive

Figure 1. Instructions for the assessment of the individual categories of the FOUR (Full Outline of Unresponsiveness) score (see Table 1). (A) For eye response (E), grade the best possible response after at least three trials in an attempt to elicit the best level of alertness.

A score of E4 indicates at least three voluntary excursions. If eyelids are closed, the examiner should open them and examine tracking of a finger or object. Tracking with the opening of one eyelid will suffice in cases of eyelid edema or facial trauma. If tracking is absent horizontally, examine vertical tracking. Alternatively, two blinks on command should be documented. This will recognize a locked-in syndrome (patient is fully aware).

A score of E3 indicates the absence of voluntary tracking with open eyes. A score of E2 indicates eyelids opening to a loud voice.

A score of E1 indicates eyelids open to pain stimulus.

A score of E0 indicates no eyelid opening to pain. (B) For motor response (M), grade the best possible response of the arms.

A score of M4 indicates that the patient demonstrated at least one of three hand positions (thumbs up, fist, or peace sign) with either hand.

A score of M3 (localization) indicates that the patient touched the examiner's hand after a painful stimulus

compressing the temporo-mandibular joint or supraorbital nerve.

A score of M2 indicates any flexion movement of the upper limbs.

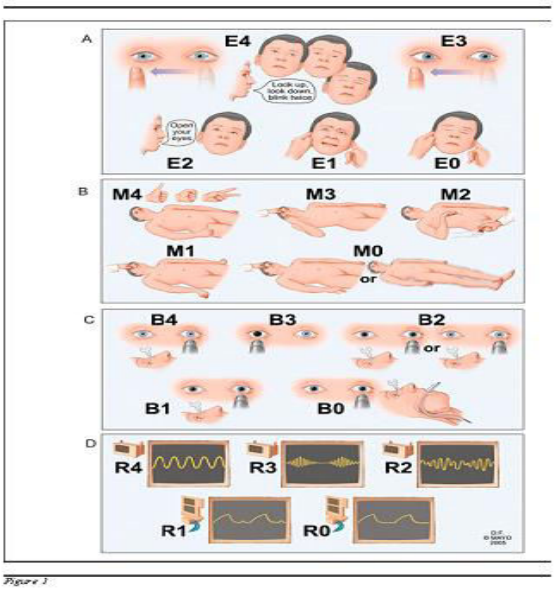
A score of M1 indicates extensor response to pain. A score of M0 indicates no motor response to pain, or myoclonus status epilepticus. (C) For brainstem reflexes (B), grade the best possible response. Examine pupillary and corneal reflexes. Preferably, corneal reflexes are tested by instilling two to three drops sterile saline on the cornea from a distance of 4 to 6 inches (this minimizes corneal trauma from repeated examinations). Sterile cotton swabs can also be used. The cough reflex to tracheal suctioning is tested only when both of these reflexes are absent.

A score of B4 indicates pupil and corneal reflexes are present.

A score of B3 indicates one pupil wide and fixed.

A score of B2 indicates either pupil or cornea reflexes are absent.

A score of B1 indicates both pupil and cornea reflexes are absent. A score of B0 indicates pupil, cornea, and cough reflex (using tracheal suctioning) are absent. (D) For respiration (R), determine spontaneous breathing pattern in a non-intubated patient and grade simply as regular (R4), or irregular (R2), Cheyne–Stokes (R3) breathing. In mechanically ventilated patients, assess the pressure waveform of spontaneous respiratory pattern or the patient. triggering of the ventilator (R1). The ventilator monitor displaying respiratory patterns can be used to identify the patient-generated breaths on the ventilator. No adjustments are made to the ventilator while the patient is graded, but grading is done preferably with PaCO2 within normal limits. A standard apnea (oxygen-diffusion) test may be needed when patient breathes at ventilator rate (R0). Figure reproduced with permission by Mayo Foundation.



RESULTS

The study cohort comprised 85 patients, with the following neurologic complaints: Suspicion CNS infection (1%); stroke (22%); seizure (14%); subarachnoid hemorrhage (3%); altered consciousness or encephalopathy (51%), and traumatic head injury (9%).

The average age of patients was 58.9 years (median, 60 years; range, 45–70 years); 72% were men. There were 40 alert patients, 25 comatose, and 20 drowsy/stuporous patients. Fifty-one percent of the evaluations were done by nurses, and 49% by physicians.

	Four score					Glasgow Coma Scale score			
Rater Pair	**Eye**	**Motor**	**Brainstem**	**Respiration**	**Total**	**Eye**	**Motor**	**Verbal**	**Total**
Nurse/Physician	0.85	0.81	0.86	0.68	0.82	0.86	073	0.87	0.82
Physician/Physician	0.77	0.84	0.97	0.91		0.90	0.83	0.93	0.89
Nurse/Nurse	0.48	0.71	0.66	0.68	0.79	0.50	0.78	0.85	0.79
Overall (95% CI)	0.78	0.80	0.81	0.78	0.82	077	0.77	0.88	0.82
	(0.70-0.87)	(0.72-.88)	(0.70-.91)	(068-.88)	(0.77-0.88)	(0.69-.85)	(0.68-0.85)	(0.81-0.96)	(076-0.87)

Table 2: Rater Agreement with the FOUR Score and the Glasgow Coma Scale as Indicated by Weighted K Values

The overall reliability was excellent for both the FOUR score (k_w = 0.82; 95% CI, 0.77– 0.88) and the GCS (k_w = 0.82; 95% CI, 0.76–0.87). The rater agreement was good to excellent for physician rater pairs. The highest degree of agreement was among the physician, and agreement was lowest among the nurse for both scales (Table 2).

Cronbach's α showed a high degree of internal consistency for FOUR score (α = 0.86 for the first rater; α = 0.87 for the second rater) and the GCS (α = 0.88 for the first rater; α = 84 for the second rater).

Table 3 presents the relations between total score and patient outcome for each of the two scales. Considering the FOUR scale total score, for every 1-point increase in total score, there is an estimated 22% reduction in the odds of in-hospital mortality (odds ratio [OR] = 0.78; 95% CI, 0.70– 0.91). A 1-point increase in total score is also associated with lower odds of poor outcome defined as a modified Rankin scale of 3 or more (OR = 0.84; 95% CI, 0.78–0.91). With the GCS scale total score, for every 1-point increase in total score, there is an estimated 28% reduced odds of experiencing in-hospital mortality under the unadjusted model (OR = 0.72; 95% CI, 0.60– 0.80). This relation remains after adjusting for age, sex, alertness group, and diagnosis (traumatic vs. non-traumatic). A 1-point increase in total score is also associated with lower odds of poor outcome (OR = 0.82; 95% CI, 0.74–0.90). This effect is attenuated slightly after considering the adjusted model (OR = 0.88; 95% CI, 0.77 –1.015).

	In-Hospital Death (N= 85; 15 events)		**Rankin of 3 to 6 (N= 85; 35 events)**	
	OR[a] (95% CI)	OR[b] (95% CI)	OR[a] (95% CI)	OR[b] (95% CI)
Four score total	0.78 (070-0.91)	0.80(0.52-0.94)	0.84 (0.78-0.91)	0.86 (0.75-0.97)
Gcs score total	0.72 (0.60-0.80)	0.79 (0.50-0.91)	0.82 (0.74-0.90)	0.88 (0.77-1.015)

Table 3. Prediction of Outcome (in-hospital death and Rankin scores of 3–6)

[a]Unadjusted logistic regression model.

[b]Logistic regression model adjusted for age, sex, consciousness group, and diagnosis (trauma vs. non-trauma).

Discussion

This is the first study of the FOUR score outside the Neurosciences Intensive Care Unit using non-neurology staff as raters. The advantages of the FOUR score have been outlined previously. This new coma scale includes important clinical neurological findings in patients with impaired consciousness and this study shows that can be assessed by emergency physicians and nurses in the ED with excellent agreement. Our raters with no specific neurological training were able to identify key neurologic signs in patients with impaired consciousness [11, 12].

The inter-rater reliability of the FOUR score and the GCS were of equivalent magnitude. This is remarkable because the raters had only minimal experience with the FOUR score. In our study, the observer agreement was highest among physician. There was perfect agreement among the physician in rating respiration and brainstem reflexes, which is an finding when communication with the attending consultant is sought. In the nurses pairs, the lowest agreement was with grading eye responses in both the FOUR score and GCS and with the interpretation of brainstem reflexes. Ratings of the eye responses are influenced by factors such as intensity of pain and loudness of voice, fluctuating alertness in between ratings, or time spent to obtain the response. The differences in observer agreement may nevertheless indicate that the nursing staff with more training should use the scales.There are significant advantages over the GCS score. The FOUR score tests essential brainstem reflexes and provides information about stages of brainstem injury that is unavailable with the GCS (13). FOUR score has the potential to recognize a locked-in syndrome, uncal herniation, brain death, and less severe neurologic injury. A more comprehensive assessment of a patient with an impaired consciousness could assist in initial decision making, assess the need for additional consultation (neurosurgeon) and more effectively triage patient to the most appropriate Intensive Care Unit, neuroradiology suite, or operating theater [14].

CONCLUSION

The FOUR score has major advantages. The 4 components provide important details of the neurologic examination such as brainstem reflexes and eye movements. It recognizes uncal herniation, a locked-in syndrome, and the beginning of a vegetative state. This detail is not provided by the GCS

REFERRENCES

1. Teasdale G, Jennett B. Assessment of coma and impaired consciousness. A practical scale. Lancet. 1974; 2:81–4.

2. Kerby JD, MacLennan PA, Burton JN, McGwin G Jr, Rue LWIII. Agreement between prehospital and emergency department Glasgow coma scores. J Trauma. 2007; 63:1026–31.

3. Menegazzi JJ, Davis EA, Sucov AN, Paris PM. Reliability of the Glasgow Coma Scale when used by emergency physicians and paramedics. J Trauma. 1993;34:46–8.

4. Ba´ez AA, Gira´ldez EM, De Pen˜a JM. Precision and reliability of the Glasgow Coma Scale score among a cohort of Latin American prehospital emergency care providers. Prehosp DisasterMed. 2007; 22:230–2.

5. Gill MR, Reiley DG, Green SM. Inter-rater reliability of Glasgow Coma Scale scores in the emergency department. Ann Emerg Med. 2004; 43:215–23.

6. Holdgate A, Ching N, Angonese L. Variability in agreement between physicians and nurses when measuring the Glasgow Coma Scale in the emergency department limits its clinical usefulness.
Emerg Med Australas. 2006;18:379–84.

7. Buechler CM, Blostein PA, Koestner A, Hurt K, Schaars M, McKernan J. Variation among trauma centers' calculation of Glasgow Coma Scale score: results of a national survey. J Trauma.1998; 45: 429–32.

8. Starmark JE, Stalhammar D, Holmgren E, et al. A comparison of the Glasgow Coma Scale and the Reaction Level Scale (RLS85). J Neurosurg .1988 69:699 – 706.

9. Benzer A, Mitterschiffthaler G, Marosi M, et al. Prediction of non-survival after trauma: Innsbruck Coma Scale. Lancet. 1991; 338:977–978.

10. Gill M, Windemuth R, Steele R, et al. A comparison of the Glasgow Coma Scale score to simplified alternative scores for the prediction of traumatic brain injury outcomes. Ann Emerg Med. 2005; 45:37– 42.

11. Wijdicks EF, Bamlet WR, Maramattom BV, et al. Validation of a new coma scale: The FOUR score. Ann Neurol.

12. Wolf CA, Wijdicks EF, Bamlet WR, et al. Further validation of the FOUR score coma scale by intensive care nurses. Mayo Clin Proc. 2007; 82:435–8.

13. Wijdicks E.FM, Bamlet WR, Maramattom BV, Manno EM, McClelland RL. Validation of a new coma scale: the FOUR score. *Ann Neurol*. 2005; 58:585-593.

14. Latha GS, Eelco FMW, Anjali B, Rahul K, Fernanda B, David L and et al. Validation of a New Coma Scale, the FOUR Score, in the Emergency Department. Neurocrit Care.2009; 10:50–54.

The New Iraqi Journal of Medicine

Original Article

Orthopedics

The role of ENDER'S nail fixation in pilon fractures: Report of 6 cases

***A.A.Faraj* ***

Abstract

Background: The armamentarium for fixing tibial pilon fractures is multitude, expensive and complex. There are however occasions were simpler, older and cheaper means of fixation useful in dealing with these fractures.

Patient and method*:* We present a series of 6 patients who underwent tibial pilon fracture fixation using percutaneous Ender's nails.

Results: Complications were minimal and 5 out of 6 patients had good results, assessed using the Iowa ankle scoring system.

Conclusions: We conclude that Ender's nail can be included in the management of tibial pilon fractures. Although it is not the typical implant for this fracture, it can be suitable for frail osteoporotic patients.

The N Iraqi J Med, August 2011; 7(3):24-28

Keywords: *Pilon fracture, Ender's nails, Iowa ankle score*

INTRODUCTION

A tibial pilon fracture is a fracture of the distal tibia involving the tibial plafond. The term pilon was first used by Destot in the early 1900 [1, 2]. It is uncommon injury accounting for 1-10% of all lower extremity fractures [3,4] and represents a challenging problem for orthopaedic surgeons.

The primary component of the force is axial through the distal tibia and the talus generally occurring as a result of high impact trauma [5, 6]. However, with the aging population and an increasing incidence of fragility fractures, the incidence of low energy fractures is increasing in the elderly population [7, 8]. This patient group inherently represents a higher surgical challenge and risk.

There is no definite consensus on their management although more recently there has been more emphasis on minimising further soft tissue trauma. There have been several studies carried out on the management of pilon fractures with varying outcomes [3]. The preservation of the soft tissue envelope along with the degree of comminution of the fracture is said to determine the complication rate and hence surgical outcome [3]. Recent times have seen the emphasis shift toward techniques which minimize further trauma to the soft tissues by using minimally invasive techniques [3, 5].

The aim of this paper is to explore yet another method albeit old, in the management of tibial pilon fractures. This method could be in reach in some hospitals around the world.

* *Department of Orthopaedics & Trauma*
Airedale General Hospital
Steeton Keighley, W.Yorkshire
Email:shevanfaraj@hotmail.com

Method

A retrospective analysis of case notes of six patients with tibial pilon fractures treated by reduction and Ender's nail fixation by one consultant over a 3 ½ year period.

There were 4 females and two males. The mean age was 67 years (42-80). The AO and Gustillo and Anderson classifications were used to classify the fractures. 3 fractures were open (1 grade II, 2 grade IIIB). Details of the fractures, classification, and method of fixation and patient co-morbidities are summarised in table 1.

Patient	Sex/Age (yrs)	AO Classification	Open/Closed	Comorbidities	Fixation
1	F/61	43 C1.2	Open (Grade II)	IHD, Factor V Leiden, Aspirin	Enders nails + screws
2	F/80	43 A2.1	Closed	Arthritis	Enders nails
3	F/42	43 C2.2	Closed	Obese (BMI 32)	Enders nails + screws
4	M/57	43 C3.2	Open (Grade IIIB)	Arthritis	Enders nails
5	F/75	43 C2.2	Open (Grade IIIB)	RF, BP, IHD, smoker, Arthritis	Enders nails
6	76f	43 C2.2	closed	fit	Enders, k wire

Table 1: Fracture configuration, method of fixation and patient co-morbidities

Operative Methods

All patients were managed in the accident and emergency department. Advanced Trauma Life Support protocols guidelines were followed for the open fractures [4]. All patients received prophylactic antibiotics with either a penicillin or cephalosporin. Following skin antisepsis, wound debridement (if required), and reduction of the fracture under image intensifier in the operating theatre. 3 stab incisions were made in the skin; medial, lateral and anterior. The fibular length was restored following the introduction of one intramedullary Ender's nail. When the medullary canal of fibula was too narrow to accomdate Ender's nail, an appropriate K-wire is used instead. If required, the larger comminuted tibial fragments were lagged using standard AO technique with small fragment screws to reduce and fix the articular fracture in an anatomical position (Table 1 - patients 1&3). The distal tibial fragment was reduced via manipulation and its position maintained by insertion of one anterolateral and one medial Ender's nail (inserted via the medial malleolus) (see figure 1). These nails were buried within the soft tissue. The fibular nails were left proud and subsequently removed in all but one case. Skin closure was with a non-absorbable monofilament suture and one case (Table 2 – patient 4) required delayed split skin grafting. An above knee plaster of Paris back-slab was then placed prior to leaving the operating theatre.

Post-operatively, once the swelling had reduced, the patients were put into an above knee lightweight cast and discharged, strictly non-weight bearing. Patients were discharged between 3 and 16 days post-operatively. The wounds were checked at between 12 and 14 days, the sutures removed and a new plaster applied. At 6 weeks the cast was changed for a below-knee, bivalved cast and they started physiotherapist-supervised exercises. They also started weight-bearing, depending on the X-ray appearances and patient factors (the 2 elderly patients were allowed to weight-bear because they were unable to cope with the concept partial weight-bearing).

RESULTS

Patients were followed up in the out-patient department where an assessment of patient function using the Iowa ankle score was carried out (table 2) [9]. The timing for this final assessment was variable (table 2).Mean time to fracture union was 15.4 weeks (range 10-20) and time to full weight-bearing 11 weeks (range 10-15). Mean follow-up (T_f) was 63.4 weeks (range 26-185). Mean range of motion of the ankle ranged from 19 degrees (range 0-30) dorsiflexion to 33 degrees (range 20-50) plantar flexion. Two patients experienced minor complications of fibular pin-site infection, which settled with appropriate oral antibiotics, and removal of the fibular pin. One patient, 18 months from injury, showed no signs of healing of the fracture and had to have reconstruction surgery. The mean Iowa ankle score in our group was 79 (table 2).

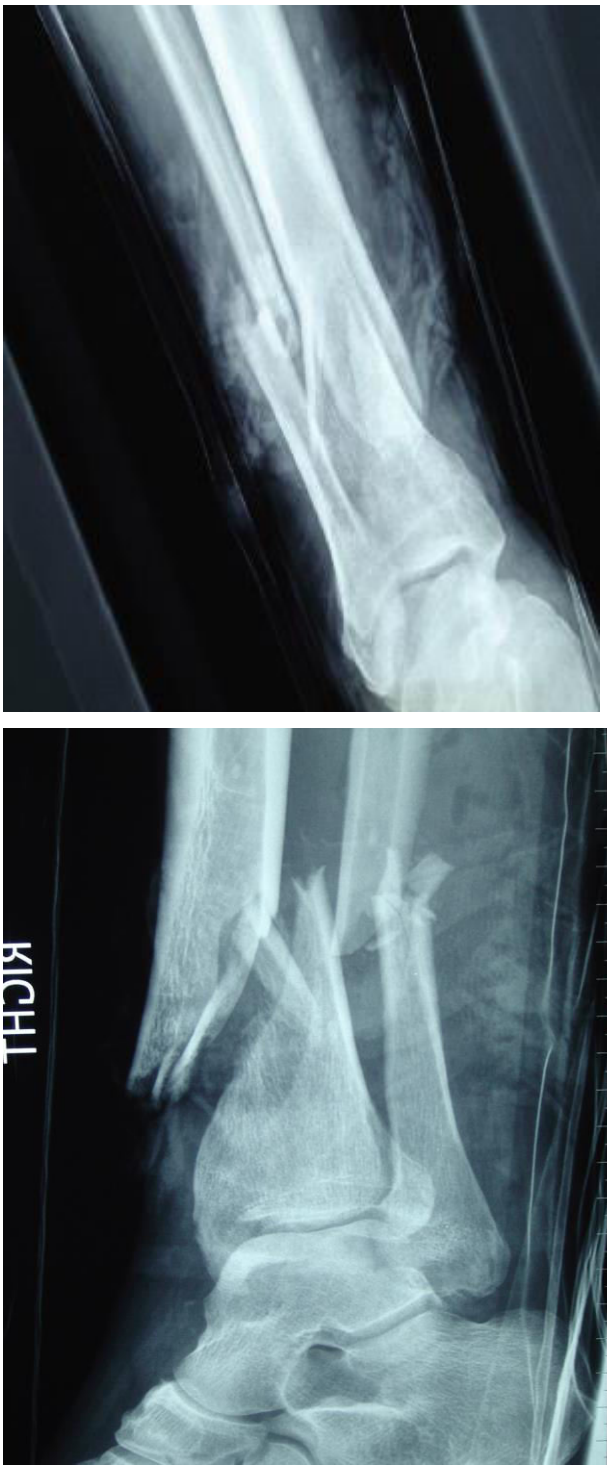


Figure 1 A: pre-operative anteroposterior and lateral radiograph

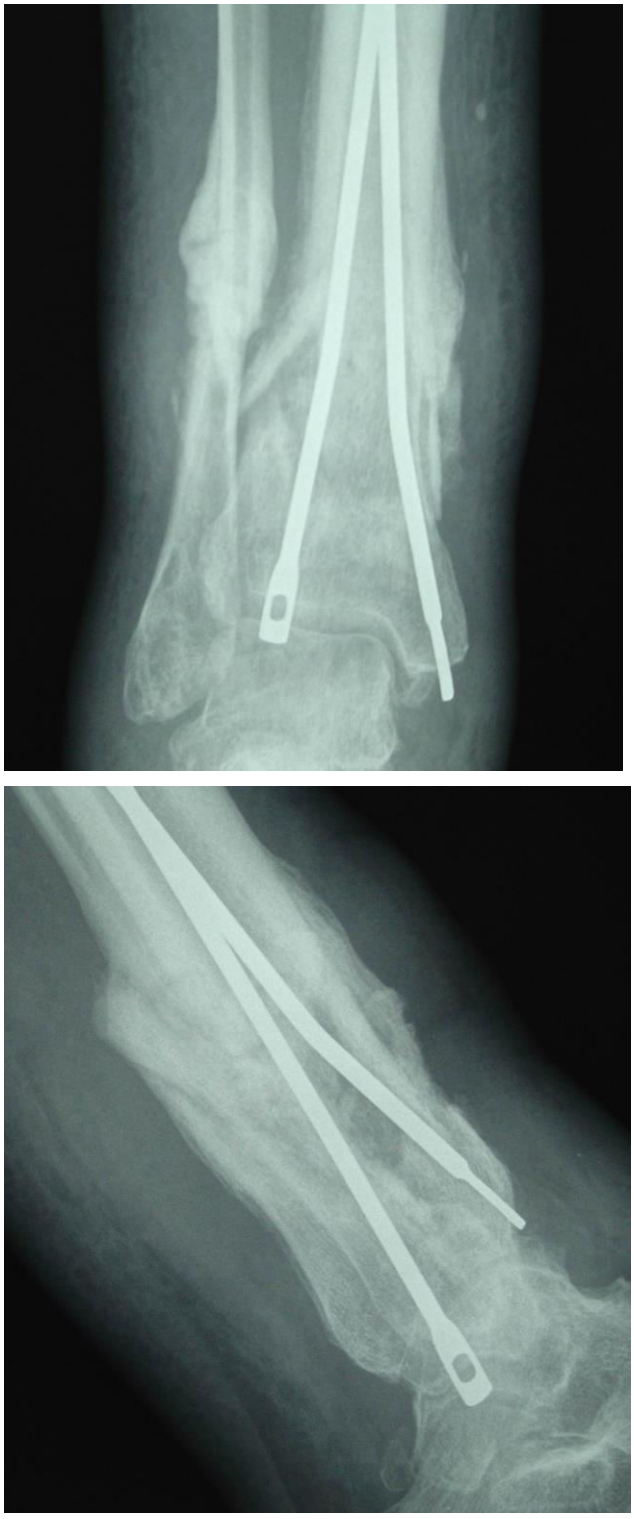


Figure 1B: post-operative anteroposterior and lateral radiograph

Patient	T_f *	Score
1	26	86
2	26	72
3	47	83
4	33	88
5	185	68
6	24	82

Table 2- Patient Iowa ankle scores at last follow-up

* Time of final post-operative follow-up (weeks)

DISCUSSION

There is no consensus on the optimal method of treating distal tibial pilon fractures. It is generally agreed that non-operative management produces poorer results and should be reserved for undisplaced fractures or patients with a poor medical prognosis [3, 6]. There is still considerable debate regarding the operative management of these fractures. In 1969, Rüedi and Allgöwer published results of open reduction and internal fixation of tibial pilon fractures showing excellent results. 74% of these patients showed good functional results and 90% returned to their occupations [10]. Since then there have been many studies and reviews published looking into different methods of operative management of tibial pilon fractures ranging from open reduction and internal fixation with plate and screws (and more recently minimally invasive techniques) to two-staged procedures using external fixators and definitive illizarov frames [3,6,11]. None of these procedures have yet become a gold standard.

Our paper is retrospective and lacks preoperative Iowa scoring system. However, an important finding of the present study was fracture healing in 5 out of 6 fractures with good Iowa score. This case series of 6 patients is not big enough to draw definite conclusion. However, the topic is relevant when dealing with pilon fracture in elderly.

More recent advances are due to recognition of the importance of the soft tissue envelope in fracture healing [3]. Rüedi and Allgöwer recommended goals of the surgical treatment of tibial pilon fractures: maintenance of length and stability of the fibula; restoration of tibial joint articular surface; restoration of bone defect; and buttressing of the medial tibia [10, 12]. In particular at the distal tibia where the soft tissue envelope is limited, the need for meticulous soft tissue handling is mandatory to reduce further periosteal stripping and microcirculatory damage, which contribute to the complications in the management of these fractures [5, 13]. The method of fixation of tibial pilon fractures using Ender's nails as described above is a percutaneous technique with minimal further soft tissue disruption. This is at the expense of no direct manipulation, and hence exact reduction, of the tibial joint surface.

One of the main aims of internal fixation is to permit early mobilisation, and although studies have shown no difference between early mobilisation and immobilisation of ankle fractures, current opinions favour the former [3, 14]. Although our patients were all placed into a cast post-operatively, they were mobilised, and started weight-bearing along with physiotherapist-supervised movement at six weeks. The plaster was bivalved and ankle exercises were encouraged. The results from the Iowa ankle score showed 3 patients had good scores (>80/100) and one patient had a fair score (>70/100). The last patient had a score of 68/100. The two patients who scored less than 80 points were both pleased with results of their surgery. There are limitations of the Iowa ankle score assessment. This scoring can be affected by pre-existing major joint arthritis causing them to have problems with day-to-day activities (e.g. climbing stairs). This was the case in both of our lower scoring cases (patients 2&5).

Conclusion

In our small case series we had acceptable results with good functional scores and no major complications. Ender's nails fixation represents a safe and minimally invasive method.

REFERRENCES

1. Destot E. Traumatismes du pied at rayons: X malleoles
, astragale, calcneum avantpied. 1911;1-10.
2. Bonnin Josiah G. Injuries to the Ankle. London: William Heinemann Medical Books. 1950; 1st Ed. ed
3. Sirkin M, Sanders R. The treatment of pilon fractures. Orthop Clin North Am. 2001; 32: 91-102, 2001.
4. A report by the British Orthopaedic Association/British Association of Plastic Surgeons Working Party on the management of open tibial fractures. Br J Plast Surg. 1997; 50: 570-83.
5. Thordarson DB. Complications after treatment of tibial pilon fractures: prevention and management strategies. J Am Acad Orthop Surg. 2000; 8: 253-65.
6. Egol KA, Wolinsky P, Koval KJ. Open reduction and internal fixation of tibial pilon fractures. Foot Ankle Clin. 2000; 5: 873-85.
7. Kannus P, Palvanen M, Niemi S, Parkkari J, Jarvinen M. Increasing number and incidence of low-trauma ankle fractures in elderly people: Finnish statistics during 1970-2000 and projections for the future. Bone. 2002; 31: 430-33.
8. Bauer M, Bengner U, Johnell O, Redlund-Johnell I. Supination-eversion fractures of the ankle joint: changes in incidence over 30 years. Foot Ankle. 1987, 8: 26-8.
9. Helfet DL, Koval K, Pappas J, Sanders RW, DiPasquale T. Intraarticular "pilon" fracture of the tibia. Clin Orthop Relat Res 1994: 221-18.
10. Ruedi TP, Allgower M. Fractures of the lower end of the tibia into the ankle joint. Injury 1969; 1: 92-99.
11. Ghera S, Santori FS, Calderaro M, Giorgini TL. Minimally invasive plate osteosynthesis in distal tibial fractures: pitfalls and surgical guidelines. Orthopedics. 2004, 27: 903-05.
12. Ruedi TP, Allgower M. The operative treatment of intra-articular fractures of the lower end of the tibia. Clin Orthop Relat Res 1979; 105-10.
13. Lerner A, Stein H. Hybrid thin wire external fixation: an effective, minimally invasive, modular surgical tool for the stabilization of periarticular fractures. Orthopedics. 2004; 27: 59-62.
14. Dogra AS, Rangan A. Early mobilisation versus immobilisation of surgically treated ankle fractures. Prospective randomised control trial. Injury 1999; 30: 417-19.

The New Iraqi Journal of Medicine

Original Article

Radiology

Differences in chest radiological findings in diabetics new smear positive pulmonary tuberculosis from non diabetics new smear positive pulmonary tuberculosis

Mohammad Yahya Abdulrazaq*, Dhafer Salman Hashim**, hayder H.Ali Al-Sikafi, Ali Niamah Al-Yasiry*******

Abstract

Background and Objectives: Over the past two decades the prevalence of diabetes mellitus has risen dramatically, and Tuberculosis is now a major global public health problem .Diabetes mellitus and pulmonary tuberculosis may coexist, and the chest radiological findings of pulmonary tuberculosis in diabetic patients may differ from non diabetic patients. To find whether there is a difference in the chest radiological findings of new smear positive pulmonary tuberculosis in diabetics and non diabetics.

Methods *:* a cross sectional study was done in the specialized center for chest and respiratory disease in Baghdad during the period from 26th of August 2010 – 26th of November 2010 , new smear positive pulmonary tuberculosis diabetic patients chest radiological findings were compared with new smear positive pulmonary tuberculosis non diabetic patients chest radiological findings .

Results: Both groups had no significant difference in the radiological findings; apical lesion was 48.38% versus 61.36% (p = 0.379), cavities were present in 41.93% versus 54.54% (p = 0.400), diffuse involvement was 41.93% versus 29.54% (p = 0.387), middle or lower lobe involvement in 16.12% versus 13.63% (p = 0.975) and bilateral involvement was 22.58% versus 20.45% (p=0.948) in the diabetics and non diabetics respectively.

Conclusions: There are similar chest radiological findings in both new smear positive diabetics and new smear positive non diabetics.

The N Iraqi J Med, December 2011; 7(3):29-32

Keywords: *pulmonary tuberculosis, diabetes mellitus, chest radiological findings*

INTRODUCTION

Tuberculosis is a contagious disease that progresses from a systemic infection caused by bacteria of the Mycobacterium tuberculosis complex. Most commonly, M. tuberculosis that is spread from person to person by airborne transmission of droplet nuclei. [1]

Tuberculosis is a major global public health problem. Approximately one-third of the world's population is infected with tuberculosis. Each year there are 9 million new cases and nearly 2 million deaths attributed to this disease [1].

Diabetes mellitus refers to a group of common metabolic disorders that share the phenotype of hyperglycemia. The worldwide prevalence of DM has risen dramatically over the past two decades. In the year 2000 , an estimated 15.2 million people had a diagnosis of diabetes mellitus in the Middle East, and this figure is expected to be increased to around 42.6 million by the year 2030 [2].

The lung is the most commonly affected organ in tuberculosis. In the 2004 CDC surveillance reports, 79.5 percent of the newly diagnosed cases of tuberculosis had lung involvement [1].

* *myahyaszh@yahoo.com*

It is seldom possible to make a completely confident diagnosis of pulmonary tuberculosis on radiological grounds alone, as almost all the manifestations of tuberculosis can be mimicked by other diseases [3].

Pulmonary tuberculosis and Diabetes mellitus may coexist, and the radiological findings of tuberculosis in diabetic patients can be differing from radiological findings of tuberculosis in non diabetic patients [4, 5, 6, 7].

But still we have some authors could not find differences in the radiological manifestations of tuberculosis [8, 9, 10, 11].

PATIENTS AND METHODS

A cross sectional study was done in the specialized center for chest and respiratory disease in Baghdad during the period 26th of August 2010 – 26th of November 2010.

Any patient attending the respiratory clinic of the specialized center for chest and respiratory disease during the study period , who diagnosed as a case of new smear positive pulmonary TB was enrolled in this study (smear positive status was confirmed by 2 sputum sampling one of which should be morning sample) .

A total numbers of 75 patients were enrolled in this study.

A full medical history and physical examination was done for each patient and a chest-x ray was ordered to each of them. The findings of chest-x ray were reported by four pulmonologists.

A blood sugar tests were ordered to all them and the American Diabetes Association criteria [2] [12] were used to diagnose the diabetics, those patients with a known history of diabetes (already on hypoglycemic medications) with normal blood sugar also reported as diabetics.

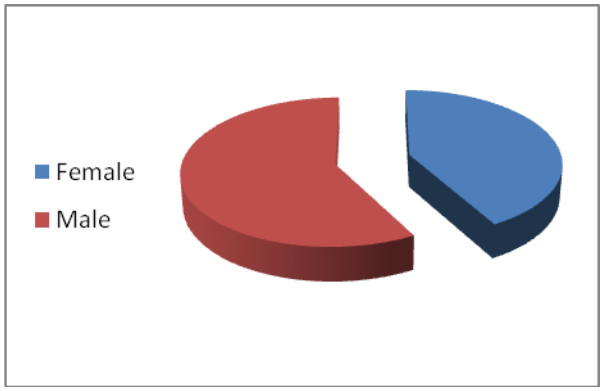
Then the radiological findings of diabetics and non diabetics were studied and compared.

Statistical analysis

Discrete variables were expressed as numbers and percents. Statistical package for social sciences version 17 (SPSS V.17) was used for data input and analysis. Z test for difference in proportions was used to test the significance of difference between two proportions of independent variable. P value was two sided asymptotic, finding with P value less than 0.05 were considered significant.

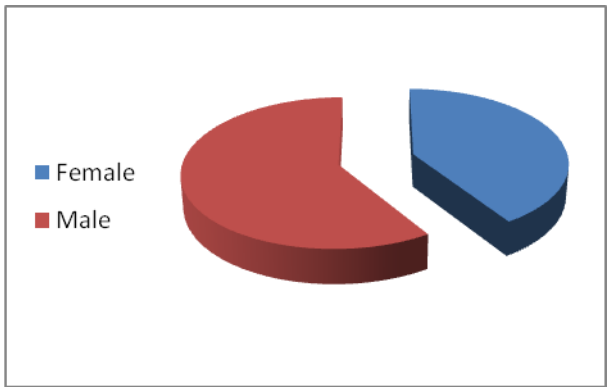
RESULTS

75 patients enrolled in this study, 31 diabetics and 44 non diabetics. Age range in diabetic group was 18-70 while in non diabetic group was 15-70.Age median for diabetic group was 52.29 while for non diabetic group 33.34. Male/Female ratio in diabetic group was 1.38 while in non diabetic group was 1.44(Pie diagram1, 2)



(Pie diagram1)

Male/Female ratio in Diabetic group

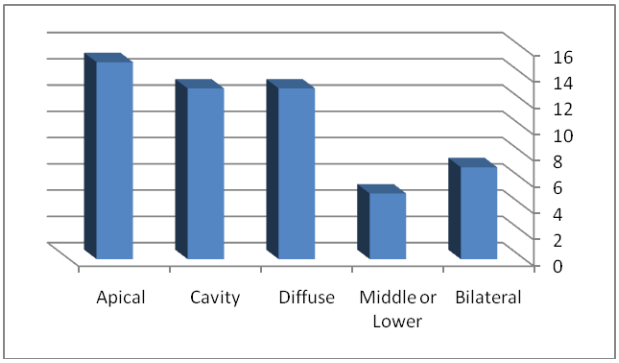


(Pie diagram2) Male/Female ratio in Non-Diabetic group

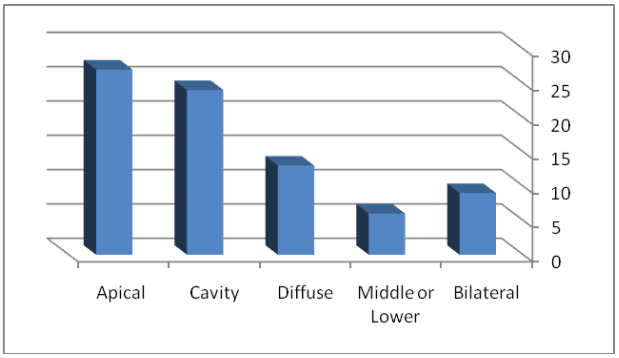
Both groups had no significant difference in the radiological findings; apical lesion was 48.38% versus 61.36% (p = 0.379), cavities were present in 41.93% versus 54.54% (p = 0.400), diffuse involvement was 41.93% versus 29.54% (p = 0.387), middle or lower lobe involvement in 16.12% versus 13.63% (p = 0.975) and bilateral involvement was 22.58% versus 20.45% (p =0.948) in the diabetics and non diabetics respectively.(table1)(Column Chart1,2).

Radiological finding	Diabetic group	Non Diabetic group	P value
apical	**48.38%**	**61.36%**	**0.379**
cavity	**41.93%**	**54.54%**	**0.400**
diffuse	**41.93%**	**29.54%**	**0.387**
Middle or lower	**16.12%**	**13.63%**	**0.975**
bilateral	**22.58%**	**20.45%**	**0.948**

(Table1) Radiological findings



(Column Chart1) Radiological finding in Diabetic group



(Column Chart2) Radiological finding in Non-Diabetic group

DISCUSSION

The association between DM and tuberculosis has been recognized, this study try to find whether there is a difference in the chest radiological findings in diabetics and non diabetics.

Age

In our study diabetic group were older than non diabetic tuberculosis patients, same finding in Perez-Guzman et al's study [13] and in Gülfem Yurteri's study [9]

Gender

In our study Males are more than Females, same finding in Yamagishi's study [14] and in Gülfem Yurteri's study [9].

Radiological finding

In our study we had no significant difference in the radiological findings whether there were apical lesions, cavities, diffuse involvement, middle or lower lobe involvement or bilateral involvement in diabetics and in non diabetics.

we have some studies could not find difference like Morris et al's study [11], Al-Wabel et al's study[15], Bacakoglu's study[16], Dr. Aisha's study [8] Gülfem Yurteri's study [9] Nissapatorn V's study [10];these findings may be explained by the fact that diabetic patients may receive more medical treatment and tuberculosis screening than the non diabetic population and for that reason the findings would be similar in both groups, also there is a study was done by Parvaneh Baghaei et al showed diabetic patients had a higher prevalence of typical presentations along with cavitary lesion(s) but no significant difference was found between the 2 groups in terms of radiological presentation But we have other studies that show difference like Wang CS's study [4] Jabbar A's study [5] Sheikh MA's study [6] Umut S et al's study [7] and Ahmed et al's study [17].

A study involving a larger number of patients and for longer duration may give results of significant value and find observations similar to those workers.

CONCLUSION

In the specialized center for chest and respiratory disease in Baghdad Pulmonary Tuberculosis have similar chest radiological findings in both new smear positive diabetics and new smear positive non diabetics.

Acknowledgements

The initial research proposal was developed during the 2010 Stop TB Action Training Course held in Tokyo, organized by the Japan International Cooperation Agency (JICA), hosted by the Research Institute of Tuberculosis, Japan Anti-Tuberculosis Association (RIT/JATA), in collaboration with the World Health Organization, the United States Centers for Disease Control and Prevention, the International Union Against Tuberculosis and Lung Disease, and the Medecine Sans Frontieres.

REFERRENCES

1- Philip A. LoBue, Michael F. Iademarco, Kenneth G Castro. The epidemiology, prevention, and control of tuberculosis. In Fishman´s pulmonary disease and disorders, Alfred P.Fishman, 4th edition, 2008: section 21 mycobacterial infection, chapter 138, pp 2447.

2- Harrison's Principles OF Internal Medicine Seventeenth Edition, Chapter 338. Diabetes Mellitus, Fauci, et al; 2008.

3- A. Gordon Leitch. Pulmonary tuberculosis: Clinical features. In Crofton and Douglas's Respiratory diseases, Anthony Seaton, Douglas Seaton, A. Gordon Leitch, 5th edition, 2000; Chapter 17 page 516.

4-Wang CS, Epidemiol Infect 2008; 18:1-8.

5-Jabbar A, East Mediterr Health J 2006; 12: 522 – 527.

6-Sheikh MA, Saudi Med J 2003; 24: 278-81.

7- Umut S, Tosun GA, Yildirim N. Radiographic location of pulmonary tuberculosis in diabetic patients. Chest 1994; 106:326.

8- Dr. Aisha, Middle east journal of family medicine, April 2010 – Volume 8, Issue 3.

9- Gülfem Yurteri, Turkish Respiratory Journal, 2004; 5 :(1):5-8.

10- Nissapatorn V. Tuberculosis in diabetic patients: a clinical perspective. Southeast Asian J Trop Med Public Health 2005; 36:213-20.

11- Morris JT, Seaworth BJ, Mc Allister CK. Pulmonary tuberculosis in diabetics. Chest 1992; 102: 539-541.

12- Cecil text book of tuberculosis of Medicine, 23rd edition, Chapter 248 – Type 2 Diabetes Mellitus, Silvio E. Inzucchi Robert S. Sherwin, 2008.

13- Perez-Guzman C, Torres-Cruz A, Villareal-Velarde H et al. Atypical radiologic images of pulmonary tuberculosis in 192 diabetic patients. Int J Tuberc Lung Dis 2001; 5:455-61

14- Yumagishi F, Suzuki K, Sasaki Y.et al; Prevalence of coexisting diabetes mellitus among patients with active pulmonary tuberculosis. Kekkaku 1996; 71; 569-72

15- Al-Wabel AH, Teklu B, Mahfouz AA, et al. Symptomatology and chest roentgenographic changes of pulmonary tuberculosis among diabetics. East Afr Med J 1997; 74:62-4.

16- Bacakoglu F, Basoglu OO, Cok G et al. Pulmonary tuberculosis in patients with diabetes mellitus. Respiration 2001; 68:595-600.

17- Ahmed MS, Reid E, and Khardori N. Respiratory infections in diabetes: Reviewing the risks and challenges. J Respir Dis. 2008; 29(7):285-293.

18- Parvaneh Baghaei Payam Tabarsi 1, Zoha Abrishami 2, Mehdi Mirsaeidi1, Yazdan Ali Faghani 2, Seyed Davood Mansouri 3, Mohammad Reza Masjedi 4 Tanaffos 2010; 9(2): 13-20.

The New Iraqi Journal of Medicine

Original Article

Gastroenterology

Some cytokines profile in gastric ulcer

***Batool Mutar Mahdi* ***

Abstract

Background AND Objective: Anti-inflammatory cytokines are a series of immunoregulatory molecules that control the proinflammatory cytokine response. Their physiologic role in inflammation and systemic inflammatory states are recognized. Cytokines are believed to have a role in the pathogenesis of gastric ulcer.
To measure the value of circulating mediators tumor necrosis factor-α (TNF-α) and interferon –gamma (IFN-γ) and their antagonists interleukin-6 (IL-6) and interleukin-10 (IL-10) in patients with gastric ulcers.
Patient and method*:* During the period from September 2008 - May 2009, 40 patients of gastric ulcers were identified at the Colonoscopic Department of Al-Kindi Teaching Hospital – Baghdad. The second control group consisted of thirty healthy volunteers' age- and sex-matched with first group from staff employees. Blood were collected and IL-6, IL-10, TNF-α and IFN-γ were measured by enzyme-linked immunosorbent assay.
Results: There was a significant increase in the serum levels of IL-10 (19.51±2.02) pg/ml (p=0.01), TNF- α (17.31±1) pg/ml (p=0.000) and IFN-γ (78.6±14.1) pg/ml (p=0.000) in patients with gastric ulcer when compared with control group. In addition to that, there was no significant difference in IL-6 level (7.99±2.37) pg/ml when compared with control group (7.5±2.4) pg/ml.
Conclusions: Immune imbalance between Th1 and Th2 cytokines secretion, enhance gastric inflammation and progression to ulceration. This may shed a light to treat gastric ulceration using immune modulator drugs especially ulcers that resist treatment by conventional medication.

The N Iraqi J Med, December 2011; 7(3):33-37

Keywords: *gastric, ulcer, cytokine and interleukin.*

INTRODUCTION

Gastric inflammation is mediated by various mechanisms implicating several proinflammatory cytokines that involved in the pathogenesis of peptic ulcer [1]. When inflammation of the gastric mucosa occurs, it leads to infiltration of neutrophils and mononuclear cells [2] that stimulating the transcription and synthesis of several pro-inflammatory cytokines like interleukin (IL)-1β, IL-2, IL-6, IL-8 and tumor necrosis factor (TNF)-α and anti-inflammatory cytokines like IL-4 and IL-10 [3].

The increased production of inflammatory cytokines results in enhanced gastric mucosal inflammation, by binding these cytokines to specific receptors on target cells. The levels of cytokines at gastric mucosa under genetic control, level of mucosal IL-1β, for example, differ significantly among the different genotypes in three polymorphisms, *IL-1B*-511, -31 and *IL-RN*[4]. . IL-1 shows enhanced suppression of gastric acid secretion, which results in more rapid development of gastric atrophy, and a consequently greater risk of developing gastric cancer [5] .IL-2 potently regulates the immune response, and plays important roles in the differentiation of CD41-positive T cells into Th1 and Th2 effecter subsets and inhibiting T-helper 17 differentiation [6,7] . IL-4 is an anti-inflammatory cytokine, which inhibits gastric mucosal inflammation and atrophy by decreasing interferon -γ (IFN-γ), which plays an important role

* *DEPATMENT OF MICROBIOLOGY*
AL-KINDI COLLEGE OF MEDICINE
BAGHDAD UNIVERSITY
AL-Nahda Square –Baghdad-Iraq
E-mail:batool1966@yahoo.com

in Th1 immune responses [8]. IL-4 also plays a central role in the maturation of T-helper cells to Th2 with a shift from a Th1 to a Th2 cell pattern, IL-4 can enhance the production of anti-inflammatory cytokines (e.g. IL-10 and IL-13) [9] . Other cytokine is IL-6 that Inhibits TNF and IL-1 production by macrophages [10] and plays an important role in host defense mechanism as a messenger between innate and adaptive systems, by stimulating IFN-γ production in T cells and promoting immunoglobulin secretion in activated B cells [11].

The current study was designed to measure circulating concentrations of mediators and antagonists in patients with gastric ulcers.

PATIENTS AND METHODS

The study consisted of a 40 adult outpatients referred to Al-Kindi Teaching Hospital – Colonoscopic Department in Baghdad for upper endoscopy between September 2008 and May 2009. They were defined as gastric ulcers by their specialized physicians.

The exclusion criteria was patients previously had prior helicobacter eradication therapy, drug-associated or other known gastric irritants, infective etiology or pathogenic bacterial, viral, parasitic, fungal and granulomatous gastritis (Crohn's associated, Sarcoid and Reactive gastritis) and radiation-associated Phlegmonous gastritis. In addition to that, subjects with history of major systemic diseases including diabetes mellitus, adrenal insufficiency, iron deficiency anemia, thyrotoxicosis, myxedema, autoimmune gastritis and Hashimoto's thyroiditis. The second control group consisted of thirty healthy volunteers' age- and sex-matched with first group from staff employees.

The study was approved by the Ethical Committee of Al-Kindi College of Medicine, Baghdad University and Al- Kindi Teaching Hospital and all samples were obtained with informed consent in accordance with the Al-Kindi Teaching Hospital Declaration.

Patients were examined by upper endoscopy and two biopsy specimens were obtained from adjacent areas of the gastric antrum and intact mucosa distant from focal lesions. Biopsies were stained with haematoxylin-eosin and examined in a blinded manner by a pathologist.

Blood samples were collected from both groups and serums were separated, stored at −20°C until analyzed. Estimation of cytokines were done (IL-6, IL-10, TNF-α and IFN-γ) by ELISA method using US Biological Kit - USA.

Statistical analysis:

Data was analyzed statistically using descriptive statistics: frequencies for tables, mean and standard deviation and inferential statistics: Student's t- test was used. P- Values <0.05 were considered statistically significant. Calculations were performed using MiniTab statistical software program 13.20.

RESULTS

A total 40 patients with gastric ulcers, their ages were range from 19–84 years (mean 45.67 years ± 15.54 SD). Twenty of them were males and the rest were females. There was no significant difference with control group as shown in table -1-. The control group formed from fifteen males (50%) and the rest were females (50%).

Estimation of IL-6 (mean 7.99± SEM 2.37 pg/ml) in gastric ulcers patients showed not significant difference with control (mean 7.5± SEM 2.4) pg/ml. Other cytokines IL-10 (mean 19.51± SEM 2.02) (p=0.01), TNF (mean 17.31± SEM 1) (p=0.000) and IFN (mean 78.6± SEM 14.1) (p=0.000) demonstrated significant higher levels in gastric ulcers patients when compared with control group as seen in tables-2-

Age in years	IC patients No.=40	Control group No.=30	P-value
Mean	45.67	44	0.629
SD	15.54	15.22	
Minimum	19	20	
Maximum	84	76	

Table-1- Age distribution in gastric ulcers patients compared with control group.

DISCUSSION

Many patients are suffering from gastritis and some of them will develop peptic ulcer disease [12], making the question what is the mechanism leading those patients with gastritis to develop peptic ulcer and others not. The inflammation of gastric mucosa in ulcerated stomach is mediated by various mechanisms involving several proinflammatory cytokines. This study showed a significant increased

in TNF-α (17.31±1.0) (P=0.000) that is in agreement with Lychkova *etal* ,2007 [13] that demonstrate diversion of functional activity of the immune system plays an important role in the pathogenesis of ulcer disease, mainly T-helper lymphocytes and cytokines produced by them. They found that ulcer is associated with massive apoptosis of epithelial cells, development of vascular reactions, edema and development of fibrinoid necrosis and infiltration of the mucosa by neutrophils, plasma cells and proliferation of fibroblasts. These processes persuaded and regulated by cytokines, particularly interleukin IL-1beta, TNF-alpha, IL-4, IL -6, IL-8, IL-12. Takeuchi *etal* 2002 [14] found that NF-κB activation followed by TNF-α release contribute to tissue damage in gastric ulcer. Consequently, the use of Pentoxifylline that has many anti-inflammatory properties including inhibition of production of tumor necrosis factor alpha (TNF-α) may accelerate ulcer healing [15, 16].

Cytokine	Gastric ulcer patients No.=40 X±SEM	Control No.=30 X±SEM	P- value
IL-6 Pg/ml	7.99±2.37	7.5±2.4	0.60
IL-10 Pg/ml	19.51±2.02	3.57±3.7	0.01
TNF-α Pg/ml	17.31±1	7.5±5.46	0.000
IFN-γ Pg/ml	78.6±14.1	8.15±6.69	0.000

Table-2- serum level of IL-6, L-10, TNF-α and IFN-γ in patients with gastric ulcer and control group.

Other cytokine is IFN-gamma that showed significant increase in our study (78.6±14.1) (p=0.000) in gastric ulcer patients which in accordance with Cinque *etal* 2006 [17] that illustrated also increase in IFN levels. IFN is a proinflammatory cytokine that plays a central role in gastric inflammation and ulceration by induction Th1 immune response.

In case of IL-6 which is showed no significant difference with control, it is in agreement with other paper that it had no relation with gastric disease [18]. It had been found that IL-6 had a correlation with disease status of gastric cancer and may be used as a new tumor marker for monitoring treatment and response of gastric cancer patients [19].

Additional cytokine was IL- 10 which is anti-inflammatory mediator showed significant increased in it is level in order to suppress the inflammatory reaction that occurred in the gastric mucosa. Other study mentioned that IL-10 may increase gastric inflammation [20]. Others found IL-10 gene polymorphism is important in Japanese gastric cancer [21] while it was not important in gastric cancer Korean population [22].

Some people had a higher level of some cytokines and other not; this may be due to gene polymorphisim of these cytokines or their receptors [23]. This imbalance in the cytokines production by Th1 and Th2 may predispose to gastric inflammation and ulceration, consequently correction of cytokine disproportion used for treatment of peptic ulcer and regeneration of gastric mucosa and healing gastric ulceration [24].

Conclusion: Immune imbalance between Th1 and Th2 cytokines secretion, enhance gastric inflammation and progression to ulceration. This may shed a light to treat gastric ulceration using immune modulator drugs especially ulcers that resist treatment by conventional medication.

Acknowledgment: I thank Al-Kindi College of medicine for their help in achievement this research.

REFERRENCES

1- Lindholm C, Quiding- Jarbrink M, Lonroth H, et al. Local cytokine response in *Helicobacter pylori*-infected subjects. Infect Immun. 1998; 66:5964–71.

2- Yuan Y, Padol IT, Hunt RH. Peptic ulcer disease today. Nat Clin Pract Gastroenterol Hepatol.2006; 3:80–9.

3- Hwang IR, Kodama T, Kikuchi S, Sakai K, Peterson LE, Graham DY, Yamaoka Y. Effect of interleukin 1 polymorphisms on gastric mucosal interleukin 1beta production in Helicobacter pyloriinfection. Gastroenterol ogy. 2002; 123:1793–1803.

4- El-Omar EM, Carrington M, Chow WH, McColl KE, Bream JH, Young HA, Herrera J, Lissowska J, Yuan CC, Rothman N, et al. Interleukin-1 polymorphisms associated with increased risk of gastric cancer. Nature. 2000; 404:398–402.

5- Sugimoto M, Furuta T, Shirai N, Nakamura A, Xiao F, Kajimura M, Sugimura H, Hishida A. Different effects of polymorphisms of tumor necrosis factor-alpha and interleukin-1 beta on development of peptic ulcer and gastric cancer. J Gastroenterol Hepatol. 2007; 22:51–59.

6- Gaffen SL, Liu KD. Overview of interleukin-2 function, production and clinical applications. Cytokine. 2004; 28:109–123.

7- Laurence A, Tato CM, Davidson TS, Kanno Y, Chen Z, Yao Z, Blank RB, Meylan F, Siegel R, Hennighausen L, et al. Interleukin-2 signaling via STAT5 constrains T helper 17 cell generation. Immunity. 2007; 26:371–381.

8- Vercelli D, Jabara HH, Lauener RP, Geha RS. IL-4 inhibits the synthesis of IFN-gamma and induces the synthesis of IgE in human mixed lymphocyte cultures. J Immunol. 1990; 144:570–573.

9- Opal SM, DePalo VA. Anti-inflammatorycytokines. Chest. 2000; 117:1162–1172.

10- Lauta VM. Interleukin-6 and the network of several cytokines in multiple myeloma: an overview of clinical and experimental data. Cytokine. 2001; 16:79–86.

11- Curfs JH, Meis JF, Hoogkamp-Korstanje JA. A primer on cytokines: sources, receptors, effects, and inducers. Clin Microbiol Rev. 1997; 10:742–780.

12- Zhang C, Yamada N, Wu YL, Wen M, Matsuhisa T, Matsukura N. Comparison of Helicobacter pylori infection and gastric mucosal histological features of gastric ulcer patients with chronic gastritis patients. World J Gastroenterol. 2005; 11: 976-981.

13- Lychkova AE, Tsaregorodtseva TM, Serova TI. Cytokine profile during experimental gastric and duodenal ulcers: the serotonin role. Eksp Klin Gastroenterol. 2010; 2:37-39.

14- Takeuchi T, Miura S, Wang L, Uehara K, Mizumori M , Kishikawa H *etal*. Nuclear Factor-κB and TNF-α Mediate Gastric Ulceration Induced by Phorbol Myristate AcetateDigestive diseases and sciences.2002; 47:2070-2078.

15- Shimizu N, Watanabe T, Arakawa T, Fujiwara Y, Higuchi K, Kuroki T. Pentoxifylline Accelerates Gastric Ulcer Healing in Rats: Roles of Tumor Necrosis Factor Alpha and Neutrophils during the Early Phase of Ulcer Healing. Digestion. 2000; 61:157-164.

16- Baraka AM, Guemei A, Gawad HA. Role of modulation of vascular endothelial growth factor and tumor necrosis factor-alpha in gastric ulcer healing in diabetic rats. Biochem Pharmacol. 2010; 79:1634-1639.

17- Cinque SM, Rocha GA, Correa-Oliveira R, Soares TF, Moura SB, Rocha AM, Nogueira AM, Cabral MM, Vieira LQ, Martins-Filho OA, Queiroz DM .The role of IFN-gamma and IL-4 in gastric mucosa inflammation associated with Helicobacter heilmannii type 1 infection. Braz J Med Biol Res. 2006; 39:253-61.

18- Hwang IR, Hsu PI, Peterson LE, Gutierrez O, Kim JG, Graham DY, Yamaoka Y. Interleukin-6 genetic polymorphisms are not related to Helicobacter pylori-associated gastroduodenal diseases. Helicobacter. 2003; 8:142-8.

19- Wu CW, Wang SR, Chao MF, Wu TC, Lui WY, P'eng FK, Chi CW.Serum interleukin-6 levels reflect disease status of gastric cancer. Am J Gastroenterol. 1996; 91:1417-22.

20- Achyut BR, Tripathi P, Ghoshal UC, Moorchung N, Mittal B. Interleukin-10 (-819 C/T) and tumor necrosis factor-alpha (-308 G/A) gene variants influence gastritis and lymphoid follicle development. Dig Dis Sci. 2008; 53:622-9.

21- Sugimoto M, Furuta T, Shirai N, Nakamura A, Kajimura M, Sugimura H, Hishida A.. Effects of interleukin-10 gene polymorphism on the development of gastric cancer and peptic ulcer in Japanese subjects. J Gastroenterol Hepatol.2007; 22:1443-9.

22- Lee JY, Kim HY, Kim KH, Kim SM, Jang MK, Park JY, Lee

JH, Kim JH, Yoo JY.Association of polymorphism of IL-10 and TNF-A genes with gastric cancer in Korea. Cancer Lett. 2005. 28; 225:207-14.

23- Sugimoto M, Yamaoka Y, Furuta T. Influence of interleukin polymorphisms on development of gastric cancer and peptic ulcer. World J Gastroenterol. 2010; 16:1188-200.

24- AskarMB, Vorob'eva NN, Trubitsyna IE, Onishchenko NA. Cytokine imbalance correction and regeneration stimulation of persistent autoimmune stomach ulcers with help of periulcer transplantation of mononuclear cells of autological bone marrow. Eksp Klin Gastroenterol. 2009; 4:42-45.

The New Iraqi Journal of Medicine

Original Article

General surgery

Retained pack after laparotomy: Risk factors, presentation and ideas for prevention

Nashwan K Mahjob * , Faris Hani Raoof **

Abstract

Aim of study: To identify risk factors that may play a rule in retained pack in surgical patient underwent laparotomy, to discuss presentation and ideas of surgeons in performing a safety checklist that can be used to minimize or prevent such complication.
Design: Retrospective, matched case control study.
Setting: Mosul medical Center at Al-jamhori and Al-batool Teaching Hospitals.
Participants: 53 patients with retained pack in their abdomen after laparotomy.
Main outcome measures: we reviewed medical records by using special formula to collect data from 37 consultant general surgeons, all with more than 10 years of official, legal and scientific responsibility. They were asked to give their experience in dealing with retained pack after laparotomy (operation that dealt with intra-abdominal viscera via abdominal wall incision excluding laparoscopic procedures) during the period between January 2000 and January 2010. Surgeons were asked to put a strategy in form of a checklist that can be used in prevention of this complication. We used a retrospective case–control design. Patients with cases were those in whom pack had been left after a laparotomy procedure; controls were patients who had undergone the same type of operations without retained pack during the same period.
Results: The study included 53 patients with retained pack in their abdomen after laparotomy, reported by 37 consultant general surgeons, from a total of 37436 laparotomies during the period between January 2000 and January 2010 at Al-jamhori and Al-Batool Teaching Hospitals, which are the main surgical and gyne-obstetrical hospitals respectively in Mosul Medical Center. The age varied from 14 to 61. There were 22 female and 31 male patients; the body mass index was more than normal in 21 patients. Emergency operation reported in 33 and elective in 20 patients, they were super major operations in 36 and major in 17 cases. Retrospective operative reports were available for 45 patients, They showed unexpected finding with operative plan changes in 28, sever bleeding that needed unorganized intra-operative blood transfusion in 19, iatrogenic organ trauma in 11 and intra-operative anesthetic complication in 5 patients. There was no record about change of staff during the operations as well as no record about counting packs at the beginning or at the end of operations. In 15 cases more than one surgical team were involved. The median date of pack detection was 24 day after surgery (range, day of surgery to 2.5 years after surgery), in 13 cases, the retained pack resulted in intestinal obstruction, abdominal mass in 10, chronic infected discharging wound in 9, small-bowel fistulae in 8, intra-abdominal abscess in 7, visceral perforation in 3, obstructive jaundice in 3 and in 1 case, the retained object resulted in death. Forty seven patients with retained pack required reoperation.
Conclusion: Emergency, super major and change in strategy of operation as well as increase body mass index are risk factors for retained pack. Intestinal obstruction, abdominal mass and chronic infected discharging wound, are the most common sequel. A safety checklist was obtained in a hope to be used and become globally acceptable to prevent such complication.

The N Iraqi J Med, December 2011; 7(3):38-45

Keywords: *Laparotomy. Pack. Laparotomy. Safety checklist.*

INTRODUCTION

Surgical care and its attendant complications represent a substantial burden of disease worthy of attention from the public health community worldwide. Surgery is performed in every community and in all regions, it's estimated that more than 234 million operations performed annually all over the world [1].This yearly volume exceeds that of childbirth [2].

Errors in surgical practice are common and may cause harm to patients and their surgeon[-3-]. Data suggest that at least half of all surgical complications are avoidable [4]. However; isolating the factors underlying specific types of errors has proved to be a

*
Assistant Professor Department of surgery
College of Medicine University of Mosul
Mosul, Iraq
Consultant general surgery
Al-Jamhori Teaching Hospital
Mosul, Iraq

formidable task. One of persistent but poorly understood error is leaving pack inside patient's abdomen that underwent surgery. In the majority of such cases, packs go un-detected despite proper procedures to prevent it [5].

The World Health Organization (WHO) published guidelines identifying multiple recommended practices to ensure the safety of surgical patients worldwide[6], but unfortunately no guidelines specifically for such complication was recorded apart from counting needle, sponges and instrument by the nurse[6], which proved to be insufficient[7,8]. Although the retention of a pack is rare event, however, the consequences are dangerous and may be life threatened [9, 10].

We try in this research to focus a light on such complication in our medical center and to perform a safety checklist that can help surgeon to reduce the rate of such complication or prevent it and whether it can be locally and globally applicable, by sharing the experience of consultant surgeons whom dealt with such condition. We are sure that the use of such checklist needs changes in the systems and behavior of individual surgical teams as well as adequate support from hospital administration.

PATIENTS AND METHODS

We developed a data form for recording surgical information about patients with retained pack after laparotomy operation during the period between January 2000 and January 2010, from 37 surgeons, all of them were qualified and authorized by the monastery of health of Iraq as specialized general surgeons in the surgical words at Al-Jamhori Teaching Hospital in Mosul Medical Center. The data included: Age, sex, weight and height of the patient, number of patient that faced the surgeon with retained pack in abdomen during the last 10 years of their surgical experience. The information regarding the offending operation included: type and indication, any intra-operative complication happened, change in the strategy of operation, any technical intra-operative organ trauma, the need for blood transfusion, number of surgical team shared, staff changed during operation, pack counting before and after the procedure. The surgeons were asked an optional question about who is the most responsible for such complication.

The information about the management of patient with retained pack included:

1- The way in which the pack was detected.

2- Time between the offending operation and detection.

3- Interference to retrieve the pack if any.

4- The patient health outcome.

We calculated the total number of laparotomies done through the time included in the study and we extracted the patients with retained pack from them. For each patient with retained pack, we identified an average of four randomly selected controls that underwent the same operation during the same period without pack retention; the data were obtained from the patient's sheath, with permission from the medical statistical unit and approval for the review of records from the directory of Al- Jamhori and Al-batool Teaching Hospitals. Given an estimated 53 operations with retained pack available for review, we determined that four controls for each operation (Medical records for 212 control patients) without such complication would give the study sufficient power to detect a risk factor present in 30 percent of patients that produced a doubling of the likelihood that a pack would be left behind. We generated descriptive statistics and performed a matched case control analysis using univariate conditional logistic regression. Variables found to be associated with an increased likelihood of retention of a pack in univariate analysis at a level of statistical significance of $P<0.05$.

Analyses of the data

We divided the risk factors into three categories:

1- Operative factors which included:

A- Type of operation.

1- Urgent operation (operation that should be performed within hours).

2- Elective operation

B- Grade of operation.

1- Super major operation (operation that includes more than one procedure with more than 24 hours of hospital admission).

2- Major operation (operation that includes single procedure with more than 24hours of hospital admission).

C- Unexpected change in the plan or strategy of operation.

1- Intra-operative newly discovered condition.

2- Sever bleeding happened during operation.

3- The need for unorganized intra-operative blood transfusion.

4- Intra-operative technical complication.

5- Intra-operative anesthetic complication.

2- Surgeon and staff factors which included:

A- Number of working team.

B- Changing of staff during operation.

C- Counting of packs before and after operation.

3- Patients factors which included:

A- Age.

B- Sex.

C- Body mass index (BMI) (weight in kg/height m^2)

The surgeons were asked to give their best ideas to prevent such complication. The ideas of surgeons and the author's recommendations were translated into a form of a practical safety checklist.

RESULTS

Thirty seven surgeons were asked to full the special formula we prepared, 5 surgeons mentioned that they faced no such complication during their surgical work, 2 surgeons not returned back the formula they received. The study recorded 53 patients with retained pack after laparotomy operation, from a total 37436 laparotomy operations at Al-jamhori and Al-batool Teaching Hospital in Mosul between January 2000 and January 2010.

Twenty two patients were dealt with by the responder surgeon, other 31 patients were treated by other surgeons after tacking permission from the first surgeon, or the condition was an emergency one, or that the first surgeon not available, apologized or asked for help from the second surgeon. Sixteen surgeons reported one case for each, 6 surgeons reported 2, and while 7 surgeons reported 3 cases and one surgeon had 4 such cases. The age of patients varied from 14 to 61 years with a median age of 34.5 years. There were 22 female and 31 male patients; the body mass index is more than normal in 21(39.6%) patients. There were 33(62.2%) emergency and 20(37.8%) elective operations, they were super major in 36(68%) and major operations in 17(32%) cases. The offending operations were shown in table one.

Type of operation	Number and % of patients with retained pack
Acute abdomen due to trauma by: Bullet(*) Penetrating wound(**) Blunt(***)	14 (26.4%) (*9) (**3) (***2)
Non traumatic acute abdomen by: Intestinal obstruction(*) perforated duodenal ulcer(**) Appendicitis(***) Ectopic gestation(****)	9 (17%) (*3) (**3) (***2) (****1)
Emergency cesarean section	8 (15%)
Elective operation for malignancy Colonic(*) Pancreatic(**)Stomach (***)Spleen(****)	6 (11.3%) (* 2) (**2) (***1) (****1)
Elective hysterectomy	3 (5.6%)
Emergency biliary system operation	2 (3.7%)
Elective open cholecystectomy	2 (3.7%)

Elective multiple hydatid cyst in the abdomen	2 (3.7%)
Elective hydatid cyst in the liver	2 (3.7%)
Elective urinary tract operation	2 (3.7%)
Elective Incesional hernia	2 (3.7%)
Elective cesarean section	1 (1.8%)

Table 1: Type, number and percentage of operations with retained pack.

The median date of detection was 24 day after surgery (range, day of surgery to 2.5 years after surgery), in 16 cases (30%) the retained pack was detected by the first 10 days after surgery, in 5 cases (9.4%), the retained pack was not detected until 2.5 years after surgery. Forty seven patients (88.6%) required reoperation for removal of the pack and management of its complication, in 5 (9.4%) patients; the packs were removed at the bedside, in one patient (1.8%), the foreign body was expelled with feces.

In 13 (24.5%) cases, the retained pack resulted in intestinal obstruction, abdominal mass in 10 (18.8%), chronic infected discharging wound in 9 (17%), small-bowel fistulae in 8 (15%), intra-abdominal abscess formation in 7 (13.2%), visceral perforation in 3 (5.6%), obstructive jaundice in 3(5.6%) and in 1 (1.8%) case, the retained pack resulted in death. The control patients were selected randomly from the pool of patients who underwent the same laparotomy operation, during the same period of time (2000-2010) without pack retention; table two shows the number of laparotomies and type of operation from which the control patients were selected.

Hospital name	Total	Emergency operation	Retained pack	No pack	Elective operation	Retained pack	No pack
Al-Jamhori	11608 (31%)	4688 (40%)	24 (0.5%)	4664 (99.5)	6920 (60%)	16 (0.2%)	6904 (99.8%)
Al-Batool	25828 (69%)	13618 (52%)	9 (0.06%)	13611 (99.94%)	12210 (48%)	4 (0.03%)	12206 (99.97%)
Total	37436	18306 (49%)	33 (0.18%)	18275 (99.82%)	19130 (51%)	20 (0.1%)	19110 (99.9%)

Table 2: Number and % of laparotomies in the involved hospital and their types.

Retrospective analyses of the operative records of the offending operations were available only in 45 conditions and 212 of the control. Table three shows the risk factors in patients with a retained pack, in comparison with control patients, and the P value.

Forty seven (88%) packs were detected by re-exploration. Other 5 retained packs (9.4%) were detected on physical examination. One (1.8%) patient brought the pack with her to medical office after she was defecated it. Ultra sound and radiography were done in 40 and 35 patients respectively; but they not

proved the condition correctly. Out of thirty surgeons how had been dealt with such condition, ten (33.3%) surgeons did not answer the optional question about the responsibility of retained pack, 10 (33.3%) blamed the leader of the team, the assistant in 6 (20%) and the nurse was blamed in 4 (13.3%) answers.

Risk factor	Patients with retained pack	Control patients	P Value
Median age — yr	34.5	37.2	
Male sex.	31/53*	145/212****	0.23
Body-mass index	21/53*-(39.6%)	34/212****-(16.3%)	0.001
Emergency operation. No, total,%	33/53*-(62.2%)	132/18375** (0.7%)	0.0001
Super major surgery No, total,%	36/53*-(68%)	82/212****-(38.6%)	0.0001
Unexpected change in plan of operation No, total,%	28/45***-(65%)	31/212****-(8.9%)	0.0001
Excessive blood loss that needed unorganized intra-operative blood transfusion No, total,%	19/45***-(44%)	32/212****-(15%)	0.0001
Intra-operative technical complication. No, total-%	11/45***-(25.5%)	19/212****-(10%)	0.01
>1 Surgical team involved No, total,%	15/45***-(34.8%)	22/212****-(10.3%)	0.001
intra-operative anesthetic complication No, total,%	5/53*-(11.6%)	11/212****-(5%)	0.39
Counts of pack	Not recorded	Not recorded	
Change in nursing staff during procedure	Not recorded	Not recorded	

Table 3: Risk factors in patients with retained pack, Control Patients, and the P value.

* Number of patients with retained pack

** Number represents the total emergency operation excluding those with retained pack.

*** Data messed in 8 patients with retained pack

**** Number of control patients

The result of a thorough discussion between the surgeons and authors, the following points were evaluated and recorded to be a safety checklist:

1- The initial pack supply should be standard in number for all laparotomy operation.*

2- The number of extra pack supply (if needed) should be standard and it's the same number of the initial supply. **

3- Only the first surgeon is allowed to call for extra packs.

4- When extra packs are requested and supplied, the first surgeon should be informed both by visual and auditory ways by the scrub nurse.

5- If nurse staff to be changed, packs should be given hand by hand.

6- The size of the pack should be standard.

7- A ribbon to be sewing with the pack for more accurate detection. ***

8- No pack should be discarded (even if they are dirty) till the end of operation, they should be collected in a special container near the scrub nurse.

9- Counting is mandatory once in all operation, but twice in:

a- All emergency operation

b- Super major operation.

c- When there is change in plan of operation.

d- More than one surgical team involved.

10 - The whole surgical team should be shared in counting packs.

11 - The act of counting should be recorded in the operative notes.

12 - Record the number of used packs in the operative notes.

13 - If there is discrepancy between supplied and counted number of packs:

a- Recheck the supplied packs by the whole team.

b- Recheck the abdominal cavity by dividing it into anatomical partitions.

c- If no pack is found, close the abdomen and record the event.

* The initial number of packs is 5 packs.

** Extra pack supply is 5 for each request.

***Radio-opaque packs may be used when intra-operative X ray facility is available and such packs can be manufactured locally and cover the need.

DISCUSSION

Although surgical care can prevent loss of life, it is also associated with a considerable risk of complications and death. Retained pack in abdominal cavity after operation, although rare, but it's one of a horrible complication in surgery [9, 10]. The incidence of retained pack after laparotomy has not been determined [7]; estimates suggest that such errors occur in 1 of every 1000 to 1500 intra-abdominal operations [7] (0.14%) in our study. The rate of retained pack is higher for operations involving an open cavity[8], abdominal cavity seems to be the most common site for such error, this may be attributed to the large cavity, multiple pouches and organs with long bowel coils the abdomen possess. Because such complication is calculated only on the basis of malpractice claims, they are most likely underestimated [10]. In the United States more than 1500 cases of a retained foreign body including pack, occur annually [8]. In our study, it's difficult to know the exact incidence of such complication because of inadequate medical and operative records, lack of post operative family doctor follow-up, absence of medical connecting information between hospitals, no use of incident reports and no Controlled Risk Insurance Company (CRICO) available in our society as well as our hospital not use the international classification of diseases, of any revision, which was used broadly to identify and record diseases and complication[9], on the other hand we are not sure that all cases were recorded .However, we know of no reason why they would differ in terms of the mechanism of causation or squeal.

In multivariate analysis, factors associated with a significantly increased risk of retention of a pack were emergency surgery and unplanned change in the operation [9, 10], it was reported that pack retained nine times as likely when an operation was performed on an emergency basis and four times as likely when an operation involved an unexpected change in procedure [10]. Each of these factors marks situations in which disorganization is increased so that it becomes more difficult to keep track of materials.

Our finding is that emergency operations were significantly more likely to involve multiple major procedures, especially in trauma and unprepared patients. Operation for trauma patients found to need more than one surgical team, had no preoperative plan, may showed excessive blood loss and subsequent transfusion, more exploration of the organs and unexpected finding is the rule. In our study 33 (62.2%) patients were operated as emergency, 14 (26.4%) due to external trauma to abdomen, mostly by high velocity bullet injury, which is indeed causes disastrous and multiple organ injury. Unexpected change in surgical procedure happen when there are anatomical abnormalities, obscuring of tissue planes by inflammation or malignancy, excessive bleeding, major technical organ trauma, unfortunate finding and major anesthetic complication, these events added more burdens on the surgical team, increase the operative time, and make them more stressfully busier by unpredictable and unpleasant condition. This was recorded in 28 (65%) of our patients.

Truly, it's difficult to estimate the actual effect of such changes as a risk factor for retained pack, but definitely, they disturb the surgical team and interrupt their concentration, making fault more common.

The age and sex of the patients play no rule as risk factors in our study and also in others [10], as packs has been left in various ages and in both sex without

significant differences from the control, while increase body mass index above normal is a significant factor, as in others [9], probably it reflects the amount of room there is in the patient's abdomen in which to lose a pack, in our study 21(39.6%) patients were regarded to be overweight.

In our study 47 (88.6%) patients needed re-exploration to retrieve the pack and or control its complications, which was in form of intestinal obstruction, prolonged wound infection, small-bowel fistulae, visceral perforation and abscess formation with one (1.8%) death. Others showed that 69% of their patients required reoperation for removal of foreign body and management of complication, where intestinal operation was the commonest presentation with 2% mortality rate-10-. Ultra-sound and radiography were done in 40 and 35 patients respectively, but they gave no accurate diagnoses, they only suggested the presence of foreign object, apart from the complication created by the retained pack.

Many methods where used globally to prevent such errors like: Only sponges detectable on radiography is to be used, packs should be counted once at the start and twice at the conclusion of all surgical procedures, writing the number of packs used on the operative board[11]. However, in the majority of cases, packs go undetected despite these procedures-5-. Previous descriptive studies have been unable to establish the human and systems related factors involved [12]. We could not reach a fixed information about the counting of packs in our studied patients neither in the control group, because of absence of such information in the operative notes, although other studies showed that, among the instances in which counts were performed, the count was reported as correct for 88 percent of patients with retained objects and 92 percent of controls; the difference between groups was not significant-10-,even so, the observation that the failure to perform these counts was not a significant risk factor according to multivariate analyses, it does not imply that such counts are not important especially in patient with high risk group [9].

The current use of intra-operative radiographic screening varies widely. A few institutions obtain radiographs in every patient whom undergoes an open cavity operation [13]. Most use radiography only in those with account that is recorded as incorrect; others imply that routine intra-operative radiographic screening in selected, high- risk categories of operations could prove to be a useful measures for detecting foreign bodies that have been inadvertently left behind[10] , some appear to have no policy regarding radiography at all[13].

On the basis of previous estimates that such incidents occur in 1 in 1500 operations involving an open abdomen, it's estimated that 300 radiographs would be needed to detect 1 retained pack. There is no such policy in our hospital daily work, and packs detectable by radiograph not routinely used, and if so, it's only to be of help if a left behind pack is to be diagnosed.

Analysis of checklist

Pack supply at the beginning of all laparotomies as well as for subsequent request should be slandered, this well eliminate fault in counting, or remembering the number of packs used and supplied. On the other hand, only the first surgeon should order for extra pack supply, this will prevent adding un- needed packs or disturb the accounts later on. The first surgeon should be informed both by visual and auditory ways by the scrub nurse for all packs on the table at the start of operation, after each request and at the end of the procedure. No pack should be discarded (even if they are so dirty) till the end of operation, they should be collected in a special container near the scrub nurse.

Although nurse staff change were not recorded in any operative notes of our patients neither control group, we are sure that this has been happened and well be happen, other studies[10] showed that in 40 to 50% of operation, with messed object, there was a change in one or more of operator staff. So, if nurse staff is to be change, packs should be given hand by hand under the vision and permission of the first surgeon.

In case where packs are designed by a special factory, the size of packs are assume to be standard, but this is not the case when pack size is manually determined when a large role is to be cut by hand, which make discrepancy in size, and this may make small size pack more prone to be lost. On the other hand, there is what's called extra-pack, which is used mostly in obstetric theater. If such type of pack is to be used, this should also be recorded.

Suturing of a colored ribbon to pack is not a new method, some with radio-opaque character. If this to be use, it should be standard for all cases, in our hospital such packs are not always available, which makes the benefit of such packs limited.

Counting packs is not only mandatory, but it should be recorded and documented in the operative notes, in published case series, some incidents appear to result from a failure to adhere to this standard[12,14], such act well be of help for legal and medical point of view.

Lastly, blaming the surgeon is not far from truth, (surgeon was blamed in 33.3% in our study), surgeon is the leader of the operative team and the most responsible person for the patient's health logically, ethically, legally and scientifically.

Conclusion

Surgical complications are a considerable cause of death and disability around the world. They are devastating to patients, costly to health care systems, depressing to the surgeon and often preventable; their prevention requires a change in systems and individual behavior. Retained pack is a rare but a serious event; it's more common in emergency operation especially those with trauma and when there is more than one major procedure included, or when the plan of operation fails to control the operative surprise. In this study we perform a safety checklist program (after through study of the condition regarding its risk factors presentation and complication) to prevent or decrease as much as possible the incidence and complications of retained pack at abdominal surgery. A concern of how feasible the checklist intervention might be for the hospitals is existing, but, we think that it is neither costly nor lengthy and it is practicable. Although further study is needed to determine the precise mechanism and durability of such checklist.

REFERRENCES

1- Weiser TG, Regenbogen SE, Thompson KD, et al. An estimation of the global volume of surgery: a modeling strategy based on available data. Lancet 2008; 372: 139-44

2- Kohn LT, Corrigan JM, Donaldson MS, eds. To err is human: building a safer health system. Washington, D.C.: National Academy Press, 1999

3- Ronsmans C, Graham WJ. Maternal mortality: who, when, where, and why Lancet 2006; 368:1189-200

4. Gawande AA, Thomas EJ, Zinner MJ, Brennan TA. The incidence and nature of surgical adverse events in Colorado and Utah in 1992. Surgery 1999; 126:66-75

5. Kable AK, Gibberd RW, Spigelman AD. Adverse events in surgical patients in Australia. Int J Qual Health Care 2002; 14: 269-76.

6- World Alliance for Patient Safety. 15. WHO guidelines for safe surgery. Geneva: World Health Organization, 2008.

7- Hyslop JW, Maull KI. Natural history of the retained surgical sponge. South Med J 1982; 75:657-60.

8- Popovic JR, Hall MJ. 1999 National Hospital Discharge Survey. Advance data from vital and health statistics. No. 319. Hyattsville Md.: National Center for Health Statistics 2001. (DHHS publication no. (PHS) 2001-1250 1-0287

9- Department of Health and Human Services. The international classification of diseases, 9th rev, clinical modification: ICD-9 CM. Washington, D.C.: Government Print ing Office, 1980. (DHHS publication no (PHS) 80-1260.).

10- Atul A, Gawande, David M. Studdert, LL.B, John O, Troyen A, Michael J. Risk factors for retained Instruments and sponges after surgery. N Engl J Med 2003; 348:229-35.

11- Pierson MA. Patient and environmental safety. In: Meeker M, Rothrock J, eds. Alexander's care of the patient in surgery. 10th ed. St. Louis: Mosby–Year Book, 1995:19-34.

12- Kaiser CW, Frideman S, Spurling KP Slowick T, Kaiser HA. The retained surgical sponge. Ann Surg 1996; 224:79-84

13- Gibbs VC, Auerbach AD. The retained surgical sponge. In: Shojania KG, Duncan BW, McDonald KM, Wachter RM, eds. Making health care safer: a critical analysis of patient safety practices. Evidence report/ technology assessment. No. 43. Rockville, Md.: Agency for Healthcare Research and Quality, 2001:255-7. (AHRQ publication no. 01-E058.)

14- Rappaport W, Haynes K. The retained surgical sponge following intra-abdominal surgery: a continuing problem. Arch Surg 1990; 125:405-7.

The New Iraqi Journal of Medicine

Original Article

Pediatrics

The burden of acute poisoning among children in north east Jordan

***Nidal Younis** **

Abstract

Background and Objective: Childhood poisoning is an important health problem which is usually accidental and is responsible for serious morbidity with mortality all over the world.
To determine the different agents involved in acute poisoning in children, to assess the clinical spectrum and outcome of poisoning in the Northeastern region of Jordan.
Patient and method*:* Retrospective chart review study carried out at Prince Hashem military hospital. All admitted cases of acute poisoning during 2010 were collected and analyzed. The spectrum of causative agents was compared with the previous studies in Jordan and other parts of the world.
Results: Poisoning among children during the study period accounted for 3.4% (102 out of 2986 admissions). Children less than 6 years accounted for 91% of all the poisoning admissions. Kerosene was the most common ingested agent (41%). Male patients 60 (59%), female patients 42 (41%) with male: female ratio 1.4:1. Antihistamines were the most common drug ingested followed by analgesics. Most poisonings were accidental (97.1%) and occurred at home. There was no mortality and all children were discharged home in good condition.
Conclusions: Lack of education, inappropriate supervision and improper dispensing are significant contributory factors to the burden of acute poisoning in pediatric age groups.

The N Iraqi J Med, December 2011; 7(3):46-50

Keywords: *Accidental, children, Jordan, poisoning*

INTRODUCTION

Acute Poisoning in children is still a universal major public health problem and a frequent cause of admission in pediatric and pediatric ICU departments, and in many cases it is preventable.[1,2] It accounts for 1% of hospital admissions annually and most prevalent between 1-5 years old.(3) Boys are more commonly involved in accidental poisoning while suicidal attempts are seen more frequently in adolescent females.[4-6]

Globally, the pattern and incidence of childhood poisoning is changing rapidly; After 1972, the incidence of accidental poisoning and mortality from drug poisoning has fallen dramatically among children less than five years of age due to the use of child resistant containers and changes in prescribing habits.[7] Risk factors to childhood poisoning include various social and demographic factors like family size, socioeconomic condition, recent change in residence, stress in the family as well as improper storage place of poison, which significantly influence the acute household poisoning cases in children.[8,9]

There is a lot of data and research about accidental childhood household poisoning from developed countries. Although acute poisoning is not infrequently seen in our daily practice in Jordan, accurate data is still lacking due to the fact that acute poisoning in many places is underestimated and most of times unreported since there is no centralized data collection. All information available is from few individual studies. [10-13]

Since the recognition of epidemiology of poisoning is important for treatment plans and proper prevention programs, the objective of this study was to determine the different agents involved, and to assess the clinical spectrum and outcome of

* *Senior Pediatric Specialist*
Prince Hashem Military Hospital
Royal Medical Services
Email: nidalyounis@yahoo.com

poisoning and intoxication in the Northeastern region of Jordan.

PATIENTS AND METHODS

This is a retrospective study carried out at Prince Hashem military hospital located in Zarqa city, which provide services to people in the Eastern and Northeastern parts of Jordan with a population of almost 1.3 million, for the period from January, 2010 to January, 2011. Children aged from birth to 14 years, who were admitted to the pediatric and pediatric ICU words with diagnosis of poisoning were identified and included in the study. Cases of food poisoning were excluded. The data collected include: age, sex, material ingested, symptoms on admission, and the outcome regarding mortality and morbidity. The spectrum of causative agents was compared with the previous studies in Jordan and other parts of the world. The statistical Package for Social Science version 10.0 for windows was used for analysis.

RESULTS

There were 102 admissions with history of poisoning, which accounts for 3.4% of the total 2986 admissions to pediatric and pediatric ICU words.

Most cases (97.1%) were accidental ingestion; whereas 3 cases (2.9%) were intentional. Mean age was 4.84 years, with age range from birth to 14 years. The majority of children (91%) were less than six years old. Male patients 60 (59%), female patients 42 (41%) with male: female ratio 1.4:1. The age and sex distribution is shown in Table 1. Kerosene was the most commonly ingested material; it was seen in 41% of cases. Accidental drug ingestion was seen in 31% and non accidental in 3%, while household corrosive agents were seen in 25% (Table2). In 2 cases (1.96%) actual chemical ingredient involved in intoxication could not be identified. The antihistamines were the most common medicinal agent ingested (8.8%), followed by analgesics (Table3). Vomiting was the most common clinical feature (Table 4). The prognosis in all cases was good; there were no deaths or any permanent sequel.

Age group	Number (%)	Male	Female	Male: female
< 1 year	6 (5.9%)	3	3	1:1
1-3 years	65 (63.7%)	40	25	1.6:1
3-6 years	22 (19.2%)	13	9	1.4:1
6-14 years	9 (8.8%)	4	5	0.8:1
Total	102 (100%)	60	42	1.4:1

Table 1: Age and sex distribution of the study population

Household Product	No. of Cases (%)
Kerosene	42 (41.2%)
Detergents	13 (12.7%)
Corrosive/chemical	5 (4.9%)
Antiseptics	3 (2.9%)
Petrol/ diesel	2 (1.96%)
Unknown (Nail polish, henna stabilizer)	2 (1.96%)

Table2: Spectrum of various household products implicated in poisoning

Drug	No. of Cases (%)
Antihistaminics	9 (8.8%)
Analgesics (nonsteroidal)	6 (5.8 %)
Antibiotics	4 (3.9%)
Iron	3 (2.9%)
Bronchodilators	2 (1.96%)
Antipsychotic	2 (1.96%)
Tricyclic antidepressants	2 (1.96%)
Anticonvulsant	2 (1.96%)
Vitamins	2 (1.96%)
Hormones	1 (0.96%)
antihypertensive	1 (0.96%)
Hypoglycemic	1 (0.96%)

Table 3: Spectrum of various drug poisonings

Clinical feature	No. of Cases (%)
Vomiting	49 (48%)
Drowsiness	40 (39%)
Respiratory distress	38 (37%)
Salivation	23 (22.5%)
Seizure	13 (12.7%)
Miosis	9 (8.8%)
Coma	8 (7.8%)
Mydriasis	7 (6.8%)
diarrhea	7 (6.8%)

Table 4: clinical features of poisoning in children

Discussion

Accidental poisoning remains an important health issue in children globally. [6] Although deaths among children with poisoning have declined dramatically over the last 40 years, there is little evidence that shows a similar decline in emergency department presentations and hospitalizations despite the prevention strategies implemented over that period. [14] The incidence of poisoning among total admissions to pediatric ward and PICU in this study was 3.4%. In reviewed similar reports from Jordan, the incidence of poisoning was never mentioned. [10-13] Reports from other countries shows a variable incidence; In Kuwait it was 1.5%, [15] in Nepal 4.3%, [16] and in India it was less than 1% of all pediatric admissions below 12 years of age. [17] All cases below 5 years of age found to be accidental and only 3 cases of

the total number (2.96%) were intentional and were seen among adolescent females. Similar results were observed in many reports from deferent countries. [14, 18, 19] This higher percentage of accidental poisoning might be due to exploratory behaviors of the young children.

This study shows a wide spectrum of agents, commonly ingested by the inappropriately supervised children. The nature of the causative agents implicated in poisoning varies with local beliefs, customs and current availability. Kerosene was found to be the most common agent involved in childhood poisoning in this study. Reports from deferent developing countries show similar results. [15,20-22] Since kerosene remains a multipurpose household product commonly available and widely used in Jordan as well as in many other developing countries, in addition to its colorless nature resembling water, and improper storage which might explain the high frequency of poisoning due to this petroleum product.

The clinical manifestation and the prognosis of poisoning are largely depending on the material ingested. In this study vomiting was the most common and was seen in 48% of the patients, followed by drowsiness and respiratory distress. Although five patients had a prolonged period of hospitalization, fortunately no deaths occurred in this study. All patients discharged home in good general condition and no long-term morbidity.

This study holds important implications for public health, and highlights the high prevalence of accidental household poisoning among the Northeastern population of Jordan. However there remain certain limitations due to the retrospective nature of the study, the small sample size and the fact that Prince Hashem hospital serve patients from other cities and rural areas, mainly of low income group. This study might not represent the true statistics as well as cannot be generalized for the whole population of Jordan. A large scale prospective multi-center study is recommended for further evaluating the incidence, geographic differences and other risk factors.

Conclusion

Kerosene is the most common source of poisoning in Northeastern Jordan. Children less than 6 years are most commonly involved. Lack of education, inappropriate supervision and improper dispensing are significant contributory factors. A poisoning national registry and 24 hour poisoning center is highly recommended to further plan prevention, first aid and health education.

Acknowledgements

Special thanks to my dear wife Dina Al-Kayed, MSc. Ph, who provide assistance in understanding the component and nature of many toxic substances and drugs, in addition to her help in writing this manuscript.

REFERRENCES

1. Litoviz TL, Baily KM, Schmitz BF, et al. Annual Report of the American Association of Poison Control Centers' Data Collection System. Am J Emerg Med 1991; 9: 461-509.
2. Wilkerson R, Northington LD, Fisher W. Ingestion of toxic substances by infants and children. What we don't know can hurt. Crit Care Nurse 2005; 25: 35–44 .
3. Lamireau T, Lianas B, Kennedy A, Fayon M, Penouil F, Demarquez JL. Epidemiology of poisoning in children, a 7-year Survey in a pediatric emergency care unit. Eur J Emerg Med 2002; 9(1): 9-14.
4. France G, Benoit LB. Hospitalizations for Pediatrics Intoxication in Washington State. Arch Pediatric Adolesc Med 2001; 155(10): 1105-10.
5. Hoffman RJ, Osterhoudt KC. Evaluation and Management of Pediatric Poisoning. Pediatrics 2002; 51-63.
6. Rodgers G, Condurache T, Reed M, Bestic M, Gal P. Poisonings. In: Behrman RE, Kleigman RM, Jenson HB. Nelson text book of paediatrics 18th edition. Philadelphia, W B Saunders; 2007: 339-357.
7. Campbell D, Oates RK. Childhood poisoning; a changing profile with scope for prevention. Med J Aust 1992; 156: 238-40.
8. Mahdi AH, Taha SA, Al Rifai MR. Epidemiology of accidental home poisoning in Riyadh (Saudi Arabia). J Epidemiol Community Health 1983; 37: 291-295.
9. Sibert R. Stress in family of children who have ingested poisons. Br Med J 1975; 3: 87-89 .
10. Abuekteish F, Daoud A, Al-Sheyyab M, Rawabdeh N, Nou'man M. Acute poisoning of children in Northern Jordan. Saud Med J 1998; 19: 447-450.
11. Bataineh H, Bataineh A. Childhood Accidental Poisoning in Tafila. Iran J Pediatr 2007; Vol 17(1): 23-26.
12. Massadeh M. The pattern of accidental drug poisoning in children. Middle East Journal of Family Medicine 2007; 5(4): 15-16.
13. Obeidat N, Abutayeh R, Hadidi K. Poisoning in Jordan: analysis of three years data from Jordan National drug and poison information center. J Med J 2010; Vol. 44 (3):298- 304.
14. Rajka T, Heyerdahl F, Hovda KE, Stiksrud B, Jacobsen D. Acute child poisonings in Oslo: a 2-year prospective study. Acta Pediatr 2007; 96: 1355-9.
15. Akhtar S, Gulati RR, Al-Anezi F. Risk Factors in Acute Poisoning in Children – A Retrospective Study. Kuwait Medical Journal 2006; 38(1): 33-36.
16. Budhathoki S, Poudel P, Shah D, et al. Clinical profile and outcome of children presenting with poisoning or intoxication: a hospital based study. Nepal Med Coll J 2009; 11(3): 170-175.
17. Singh S, Singhi S, Sood NK, Kumar L, Walia BNS. Changing pattern of childhood poisoning (1970-1989): experience of a large north Indian hospital. Indian Pediatr 1995; 32: 331-6.
18. Rifdah EI. Childhood poisoning in Dublin. Irish Med J1991; 84: 87-89.
19. Yates Kim M. Accidental poisoning in New Zealand. Emergency Medicine 2003; 15(3): 244-249.
20. Assar S, Hatami S, Lak E, Pipelzadeh M, Joorabian M. Acute poisoning in children. Pak J Med Sci 2009; 25(1): 51-54.
21. Luca G. Kerosene oil poisoning in children: A hospital based prospective study in Srilanka. Indian J Pediatr. 1994; 61: 683-687 .
22. Nagi NA, Abdullah ZA. Kerosene poisoning in children in Iraq. Postgrad Med J 1995; 71: 419-422 .

The New Iraqi Journal of Medicine

Original Article

Infectious disorders

Early detection of bacterial sepsis in newborns

Khaled Amro *, Jürgen Dinger **

Abstract

Objective : Neonatal infections are by far the most common cause of morbidity and mortality in infancy.
The aim of our study to determine the usefulness interleukin-6 level and positivity of blood culture in neonatal intensive care unit with suspicion of bacterial infection.

Methods: This retrospective study conducted over a period of two years 2009-2010 Data collected using patient's file at pediatric and neonatal care unit of "Carl Gustav Carus" Technical University Hospital, Dresden-Germany. Where we review 778 file of different age group of newborns from 28 to 42 week gestational age. We compared the positive bacterial blood culture result with inflammatory markers, i.e. interleukin-6 (IL-6) and C-reactive protein (CRP). Blood samples were collected at the time of admission and before the first antibiotic dose for complete blood count, blood culture, and interleukin-6 (IL-6), C-reactive protein (CRP) estimated were done.

Results: Of the 73 blood samples clinically having suspension of sepsis, there were twenty two samples revealed positive blood cultures for bacteria. The level of interleukin in first hour was extremely high and normal or minimal elevation in C- reactive protein. The whole group median IL-6 was 100 pg/ml. High level groups (IL-6 > 1000 pg/ml) was formed by 17 Newborns, and low level group (IL-6 < 350 pg/ml) by 5 newborns. And CRP maximum level was 12 mg/l in eight patients.

Conclusions: We conclude that high IL-6 plasma level measurement might correlate with positive bacterial blood culture in neonatal sepsis.

The N Iraqi J Med, December 2011; 7(3):51-56

Keywords: *C-reactive Protein; Interleukin-6 ; Sepsis*

INTRODUCTION

Neonatal sepsis refers to a systemic infection with positive blood or other central culture. Sepsis occurs when bacteria infect the bloodstream of the "immunologically compromised" newborn host. Clinical diagnosis of sepsis in newborn infants is not easy because symptoms and signs are non-specific. There is no laboratory test with 100% specificity and sensitivity, to detect bacteraemia in neonate but search has continued for a reliable test. The neonates with "risk factors" for neonatal sepsis are thus treated with broad spectrum antibiotics and require prolonged hospitalization [1]. Mortality has decreased in recent years for term, low-birth weight, and very-low-birth weight infants, possibly due to the shift in predominant organisms from gram-negative to gram-positive [2]. Blood cultures are the gold standard for diagnosis of sepsis; however, the results of the test are available only after 48-72 hours. The positivity rates vary widely, ranging from 30 to 87%. [3]. Interleukin-6 is a rapid-response inflammatory protein with a short plasma half-life. [4]. The proinflammatory cytokine interleukin-6 consist of a series of phosphoglycoproteins with a molecular weight ranging from 21 to 45 kDa and the serum reference limit of IL-6 is less than 10 pg/ml in healthy individuals [5-6]. In response to inflammatory tissue injury, IL-6 is a mediator of the acute phase response. Previous clinical studies demonstrated consistently

* *Pediatric Intensivist from Royal Medical Services Amman- Jordan. Queen Rania Al Abdullah Hospital for Children*
E mail: drkhaledam64@yahoo.com
***Pediatric Intensivist and Neonatologist from Department of Pediatrics, Medical Faculty, "Carl Gustav Carus" Technical University, Dresden-Germany*

elevated IL-6 level in patients with sepsis, and that IL-6 levels above 1000 pg/ml are generally associated with an increased mortality rate in critically ill patients [7-9]. Undetectable concentrations may be measured in septic neonates at the time of suspected infection onset because the interleukin-6 concentration has already returned to baseline. By contrast, C-reactive protein, an acute phase protein stimulated by interleukin-6 rises to abnormal concentrations in neonates 24–48 h after the onset of Infection-time when interleukin-6 concentrations may have already fallen to within the normal range. Levels of C-reactive protein (CRP), an acute phase protein associated with tissue injury, are elevated at some point in 50-90% of infants with systemic bacterial infections [10]. Moreover, CRP is also reported to elevate in non-infectious conditions like meconium aspiration, birth asphyxia and tissue injury [11-13]. The positive predictive value of CRP for neonatal septicemia is reported to be <50% [14]. So the value of CRP in sepsis workup is questionable. Therefore, the combination of interleukin-6 an early marker of infection, with C-reactive protein (CRP), a later sepsis marker, may allow the clinician to monitor the evolution of neonatal infection and detect more accurately infection among neonates. An early detection of infections among neonates will allow better planning for medical treatment and preventing further physiological damage due to infection. This study intends to measure both markers although interleukin is more accurate in early diagnosis bacterial sepsis in neonatal critical care unites. Studies that have measured interleukin-6 and CRP together show that the combination is more sensitive than either marker alone, with little change in the specificity, and hence few false-positive results. [15-16]. Therefore, the purpose of this study was to evaluate the high level of IL-6 in early detection of positive bacterial blood culture in first hour of newborn admission with clinical sepsis to intensive care unit.

Methods

Design

This study used the retrospective approach to review medical records for newborns who were admitted to intensive care unit of Carl Gustav Carus university hospital in Dresden- Germany, between January 2009 and December 2010.

Sample and setting

A total of 778 newborn represented the total number of newborns in the PICU over the two years period. Data collected in regards to documentation of blood culture results and interleukin-6 and C-reactive protein tests. Among these there were 73 newborns suspected for septicaemia, and 22 had positive blood culture for bacteria. For the purpose of the study, all newborns presented with positive signs and symptoms of septicemia with/without pneumonia and/or meningitis had been investigated retrospectively. Neonates were excluded from our study if they had: a) major congenital anomaly; b) inborn errors of metabolism, c) hemolytic jaundice or respiratory distress syndrome (due to surfactant deficiency.). Informed consent was obtained from the parents of each newborn in the file of each newborn at time of admission.

Data collection

Medical records reviewed maturity, age at onset, sex, birth weight, symptoms and signs along with the maternal risk factors. The cases with suspect sepsis were screened for interleukin-6, C- reactive protein, and blood culture. Other investigations were done previously as required. Some of these neonates were asymptomatic but were evaluated for sepsis because of maternal intrapartum sepsis risk factors like prolonged rupture of membranes, maternal urinary tract infection, maternal intrapartum fever >38°C, chorioamnionitis, and excessive vaginal discharge.The criterion standard for diagnosing sepsis is the positive organism-specific blood culture, at least in the absence of maternal intrapartum antibiotic prophylaxis. Laboratory test for blood culture, Interleukin-6 and C-reactive protein were obtained from peripheral or umbilical vein for every newborn admitted in critical care unite for routine culture of aerobic and anaerobic bacteria. Cultures of cerebrospinal fluid and urine were performed when appropriate. In addition, tracheal samples from intubated patients were cultured for bacteriology and screening for IgM antibodies to Toxoplasma, rubella virus, cytomegalovirus, herpes simplex virus, and Treponema pallidum was done in the first few postnatal days if congenital infection seemed likely. Our evaluated demographic characters, blood culture results and IL-6 with CRP levels of patients, and then we compared result of interleukin-6 and C-reactive protein with positive blood culture for bacteria. Our defined clinical sepsis according to the presence of the following parameters on clinical, laboratory or cultural screen [16-17]: Clinical signs consistent with infection (at least two from the following categories): Table (1).

	Clinical signs	Data
Respiratory	Ta Tachypnea (respiratory rate >60 bpm, in full term newborn and >70 bpm in preterm baby). Subcostal and/or intercostals retractions, grunting, apnea >20seconds.	
Cardiovascular	Po Poor perfusion, capillary refill >3 s, metabolic acidosis with pH <7.25, tachycardia >170 bpm, Br bradycardia <90 bpm, hypotension with B blood pressure < 2 SD of the mean for age and weight	
Neurologic	H Hypotonic, lethargy, convulsions.	
Gastrointestinal	V Vomiting, rejection of food, abdominal distention, H hepatomegaly, poor peripheral perfusion.	
Temperature	H Hypothermia <36 °C, hyperthermia >37.9 °C);	

Table: 1 Clinical signs of neonatal sepsis

RESULTS

A total of 778 newborns that were screened retrospectively represent all hospitalized neonates in critical care. Of these was 254 (32.6%) full term (>37 gestational age) and 524 (67.4%) preterm (>28week gestational age). Among the total number of newborns, 73 (9.4%) newborn met inclusion criteria. Twenty two (30%) newborn had positive and 51(70%) negative blood culture.

Of newborns suspected of neonatal sepsis with negative blood culture and negative CRP, three had slightly elevation level of IL-6. More over, the statistical analysis showed no significant difference in regards to gender and gestational age of both groups (p >.05). in addition, for those 22 newborns diagnosed with sepsis, the mean IL-6 was 100 pg/ml. High level groups (IL-6 > 1000 pg/ml) was formed by 17 newborns, and low level group (IL-6 < 350 pg/ml) by 5 newborns. And CRP maximum level was 12 mg/l in eight newborns.

As shown in table 2, the analysis showed that the most common isolate microorganism from blood culture was *E.coli* (n = 7, 9.5%) patients, and the least common was *Klebsiella* spp., with two (2.7%) patients in all the newborn with bacterial sepsis. IL-6 plasma levels were

microorganism	frequency	%
No microorganism	51	70%
E.coli	7	9.5%
Coagulase Neg. Staph	5	6.8%
Streptococcus pneumonia	4	5.5%
Pseudomonas aeruginosa	4	5.5%
Klebsiella spp.	2	2.7%
Total	73	100%

Table: (2): Most common isolate microorganism from blood culture in 73 infants with clinical suspected sepsis.

significantly elevated at the time of first blood sample which was more than 30000pg/ml and consist with positive bacterial sepsis mainly gram negative bacteria. Moreover, the analysis showed that

there was no significant correlation between gestational age (r = 0.24; *P* >0.05) and gender (r = 0.27; p >0 .05) and the IL-6 plasma level among newborns with positive blood culture.

Variable	IL-6 (pg/ml) <50pg/ml	CRP (mg/l) <5mg/l
Blood culture positive (E.coli., Streptococcus pneumonia,	1,200-50,000	5-22
Pseudomonas aeruginosa, Klebsiella.)	200-1000	1-5
Coagulase Neg. Staph.		
Blood culture negative	10-100	negative<1

Table (3): Levels of interleukin-6 (IL-6) and C-reactive protein (CRP) in 73 infants with clinical suspected sepsis.

In addition, Serum IL-6 levels were higher in neonates with positive blood culture especially in gram negative bacteria compared to coagulase negative staphylococcus than in the non-infected neonates and those with negative blood culture ($p < 0.001$ and $p < 0.01$, respectively). And the level of CRP in first hour of admission was not significantly elevated. As in (table 3) the level of IL-6 was 20000 and 45000pg/mlin gram negative bacteria especially E.Coli and Pseudomonas also it was seen in Strep. Pneumonia but in staphylococcus the level of interleukin-6 was not significantly elevated it reach maximum 1000pg/ml, and when the level of IL-6 less than 50pg/ml the culture is negative in all.

DISCUSSION

This retrospective clinical study was undertaken to identify a serum biomarker panel to diagnose bacterial sepsis in newborn admitted to neonatal critical care unit. It has been found that IL-6 was reacting with maximum plasma concentrations at the time when the infants were suspected of having sepsis. CRP were late reacting with maximum concentrations at 24 hour, especially we noted that when the cytokine values were decreasing, CRP had just started to increase**.** Early recognition of neonatal sepsis and prompt initiation of appropriate antibiotic therapy is essential for the successful treatment of bacterial infections in the neonatal period. Clinical symptoms and signs of neonatal sepsis can be very non-specific and, therefore, easily misleading. The major problem in neonatal infections is the identification of the infected infant and the equally important task of identifying the non-infected infant [17]. The incidence of sepsis in neonatal intensive care units (NICU) is high due to immature management of patients needs, and consequently, another confounding factor is the potential transplacental transfer of antibiotics administered to mothers during the pre- and intrapartum period which might increase the likelihood of culture-negative sepsis [18-19]. It is in this group of patients that the availability of a test that rapidly and reliably identified the presence of sepsis would be immensely valuable. Such a test would radically alter neonatal prescribing practices and limit the unnecessary administration of antibiotics to uninfected infants. That's the reason our study excluded all newborns who's mother received antibiotic before delivery.

Many newborn are treated with several days of antibiotics because of possible infection while waiting for negative bacteriologic cultures. In our retrospective chart reviews found that IL6 is an important cytokine of the early host response to infection. Its concentration increases sharply after exposure to bacterial products and precedes the increase in CRP. Many studies have tried to find reliable early reacting cytokines for detection of bacterial sepsis in neonatal period [20]. Evaluation of possible infection is sometimes extremely difficult in the neonatal bacterial sepsis. Therefore antibiotics may be used more often than necessary in the NICU, which increases the risk of antibiotic resistance [21]. The aim of retrospective study was to analyse the dynamics markers during the time of admission after the suspicion of sepsis, and on the basis of the results to test how well a combination of an early high level of interleukin-6 correlated with positive culture for bacteria mainly gram negative The inflammatory process in sepsis is biochemically very complex. From laboratory and clinical studies it is known that some proinflammatory cytokines peak very fast within one to four hours after a sepsis stimulus [20-21].

C-reactive protein (CRP) rises to a maximum 24 hours after the septic stimulus [22]. CRP is induced by proinflammatory cytokines [23]. In our retrospective chart reviews we evaluate the level of C-reactive protein comparing with interleukin-6 in

detection of early bacterial infection in neonate, and it shown that IL-6 concentrations are significantly elevated in neonates with bacterial infections during the time of admission to NICU compared with those of septic neonates with negative blood culture. In other study maintained that umbilical cord blood IL6 has been consistently shown to be a sensitive marker for diagnosing neonatal infection within 72 hours of birth, the sensitivities and negative predictive values being 87–100% and 93–100 %. [24-35]. we hypothesize that IL-6 appears to be a highly sensitive marker of sepsis in the immediate postnatal period. This high sensitivity for early onset-sepsis is related to its rapid response time, which is much faster than that of CRP and thus should help to gain time for diagnosis of sepsis. Our studies demonstrate very high serum interleukin-6 levels in all neonates with proven or clinically diagnosed bacterial infection. Neonates with viral infection, bacterial colonization, or respiratory distress of numerous causes, including hypoxemia, had normal or only slightly increased serum interleukin-6 levels.

In summary, we have the conviction that measurement of interleukin-6 alone would be sufficiently sensitive to diagnose bacterial infection in neonatal critical care unit. Using sensitivity of interleukin-6 can give a guide to make a better decision to treat those with positive reports using antibiotics

Conclusion

This study provides evidence that IL-6 is a better diagnostic marker of neonatal sepsis at the time of admission to critical care unites with suspicion of sepsis. The study revealed that interleukin-6 measurements may be of value in the early diagnosis of neonatal bacterial infection. however, CRP measured at the time of admission did not discriminate neonate with culture-proven sepsis from uninfected neonates. Although Interleukin-6 alone is not sufficiently sensitive to make a diagnosis of neonatal infection; it can help to detect positive bacterial culture in septic neonatal admission.

Acknowledgments

We wish to thank Prof.Dr.med. M. Rüdiger, Head of the Department of Neonatology and Pediatic Intensive Care, and OA Dr. med. Sebastian Brenner Head of PICU & Tutor Medical Faculty, “Carl Gustav Carus” Technical University, Dresden-Germany
for there advice and encouragement.

REFERRENCES

1. Natália C, Carvalho, Rozilda L, de Souza, Felipe Dal-Pizzol1, Vanessa M,Andrade. Comet Assay in Neonatal Sepsis. Indian J Pediatr 2010; 77 (8): 875-877
2. Ronald Perkin M , James D. Swift , Dale A. Newton , Nick G. Anas Pediatric Hospital Medicine Textbook of Inpatient Management, 2nd Edition (2008) 116pp. 593-599.
3. Gerdes JS. Diagnosis and management of bacterial infections in the neonate. Pediatr Clin North Am 2004;51 pp.939-59.
4. Ng PC, Cheng SH and Chui KM et al. Diagnosis of late onset neonatal sepsis with cytokines,adhesion molecule, and C-reactive protein in preterm very low birth weight infants. Arch Dis Child 1997; 77. F221–F227.
5. Thomas L, Messinger M,Pathobiochemieund Labordiagnostikder Entzuendung. Lab. Med. 1993; 17: 179-193.
6. Volk H.D, Keyüer G, Burmester G.R., Zytokine und Zytokin-Rezeptoren, in: L. Thomas (Ed.), Labor und Diagnose: Indikation und Bewertung von Laborbefunden fuer die medizinische Diagnostik, TH-Books-Verl.-Ges., Frankfurt/Main 1998; 5: 782-191.
7. Casey LC, Bal RA, Bone RC, Plasma cytokine and endotoxin levels correlate with survival in patients with the sepsis syndrome, Ann. Intern. Med 1993; 119:771-778.
8. Martin C, Saux P, Mege JL, Perrin G, Papazian L, Gouin F, Prognosti values of serum cytokines in septic shock, Intensive Care Med 1994; 20: 272-277.

9. Presterl E, Lassnigg A, Mueller-Uri P, El-Menyawi I, Graninger W, Cytokines in sepsis due to Candida albicans and in bacterial sepsis. Eur. Cytokine Netw 1999; 10:423-430.
10. Hawk M. C-reactive protein in neonatal sepsis. Neonatal Netw 2008; 27 (2): 117-120.
11. Ainbender E, Cabatu EE, Guzman DM, Sweet AY. Serum C-reactive protein and problems of newborn infants. J Pediatric 1982;101:438-440.
12. Meeteran Schouten-Van, N.Y.N, Rietveld A,Moolenar AJ et al. Influence of perinatal conditions on C-reactive protein production. J Pediatrics 1992; 120:621-624.
13. Ito H, Kishikawa T, Yamakawa Y. Serum acute phase reactants in pediatric patients; especially in neonates. Jpn J Surg 1983; 13:506-511.
14. Benitz We, MY Han, A. Madan P. Ramachandra. Serial serum C-reactive protein levels in the diagnosis of neonatal infection. Pediatrics 1998; 102(4): E41.
15. Terregino CA, BL. Lopez DJ. Karras AJ. Killian, GK. Arnold. Endogenous mediators in emergency department patients with presumed sepsis: are level associated with progression to severe sepsis and death? Ann. Emerg. Med. 2000; 35:26-34.
16. Edgar JDM, DC Wilson and SA McMillan et al, Predictive value of soluble immunological mediators in neonatal infection. Clin Sci 87(1994), pp. 165–171.
17. Doellner H, KJ Arntzen and PE Haereid et al.interleukin-6 concentrations in neonates evaluated for sepsis. J Pediatr 132(1998); pp. 295–299.
18. Assumma M, F Signore L Pacifico, N Rossi, J F Osborn C Chiesa. Serum procalcitonin concentrations in term delivering mothers and their healthy offspring: a longitudinal study. Clin. Chem 2000; 46:1583–1587.
19. Chiesa C, G Pellegrini , A Panero et al. C-reactive protein, interleukin-6, and procalcitonin in the immediate postnatal period: influence of illness severity, risk status, antenatal and perinatal complications, and infection. Clin. Chem 2003;49:60–68
20. Mehr S, Doyle LW. Cytokines as markers of bacterial sepsis in newborn infants: a review. Pediatr Infect Dis J 2000; 19:879-87.
21. Balslev T, B. Kristensen, F. Ebbesen, H. Schumacher, B. Korsager. Gentamicin-resistant Enterobacteriaceae in a neonatal intensive care unit. Acta Paediatr 1993; 82:792-793.
22. Dandona P, D Nix, MF Wilson, A Aljada, J Love, M Assicot et al. Procalcitonin increase after endotoxin injection in normal subjects. J Clin Endocrinol Metab 1994; 79:1605-8.
23. Kuster HM, Weiss AE.Willeitner S. et al. Interleukin-1 receptor antagonist and interleukin-6 for early diagnosis of neonatal sepsis 2 days before clinical manifestation. Lancet 1998; 352:1271-7.
24. Tavares E, Maldonado R,Ojeda ML,Minano FJ. Circulating inflammatory mediators during start of fever in differential diagnosis of gram-negative and gram-positive infections in leukopenic rats. Clin Diagn Lab Immunol 2005; 12 :1085-93.
25. Berner R, Niemeyer CM, LeititisJU, et al. Plasma levels and gene expression of granulocyte colony-stimulating factor, tumor necrosis factor-alpha, interleukin (IL)-1-beta and soluble intercellular adhesion molecule-1 in neonatal early onset sepsis. Pediatr Res 1998; 44 :69–77.

The New Iraqi Journal of Medicine

Original Article

Health care services

The influence of patient expectations on perceived quality of health services

Veselin Dickov *, Boris Kuzman **

Abstract

Globalization of world markets faster and innovative technical and technological progress is almost completely changed the business environment. Today, each order service businesses and even health services must be locally and globally competitive, because survival in the market, because the competition knows no bounds. In the modern business environment, health care organizations regardless of ownership structure (private, government or public) are faced with changing demands of healthcare consumers - patients, innovative technologies, increasing pressure on costs and quality of health care services. Due to constant changes in the competitiveness of health care organizations must devote significant time and resources, both financial and human resources, and energy to their own success criteria and the quality of business in achieving the set strategic objectives. Healthcare organizations today want success in a turbulent and complex business environment is expected to acquire such a business policy that will create a health care institution capable of being able to ever doing three important things - to improve, to expand and innovate the quality of their health service orientation.

The N Iraqi J Med, December 2011; 7(3):57-67

Keywords: *The quality of health services, Patient choice, Private or government health institutions*

Health services are considered services performed in the primary, specialist services and hospital care in the Republic of Serbia, in accordance with the Law on Health Care to be implemented for the purposes of treatment, provided that these expenses paid from personal funds of citizens then the base, supplemental or additional health insurance[1].

**Assc.Prof. dr Veselin Faculty of International Management, European University Carigradska 32; 11 000 Belgrade Serbia e-mail: dickov@hotmail.com*

***Boris Kuzma INSTITUTE OF AGRICULTURAL ECONOMIC Volgina Street 15. 11060 Belgrade, Serbiae E-mail: kuzmanboris@yahoo.com*

Health services include in particular: medical examinations, diagnostic and laboratory tests, diagnostic and therapeutic procedures, including surgery and structural materials, hospital health care and medical rehabilitation, dental care and prosthetic replacements, drugs that are registered in the Republic of Serbia and prescribed prescription and

cannot be bought without prescriptions, paid co-payments and prescription drugs prescribed and purchased in the Republic of Serbia, who are not registered with us and cannot be bought without prescriptions, orthopedic supplies, eye and hearing aids, aids to enable high volume of speech, including and repair tools, spare parts and second, according to the Regulation on conditions and manner of exercising the right of orthopedic and other aids. [1].

Starting from the basic characteristics of the model for measuring the quality of the paper

presenting the results of a study conducted among users of health services and measuring the impact of their previous expectations in the perception of service quality using SERVQUAL weighted model based on the differences and relations between the perceived and expected quality [2]. The research topic is the measurement of perceived service private and social health institutions and compares the results to estimate the perceived quality of health services and the impact of expectations on the level of perceived quality. The results showed that the level of previous expectations of an exceptionally high level of importance for the perception of service quality. Subjects with low expectations and a modest experience in the treatment showed a low level of claims against health care institution in relation to demanding patients. This led to the positive difference between the perceived and expected quality of these customer relationships implying a higher perceived value as expected. In addition respondents who rated the services of state institutions have a lower level of expectations in terms of their capabilities and quality of services they can provide .The study confirmed that using the model of measuring the quality necessary to take account of previous expectations of respondents and their characteristics and requirements facing service providers.[3] [4] [5]

Defining research problems

Service quality is commonly studied in the field of literature management services. Efforts to understand and identify the quality of health services for years. It turned out that the long term the most important factor that affects the business performance of the quality of services offered by health institutions in relation to its competitive. As a result, the development of theory, problems of quality measurement and quality becomes more important place in the theory of service management. In doing so, the basic problems and disagreements among authors regarding the possibility that some models offer, and benchmarks to measure within the model [6]. When it comes to service quality, its definition and measurement, it is necessary to take into account the following:

a) When defining the quality of services there is general agreement among authors that the quality of service attitude or global evaluation of the superiority of the service. However there is no agreement on the exact nature of this paragraph. Some authors believe that the attitude of the service quality is formed by comparing the expectations and perceived performance (based on the theory disconfirmation) [7] [8] others are of opinion that this is the result of comparing performance with ideal standards [7], while there are views expressed and that attitudes about the quality of service only a result of the perception of performance quality [9]. These differences in the opinions of the author are clearly visible in the models. [10]

b) Defining the concept of service quality is very closely related to the definition and meaning of the concept of customer satisfaction. It is important to emphasize that it is not an identical, but the interrelated categories. The authors agree that the quality of services varies from customer satisfaction, stating:

That the quality of service attitude on service firms, while satisfaction relating to individual service encounters [11] [12] .According to this view the customer can be satisfied with the individual service encounter while his perception of the quality of the institutions observed negative. As a result, the buyer must not have any personal experience in the service encounter with a service company to form a view on the quality of its services (this is strongly reminiscent of the pre-formation of perceptions about the company based on the image, which delights the public, with potential and actual users and customers), but to the perceived level of dies / satisfaction of the buyer must "pass" through the utility meet and form a service experience.

It is a different category, although the quality of services does not constitute a generalized attitude, but also very specifically to a particular transaction. [13].

That the term "customer satisfaction" means a measure of cumulative, but that is [not the same quality of service, causing further confusion and misunderstanding;

Between these two concepts, there are many similarities, and that their observation and analysis in the future must be approached through the integrated study of the concept of "rating by consumers" [14]

That these two dimensions are the cause and effect relationship. What is not consent either of these factors prior to the following: quality of service satisfaction or satisfaction with service quality [15].

Finally, when it comes to measurement, there are two key elements in measuring the quality of health services: Identification of the patient's requirements and expectations of service quality. It is well known that customers evaluate the service they receive and their expectations are of critical importance in determining the level of satisfaction [16].

Perception of the patient. Perceived quality reflects the opinion of patients about the superiority or global service excellence [17]. In light of these factors was developed model for measuring quality - SERVQUAL scale which served as the basis for the development of a whole series of modified models and measurements [17].

On this basis it is possible to summarize the differences that appear in the attitudes of academics and research dealing with issues of quality health services, opportunities and models for measuring quality. It is the differences in conceptual terms, in terms of defining the categories of quality and satisfaction, but also models, time, size and method of measurement used by the authors:

Determining the purpose of designing the model and measuring the attitudes of patients (diagnosis or prediction)

Choice of models for measuring quality (SERVQUAL, SERVPERF ...).
The number of dimensions that are measured (or uniform number depending on the service environment) [18]

The measurement of expected and perceived or only perceived quality

Time measurement of expectations (before or after the service experience)

Using the scale formed on the basis of measuring the difference between perceived and expected service, or based on measurement of the ratio (quotient), or the use of semantic differential scales to measure the difference.

A. Model for measuring the quality of health services

It is possible to identify several models for measuring the quality of health services, as a result of theory and testing different models of sustainability. Basic features of the originating just behind the differences are listed. It is several different models derived from measurements and comparisons of perceptions and expectations, and the basic SERVQUAL model [17]. The main differences between the models derived stem from commitments to use the measured subjective expectation or ideal level of service.
According to this view the patient may be satisfied with the individual service encounter in a medical Institution while his perception of the quality of the institutions observed negative. As a result, the patient must not have any personal experience in the service encounter with a health organization to form its opinion on the quality of service (this is strongly reminiscent of the pre-formation of perceptions based on the image, which delights the public, with potential and current customers and patients), but that would be perceived a certain level does not - customer satisfaction has to "pass" through the service encounter and create a service experience [18]

1.1. The creators of SERVQUAL model advocates the view that the primary purpose of measuring service quality diagnosing the current situation and the level of quality and of higher perceived quality in relation to the expected measured through five basic dimensions of quality (tangibles, reliability, responsibility, security , empathy) [19].

SERVQUAL: Service quality = performance – expectation

Weighted SERVQUAL: service quality = importance of dimension x (performance - expectations) of performance

According to this model, the positive difference is a better service than expected and the quality of service that exceeds expectations, the perception of higher quality. On the other hand, a negative difference implies poor service and poor quality services. If the difference between perceived and expected quality of zero implies a satisfactory quality and meet patient expectations. [20].

1.2. Variant SERVQUAL based on the comparison of perceived quality with defined ideal quality as a common measure adopted was created as a result of the perceived conceptual and operational problems in defining the meaning of expectations, and possible ambiguities in the theoretical evaluation and interpretation of model based on measuring the gap [21] . These problems are due to intrinsic differences in the level of expectations among respondents, depending on their previous experience, knowledge, and even demands posed by the service providers - health professionals. However, today the world's efforts to offer individualized health service and adapt to specific requirements and patient and service users becomes very problematic definition of "universally accepted ideal category." This is exactly what makes the need for analysis of the impact on expectations and perceptions of the quality of activities requires the identification of certain groups of users by healthcare organizations

that will facilitate the creation of appropriate quality management strategy [22].

1.3. Based on the analysis and testing of the SERVQUAL model, its validity and justification, conceived the model of measuring quality of health services based on the measured performance dimension of service quality. Its authors Cronin and Taylor (1994) representing the view, based on tests conducted and research is the most reliable data on the quality of services given non ponderosa measuring and grading the perception of individual performance dimensions of quality [23]

SERVPERF: Service quality = performance Weighted SERVPERF: service quality = importance of dimension x performance

1.4. In addition to these models derived from the original SERVQUAL model uses a series of other models most notably Kano model Measurement model and the technical and functional quality [7] Is important to emphasize that the Kano model is based on the presumed expectations of health services on the basis of which the dimensions of service quality are assessed and grouped at the base, and differentiating variables that cause excitement. [8]. Just based on that service companies are able to differentiate their offer in comparison to its competitors and ensure customer loyalty. [9]

B. The role of expectations in the measurement of quality of health services

As can be seen from the previous exposure there is no agreement among authors about the justification of measuring the level of expectations in terms of quality of service, his objectification but no definition. Even the proponents of the theory of measuring service quality based on the theory disconfirmation define expectations in different ways: as wishes, demands that the service provider should have to meet, as normative expectations, ideal standards, what the buyers are hoping that will receive, as well as adequate service [17]. In doing so, distinguish between expectations that relate to the satisfaction and expectations that are related to the quality, but it has not been fully and appropriately incorporated in the model of measuring quality of health services, but is more a matter of definition and conceptualization of the term and category expectations . Thus, expectations regarding satisfaction of seeing the patient as a prediction of what will likely happen during a specific service encounter, whereas expectations for service quality, consider the patient's wishes or demands, or what would, in the opinion of respondents, service provider should offer. For example, a patient can say that the health worker will be cold and unfriendly during a specific service encounter (the expectations in terms of satisfaction), but he may want a doctor to be benevolent and friendly (in terms of expectations of service). Although disconfirmation also used as a basis for measuring the quality structure is completely different from those used for measuring the quality of health services [24]. Expectations of different dimensions than defining the challenges and problems, due to the fact that the model does not confirm –disconfirmation. implies that it is necessary that the level of perceived performance, or level of services provided must always exceed the expectations that patients perceived high quality. This situation is not appropriate to the classical conception of the ideal points of specific performance, which reflects the wishes of service users. According to this model which is not to be reflected in the decline of quality when the level of performance exceeds the ideal point. Apart from the problems and inconsistencies in the conceptual definition, the category of application expectations in models of measuring quality of service may occur the following problems: [25].

The tendency of the patient to overemphasize own expectations after the service experience; [26].

Distorted picture of improving performance in light of the concept of value and the price paid;

The influence of experience on service expectations (if measured expectations and perceptions performed simultaneously, or after the service encounter) [27].

Theoretical and practical solutions

The average patient in Serbia a year for treatment of health insurance for cash spend 377 euros or 107 euros more than the average resident of Serbia, through compulsory insurance, set aside for health! Out of seven million policyholders (half of them do not pay contributions for health care, which is 12.3 percent of income), health care, according to recent data, used during the year was 4.5 million

people. Each of them is the health care system, to review, by referral, the diagnostic procedure, or control, on average, "entered" 17 times! For a total of 78 million service for a year. These patients have been spent not only what they themselves opt for insurance, you pay a contribution, but also money that the insured regularly insurance and do not use

health care. These patients have spent not only what they themselves singled out for insurance if you pay contributions, but the money of persons who regularly paid insurance and does not use health care. From their pockets patients further, through participation, paid for treatment last year seven billion dinars. [1]. Three billion were provided through the participation of drugs and four to participate in the cost of insurance per year healthy. U cash being left around two billion euros. Hence funded salaries 104 000 employees in health care, work of health facilities, drugs, sickness, aids ... Every day in hospitals lies 23 000 patients. The average lay 11 days. That's nine million hospital days per year. Healthy only one patient, sometimes costing more than 1600 average annual insured aside for health. Health care is free only in the heads "of those who do not understand how to operate the health system, in practice, everything has a price. [1]. Paid by the insured through a contribution. Just as one pays, the two are treated, because the insurance money from the cash spent - in solidarity. "Health of citizens is not only the obligation and responsibility of health services, but the duty of every individual and society as a whole. Health policy must be directed toward significantly greater decentralization of the system and combining public and private practice, wherever possible, particularly in primary health care. Primary health care has in practice, not just on paper to become an "input screen, or entering the system. Primary health care should solve 85% of health needs, and that the secondary and tertiary levels reach only those who were really necessary. There are no effective or sustainable health systems without defining clear models and stable sources of funding. The first misconception that needs to be broken is that something for free. Each service is paid and has a price. False is every solidarity in which everyone involved. Disadvantaged citizens are considered to be insured, while the state is exempted from paying health insurance contributions of those citizens. The first step towards creating opportunities for involvement of private service providers in the system is through the personal physician of choice. Policyholders should be given the opportunity to the choice of personal physicians, where they live and work, have a choice among all physicians who do meet the requirements. Organization and establishment of efficient health care system must be accompanied by policies designed for human resources. The introduction of pluralism at the level of service providers and funding the foundation of the third essential characteristic of the reform and this is a free choice of doctors by the public. Under the conditions and pursuant to the Act on health care, private practice and carry out health workers to: medical doctors and dentists in private practice, pharmacists in private pharmacies, masters in medical biochemistry in private medical - biochemical laboratories, and nurses-medical technicians, senior dentists, dental technicians and physiotherapists. With the free choice of doctors in government or private sector and the insurance money that accompanies it, the citizen finally gets the opportunity to exercise their health rights. Non monopolizations basic principles of modern health care the patient is free to choose doctors "and" money follows the patient "not otherwise provided by law. Monopoly service provider in the state sector is stronger, contrary to the intentions and successful reforms in transition countries. Also, the law is based on a monopoly of the state compulsory health fund, although many post-communist countries spend a smaller share of gross domestic product for the health of Serbia and funded health care system from multiple public and private health insurance. The patient is still not able to freely choose a doctor in private or public sector, which is contrary to EU standards. This reduces productivity, efficiency and quality of health care but because given a strong incentive for corruption. From economics we know that legislation that protects monopolies generator system corruption. Unclear is the definition of "basic package of services" by government and health ministry have always entitled to change the scope and content so that a citizen can never know what he gets for his contribution to the mandatory health insurance. This is contrary to basic human rights under the contractual relationship between insured and insurance. As well as undermining economic sustainability system reduces the uncertainty and fiscal disciplines of citizens for carrying out the obligations of contribution for health insurance. But on these legal and economic paradoxes show that the proposed concept of insurance is far below the standards of modern health care system and to experiment with a purely propaganda purpose.

RESEARCH

In order to test the hypothesis that the level of previous expectations, which are significantly different for different segments of the patient, has a significant impact on the perception of service quality as a prerequisite for building satisfaction and loyalty, we conducted a survey among the population of Belgrade and Novi Sad. The aim was to measure the quality of health services that customers provide health organizations with predominantly or exclusively private property and called state, public health institutions, using weighted SERVQUAL model. Therefore, we decided to explore the level of expectations and perceptions of services that clients have when it comes to public and private health institutions without specifying any of them. Model selection is a consequence of the fact that previous studies the quality of health services and perceptions

of the quality conducted on several occasions in Serbia, in the form of various surveys, focus groups and discussions showed that there were significant differences in the expectations that patients have the potential when it comes to private and public institutions and the level of trust towards these two groups.

Thus, expectations regarding satisfaction of seeing patients as a prediction of what will likely happen during a specific service encounter, whereas expectations for service quality, consider the patient's wishes or demands, or what would, in the opinion of respondents, service provider should offer. In contrast to this model is applicable for so-called absolute. Vector of attributes for which it is desirable that the performance level is as high as possible. Apart from the fact that the Serb population has more confidence in the private sector, one of them and expect more in terms of level of service, professionalism and individualization of services. Accordingly, we wanted to test the hypothesis that the differences in the level of expectations that show patients have an impact on the level of perceived quality and satisfaction with services provided by the institution. To verify this hypothesis it was necessary to spend several discussions within the group formed, distribute, fill out, process and analyze data from the original questionnaire, and then discuss the findings, which were obtained from subjects [28].

MATERIALS AND METHODS

Methodology

The implementation of the research used the original questionnaire SERVQUAL model which contains 22 statements, since we appreciate that it is the same in its entirety to be eligible for the analysis of the different dimensions of service offerings. During the investigation, we formed four focus groups involving business people who may be treated in the private sector (group E8), postgraduate students who are customers of private (E11) and public health organizations (E10) and finally a group composed of patients who are beneficiaries of public health (E12). In the case of the last group did not exist some important guidelines and characteristics that were linked. Were selected randomly, and the main selection criterion was that they were to use health services public health. During the investigation, in accordance with the methodology of SERVQUAL model, each group is ongoing discussion about the peculiarities and characteristics of services received instructions on how to fill out a questionnaire, in part related to the assessment of certain dimensions and characteristics that must be characterized by "health care organization that provides emergency services».Also in this section were required to assess the relevance, importance of some of these dimensions, from their perspective, the perception of quality services. After that, the custom form, evaluated their own institution or organization in which the lenses longer than 6 months and with which they had made contact regarding the use of different types of services, which allowed them to gain a comprehensive picture of the characteristics and allow the perception of quality of different types of services. The study was conducted on respondents who live in Belgrade, which is likely to affect the results especially in terms of higher levels of expectation and critical attitude. On the other hand, if we take into account the fact that Belgrade is the center of economic and financial flows of Serbia, and that the purchasing power of the level of demand for most products and services right here at the highest level, it is logical to organize any research just in conditions where there is greatest competition among health care institutions in an effort to win patients [1].

Sample structure

41 The questionnaire was distributed to participants during the discussions conducted in focus groups. The first group consisted of respondents are business people, they are 8 (E8). 62.5% of them were male and 37.5% women, aged between 30 and 50 and all are employed in positions of director (general and executive). Postgraduate students MBA (E11 and later E10) were students of the Faculty of International Management, European University in Belgrade. All the participants before the study attended classes in the subject of management services. 54.54% and 60% were women, and all were aged between 25 and 30 years. 72.72% or 80% of them are working and studying as an external student. It defines their experience as users of health services. Finally a third group of subjects we have created in collaboration with one of the state health organizations (but not announced to the subjects). 12 "ordinary" users of medical services who agreed to participate and cooperate in the implementation of research. Two-thirds of them were men, a third woman, aged between 45 and 50 years and lived in the city, the employees, not owners of private businesses or activities so that they only used the services of the government sector.

Results

According to the methodology of weighted SERVQUAL model of the respondents are asked to identify the level of individual characteristics (dimensions in SERVQUAL) which should ensure a hypothetical "excellent" health care organization, and then to rate the importance of individual dimensions

of service from their own perspective. At this stage the respondents were asked the amount of 100 points divided into five service dimensions. In Tables 1 and 2 are presented the results obtained:

Service size	Standard deviation	Medium	Rang	Standard deviation	Medium	Rang
Tangibles	3.80	12.25	5	2.37	18.81	4
Reliability	7.78	31.00	1	1.87	22.36	1
Responsibility	4.18	23.00	2	2.89	20.27	2
Security	2.57	17.88	3	2.09	19.00	3
Empathy	4.31	15.88	4	2.26	18.63	5

Table 1. The mean value of the SERVQUAL dimensions E8 and E11 Focus Groups

	MBA students who evaluate the public health institution			Patients state institutions		
Service size	Standard deviation	Medium	Rang	Standard deviation	Medium	Rang
Tangibles	4.67	12.70	5	3.42	16.58	4
Reliability	4.23	28.10	1	4.35	26.42	2
Responsibility	5.00	24.50	2	2.31	22.67	3
Security	5.08	20.60	3	2.69	27.92	1
Empathy	5.34	14.10	4	3.38	16.42	5

Table 2. The mean value of the SERVQUAL dimensions E10 and E12 Focus Groups

SD	E	P	SQ (P-E)	R	W %	SQW	SQWR	SQ (P/E)	SQR	SQW	SQWR
Tangibles	6.00	5.88	-0.12	5	12.25	-0.07	5	0.98	1	0.65	4
Reliability	6.02	5.65	-0,37	3	31.00	-0.52	1	0.94	2	1.32	5
Respnsibility	5.91	5.56	-0.35	4	23.00	-0.36	4	0.94	2	0.98	1
Security	5.84	5.25	-0.59	2	17.88	-0.48	2	0.90	4	0.73	2
Empathy	5.78	5.15	-0.63	1	15.88	-0.45	3	0.89	5	0.64	3
	-0.41			-0.38			0.93			0.82	

Table 3. Business people dimension of the quality assessment of private health institutions (E 8)

From these results we can see that there are no significant differences in relative importance when it comes to the first three groups - business people and MBA students, especially when it comes to the three most important dimensions. According to the estimates of the three groups most important dimension of service reliability and immediately after her responsibility. In doing so, the major difference

between these two dimensions only records in a group of business people, the reliability of 31.00 and responsibilities 23.00, the other two groups the difference is much smaller 22:36, by 20:27, with

postgraduate students who were assessed and 28 private institutions, 10 to 24.50 in the same group that carried out the assessment of the state.

SD	E	P	SQ (P-E)	R	W %	SQW	SQWR	SQ (P/E)	SQR	SQW	SQWR
Tangibles	5.82	5.65	-0.17	5	12.70	-0.1	5	0.97	1	0.56	5
Reliability	6.02	5.38	-0.64	1	28.10	-0.82	1	0.89	4	1.13	1
Responsibility	5.75	5.38	-0.37	4	24.50	-0.41	3	0.94	2	1.04	2
Security	5.62	4.98	-0.64	1	20.60	-0.6	2	0.88	5	0.82	3
Empathy	5.76	5.24	-0.52	3	14.10	-0.33	4	0.91	3	0.58	4
	-0.47			-0.45			0.92			0.83	

Table 4. MBA students - the dimension of the quality assessment of private health facilities (E11)

SD	E	P	SQ (P-E)	R	W %	SQW	SQWR	SQ(P/E)	SQR	SQW	SQWR
Tangibles	5.40	4.52	-0.88	4	18.81	-0.75	4	0.83	4	0.71	4
Reliability	5.89	4.96	-0.93	3	22.36	-0.94	2	0.84	3	0.85	1
Responsibility	5.11	4.11	-1.00	2	20.27	-0.92	3	0.89	2	0.74	3
Security	5.33	4.23	-1.16	1	19.00	-1.00	1	0.79	5	0.68	5
Empathy	5.47	5.47	0.00	5	18.63	0.00	-	1	1	0.84	2
	-0.79			-0.72			0.85			0.76	

Table 5. MBA student assessment dimensions of the state, public health institutions (E10)

SD	E	P	SQ (P-E)	R	W %	SQW	SQWR	SQ(P/E)	SQR	SQW	SQWR
Tangibles	3.94	4.44	0.5	3	16.58	0.37	1	1.12	1	0.84	4
Reliability	4.16	4.18	0.02	5	26.42	0.15	4	1.00	5	1.20	1
Responsibility	3.75	4.06	0.31	2	22.67	0.32	3	1.08	3	1.11	2
Security	3.67	4.12	0.45	1	17.92	0.37	1	1.12	1	0.91	3
Empathy	3.83	3.88	0.05	3	16.42	0.04	5	1.01	4	0.75	5
	0.27			0.25			1.07			0.96	

Table 6. "Ordinary patients' ratings of dimensions of the state public health institutions (E12)

The only difference that appears in the ranking of service dimensions among the three groups related to the position of tangibility and empathy. These two dimensions are ranked according to significance in the fourth and fifth place in the group of E11, in the group E8 and E10 in the fifth and fourth respectively. In contrast we can see a significantly different order of importance of service dimensions observed in E12's. In this case the most important dimension of security, which implies the ability of employees to perform assigned tasks and to ensure customer confidence, then the reliability and accountability? The order of tangibility and empathy is the same as MBA students are assessed a private health institution.

The results show a negative gap servquala SQ (PE) SQW between perceived and expected service, the first three groups, as a result of the fact that services are provided, perceived by the patient's lower than expected, and different levels of perceived deviations from the expected quality of SQ (P / E), as a measure of patient satisfaction with quality of service compared to the expected. In fact the biggest difference can be observed when evaluating the differences between perceived and expected quality of state institutions, as measured by the MBA students. Much smaller differences were found among the private, as measured by students and business people. (Where there is little difference in the amount of negative differences measured for public institutions.) Simultaneously calculate the relationship between perceived / expected, which implies a certain level of customer satisfaction by filling out the promise just the opposite is ranked in relation to height and rank the observed gap. So the dimensions in which the largest gap observed patients are generally the most dissatisfied. Significantly, also noted that the overall height differences between higher before comparing the results measured for each dimension of service to its relative importance, but also that the height of the observed differences, after correction by a factor of increasing importance for the reliability dimension in all three measurements. When it comes to private institutions can be seen that the largest gap recorded in the reliability of such dimensions of service which, in the opinion of respondents, the most important for measuring the quality of service, then the security . From all the foregoing results that are exactly the dimensions that the subjects per group for each institution for which the measurement was carried out as the key rate was recorded and the largest deviation in the difference of the perceived and expected quality, which is the assumption appearance dissatisfaction. It is important to emphasize that these deviations is much higher for state institutions, which confirms the fact that foreign and private capital in the health sector increased the service quality perceived by the patient. It is evident that at the same time increased the level of expectations, not only in private, but also in government service, although the latter to a lesser extent.

It is interesting to note the results measured in the last group of E12. Specifically, this group recorded positive results, or measured client satisfaction with services provided. It is the largest positive gap, hence the higher than expected level of perceived noted in the security sphere, the dimensions of the clients from these groups consider most important and tangibles, and then in the sphere of responsibility and reliability and ultimately compassion. The cause of these results, the conclusions drawn from the discussion that followed the measurements, lies in low expectations of this group of patients. In this sense, the level of services provided state institutions, private competition caused pressed to raise service quality and satisfaction caused by a patient with low expectations.

Conclusions

The measurement results, especially the information obtained during the discussion of the results obtained show that the increasing presence of private health care organizations on the health market in Serbia increased the level of competition in the field of supply health services, and in this context and influence on improving the quality of services offered to patients [28]. However, at the same time led to a higher level of expectations among patients, especially due to the traditionally used elements of marketing mix where surgeries are trying to attract new patients and recapture them from the competition. Experience, however, show that he still recorded a negative difference of the perceived and expected quality and the negative perception of the quality provided by private organizations, especially when it comes to state clinics rated by "demanding customers", those who had the opportunity to compare competitive services and whose level of application increases. At the same time on the market, still, there's a relatively important part of low expectations, which are satisfied or fairly satisfied, average (or even below average) health services. This is primarily a consequence of their earlier negative experience and relatively simple request that they put in front of the institution. Here, however, important to emphasize that in the case assessment both categories (private and government) by the same group of subjects there is a different level of expectations in respect of the same dimensions. Namely, the same size have a higher service level expectations of respondents from MBA students

when it comes to private, as compared to the level of expectation for state health organizations.

Based on the results of the study can be concluded that:

The level of previous expectations of health services in the Serbian market has a significant influence on perceived service quality;

The prior information and user experience have crucial influence on the formation level of expectations. This is so present that the subjects of the same group formed a different level of expectations when it comes to private or government health institutions, due primarily to the knowledge of their capabilities, and experience they have had

Patients' needs and requirements that are placed before the health organization is significantly affected by comparison of results based on the difference between perceived and expected services show that the overall service quality gap is less when calculating the weighted differences, which implies lower tolerance when it comes to using information about the importance of (importance) of individual variables for the patients.

In contrast with these results, the expected relationship between the perceived quality of customer satisfaction indicates the degree of health services. It is important to note that the level of satisfaction is highest among the four groups of subjects, which is logical, given the positive difference of the perceived and expected quality.

Is important to emphasize that the calculation of patient satisfaction through the relationship of perceived and expected quality shows a lower level of satisfaction when using a weighted model, and calculating the importance of individual dimensions .

REFERRENCES

1-Dickov V, Dickov A, Milicevic B. FREEDOM FROM DISEASE - Health protection system in Serbia - management approach. International Journal Total Quality Management and Excellence 2010; 38 (2): 119-126.

2- Bolton RN, Drew JH .A Longitudinal Analysis of the Impact of Service Changes on Customer Attitudes. Journal of Marketing 1991a; 55 (1): 1-9.

3- Bolton RD, Drew JH. A Multistage Model of Customers' Assessments of Service Quality and Value. Journal of Consumer Research 1991b; 17: 375-384.

4-Boulding W, Karla A, Staelin R, Zeithaml V.A. A Dynamic, Process Model of Service Quality: From Expectations to Behavioural Intentions. Journal of Marketing Research 1993; 30 February: 7-27.

5-Brown SW, Swartz TA. A Gap Analysis of Professional Service Quality. Journal of Marketing 1989; 53:92-98.

6- Carman JH. Consumer Perceptions of Service Quality: An Assesment of SERVQUAL dimensions. Journal of Retailing 1990; 66(1):33-55.

7-Cronin J.J, Taylor S.A. Measuring Service Quality: a Re-examination and Extention. Journal of Marketing 1992; 56:55-68.

8- Gronroos C.Strategic Management and Marketing in Service Sector. Marketing Science Institute, Cambridge 1982; MA: 25-28.

9- Gronroos C.Service Management and Marketing. Lexington Books, Lexington 1990; MA: 15-18.

10- Gronroos C.The Perceived Service Quality Concept – a Mistake? Managing Service Quality 2001; 11(3):150-208.

11-Iacoubucci D,Ostrom A.L,Braig B.M,Bezjianž-Avery A. canonical Model of Consumer Evaluations and Theoretical Bases of Expectations in Swartz, T.A. Bowen, D.E. and Brown, S.W. (eds).Advances in Services Marketing and Management 1996;5 JAI Press, Greenwich,CT:1-44.

12- Kang GD, James J.Service Quality Dimensions: An Examination of Gronroos's Service Quality Model. Managing Service Quality 2004; 14(4):266-277.

13- Kano N, Seraku N,Takahashi F,Tsuji S. Attractive Quality and Must-be Quality (Hinshitsu Quality).The Journal of Japanese Society for Quality Control 1984;14 (2):39-48.

14- Kim Y, Lee S, Yun D.Integrating Current and Competitive Service Quality Level Analyses for Service-Quality Improvement Programs. Managing Service Quality 2004; 14 (4):288-296.

15- Leugenia HC.Analyzing the Value of Service Quality Management: Gaining Competitive Advantages. International Journal of Value-Based Management 2003; 16:131-152.

16- Oliver R.L. A Cognitive Model of the Antecedents and Outcomes of Satisfaction Decision. Journal of Marketing Research 1980; 17:460-469.

17-Oliver R.L.Measurement and Evaluation of Satisfaction Processes in Retail Settings. Journal of Retailing 1981; 57: 25-48.

[1]Parasuraman A, Zeithaml VA, Berry L.L.A Conceptual Model of Service Quality and Its Implications for Future Research. Journal of Marketing 1985; 49:41-50.

18- Parasuraman A, Zeithaml VA, Berry L.L.SERVQUAL.A Multiple-Item Scale for Measuring Consumer Perceptions of Service Quality. Journal of Retailing 1988; 64:12-40.

19- Parasuraman A, Berry L.L, Zeithaml V.A. Refinement and Reassessment of the SERVQUAL of the

SERVQUAL scale.MSI working paper 1991.
Parasuraman A, Berry LL.Alternative Scales for Measuring Service Quality: A Comparative Assessment Based on Psychometric and Diagnostic Criteria. Journal of Retailing 1994a; 70(2):201-230.

20- Parasuraman A,Zeithaml VA,Berry LL.Reassessment of expectations as a Comparison Standard in Measuring Service Quality: Implication for Future Research. Journal of Marketing 1994b; 58: 111-124.
21-Robinson S.Measuring Service Quality: Current Thinking and Future Requirements. Marketing Intelligence and Planning 1999; 17/1:21-32.
22- Tan PL, Foo S.Service Quality Assessment: A Case Study of A Singapore Statutory Board Library. Singapore Journal of Library and Information Management 1999 ;(28):1-23.
23-Smith A.Measuring Service Quality: is SERVQUAL now redundant? Journal of Marketing Management 1995; 11:257-276.
24-Teas R.K.Expectation, Performance, Evaluation and Consumers' Perceptions of Quality. Journal of Marketing 1993; 57:18-34.
25- Teas RK.Expectations as a Comparison Standard in Measuring Service Quality: an Assesment of a Reassessment. Journal of Marketing 1994; 58:132-149.
26- Thongsamak S.Service Qualiti: Its Measurement and Relationship with Customer Satisfaction.2001; ISE 501.
27- Woodside AG, Frey LL, Daly RT. Linking Service Quality, Customer Satisfaction and Behavioral Inention.Journal of Health Care Marketing 1989; 9 December: 5-17.
28- Dickov V,Nerandjic B,Perovic V.Ekonomika moderna,Stilos, FTN, Novi Sad 2004:9-23.

The New Iraqi Journal of Medicine

Original Article

ENT

Screening for hearing impairment among the elderly using hearing handicap inventory for the elderly- screening (HHIE-S)

Rosdina AK , Leelavathi M , MN Azimah , NA Aziz

Abstract

Background: Pure Tone Audiometry (PTA) is the gold-standard to measure hearing impairment however; it is less suitable for mass-screening due to lack of availability and cost. The aim of this study was to detect the prevalence of hearing impairment using Hearing Handicap Inventory for the Elderly- Screening (HHIE-S) and comparing its precision to Pure Tone Audiometry (PTA).

Patient and method*:* A cross sectional study was done among elderly patients using the Hearing Handicap Inventory for the Elderly-Screening (HHIE-S) and followed by Pure Tone Audiometry (PTA) test.

Results: A total of 111elderly completed both the questionnaire and audiometry testing. The prevalence of hearing impairment using HHIE-S is 19.8% whilst PTA assessment recorded prevalence of 36.9%. The HHIE-S questionnaire yielded a sensitivity of 31.7% at pure tone audiometry cut off level of 25dBHL and improved to 60.0% at 40dHBL, however the Positive Predictive Value (PPV) and Negative Predictive Value (NPV) reduced from 59% to 13.4% and 68.5% to 63% respectively.

Conclusions: The prevalence of self reported hearing impairment using HHIE-S is lower compared to the gold-standard PTA. The results show that HHIE-S has a tendency to under-detect hearing impairment. Hearing impairment may be under-reported due to the acceptance that it is the normal process of ageing. The HHIE-S is a relatively good screening tool for moderate hearing impairment. However, it may not be a better alternative to PTA especially in detecting the mild hearing loss.

The N Iraqi J Med, December 2011; 7(3):68-72

Keywords: *Hearing loss, mass screening, audiometry, pure tone*

INTRODUCTION

The ageing population is expected to increase worldwide due to the improved socioeconomic status, health facilities and decreasing mortality rate. Malaysia is a multicultural country consisting different ethnic groups with the Malay indigenous group being the majority (58%), followed by Chinese (26%) and Indians (7%).The elderly population in Malaysia is projected to make up to approximately 9.5% of the total population by 2020, hence increasing the prevalence of age-related health problems [1]. Hearing impairment is a common problem among the elderly and often perceived as a normal part of ageing. Undetected, it can cause various problems namely; functional decline, anxiety, depression, and social isolation [2]. The gold standard method for evaluating hearing impairment is by using an audiogram [3]. However, this audiometric assessment is not regularly performed as a screening tool due to its inaccessibility and expensive cost. Detecting the early stage of hearing impairment is important as it can reduce both untoward complications and higher medical cost among the elderly. Hence, a cost effective physician friendly hearing assessment tool is required. Studies have shown that the Hearing Handicap Inventory for the Elderly-Screening (HHIE-S) is a reliable screening tool for identifying hearing handicap and measuring the effects of hearing impairment in the elderly [4, 5] .The aim of this study is to determine the prevalence of self-reported hearing impairment among elderly using Hearing Handicap Inventory in Elderly-

* *Kelinik Kesihatan Senggarang , Batu Pahat , Johor*
Email : dinazai01@yahoo.com
Department of Family Medicine, Medical Faculty, Universiti Kebangsaan Malaysia Medical Center.

Screening (HHIE-S) questionnaire and comparing its precision to Pure Tone Audiometry (PTA).

PATIENTS AND METHODS

A cross sectional study was performed in 2006 using universal sampling of all patients 60 years and above at a rural health clinic Malaysia. Those who were acutely ill, illiterate, demented based on the Elderly Cognitive Assessment Questionnaire (ECAQ) and those who refused to participate, were excluded from the study. The selected patients completed the self-administered Hearing Handicap Inventory in Elderly– Screening (HHIE-S) questionnaire. They were then subjected to hearing assessment using the Pure Tone Audiometry (PTA).

The HHIE-S consists of 10-items questionnaire, which assessed the social and emotional perception of hearing impairment. Individuals who perceived hearing impairment were further tested and prescribed appropriate hearing aids if required. The original HHIE-S (English) was translated to the Malay language using forward and back translation by two non-medical language experts and an internal consistency (Cronbach's alpha) of 0.88 was obtained. Responses were individually scored with a minimum score of 0 and maximum 40 points. ("yes" scored 4 points, "sometimes" 2 points or "no" 0 points). A score of 8 or more was defined as presence of hearing loss [6].

PTA (Amploid 171 audiometer) was performed at a nearby tertiary hospital after otoscopic examination (Welch-Allyn audioscope) for any impacted wax. Hearing impairment was measured using the pure tone audiometry at frequencies of 250, 500, 1000, 2000 and 4000 Hz. Hearing impairment was defined as mild (26-40dBHL), moderate (41-60dBHL), severe (61-80dBHL) and profound (≥ 81 dHBL) using PTA testing. Normal hearing was defined as 10-25 dBHL [7].

RESULTS

A total of 138 elderly were selected and 80.4% (n=111) completed both the questionnaire and audiometry testing. The age range of the study population is 60 to 93 with a mean of 68 ± 6 years. Females constituted 53.2% (n=59) while males 46.8% (n= 52). The participation of Malay ethnic group is 60.4% (n=67), followed by Chinese 38.7% (n=43) and Indians 0.9% (n=1). The participation of Indians is low as they are mainly concentrated in urban areas.

The prevalence of hearing impairment using HHIE-S is 19.8% (n=22) while the prevalence of hearing loss by PTA is 36.9% (n=41). Older people (mean age of 70.8) admitted to hearing impairment using the HHIE-S (p=0.02). However there was no significant association between self reported hearing impairment using the HHIE-S for gender and ethnicity. (Table 1).

Among 89 subjects who denied hearing impairment using HHIE-S (score less than 8), 31.5% (n=28) actually had hearing loss measured by PTA. More than half (59.1%; n=13) of the 22 subjects who screened positive with HHIE-S (score more than 8), had hearing loss when tested with PTA. The HHIE-S questionnaire yielded a sensitivity of 31.7% at pure tone audiometry cut off level of more than 25dBHL (mild hearing loss) but improved to 60.0% at a higher cut off value at 40dBHL (moderate hearing loss). However, the specificity, Positive Predictive Value (PPV) and Negative Predictive Value (NPV) declined when the PTA threshold level was increased (Table 2).

Discussion

The prevalence of self reported hearing impairment in this study using the HHIE-S is about 1.8 times lower than prevalence measured by the gold standard PTA (36.9%). This showed that the elderly under reported their hearing status probably due to the perception that it is a normal part of ageing process. This prevalence is higher when compared to a study done on Chinese Americans (10%) [8].This could be due to the difference in the population itself or their perception of hearing impairment. Hearing impairment increased with age and this is a predicted relationship secondary to presbyacusis [9]. There is no relationship between gender and ethnicity with hearing impairment. Previous studies have documented controversial evidence where some studies reported increased prevalence among males while others reported inverse relationship [9, 10].

Factors tested	HHIE-S score 0-8	HHIE-S score > 8	Test	p-value
	Number (%)	Number (%)		
			T-test	
Mean age	67.67	70.82	-2.215	0.02
Gender				
Male	40 (79.9%)	12 (23%)	χ^2	0.42
Female	49 (83.0%)	10 (16.9%)		
Ethnic				
Malay	52 (77.6%)	15 (22.3%)		
			χ^2	0.07
Non-Malay (Chinese & Indian)	37 (84.1%)	7 (15.9%)		

Table 1: Factors associated with hearing impairment using HHIE-S

Hearing Loss measured at two PTA threshold (dBHL)	Sensitivity	Specificity	PPV	NPV
>25 dBHL Mild hearing loss	**31.7%**	**87.1%**	**59.0%**	**68.5%**
>40 dBHL Moderate hearing loss	**60.0%**	**15.3%**	**13.4%**	**63.0%**

Table 2. Diagnostic performance of HHIE-S versus audiometry at different threshold levels

About 31.5 % out of the 89 patients who denied hearing problem are noted to have hearing impairment by PTA. Similar observation was noted by Jupiter et al [11]. This indicates that self assessed hearing loss is under reported probably because the elderly do not perceive it as a handicap, instead

accepted it as a norm. Other possibilities include denial and social stigma. Some patients may not report hearing loss in quiet setting, but have difficulty understanding speech in social settings where the ambient noise interferes with auditory acuity. Patients in this study are mainly retirees in a rural setting hence possibility of limited exposure to noise to have noticed any hearing problem.

The high specificity and negative predictive value (NPPV) at pure tone average level > 25dBHL, means the HHIE-S more accurately identify those without mild hearing impairment rather than identifying those with hearing impairment. In this study the low sensitivity of HHIE-S is comparable with a similar study among Chinese American [8]. Other studies have shown variable sensitivity, specificity and predictive values suggesting that the prevalence of the hearing impairment is an important determinant of these values [10, 12]. Although the sensitivity improved when tested higher cut off value (> 40 dBHL) the specificity, PPV and NPV deteriorated suggesting that HHIE-S is more useful to detect moderate hearing impairment but less valuable in eliminating those without moderate hearing impairment. This is probably because the socially adequate hearing or serviceable hearing is around 40 dBHL [13].

Conclusion

The prevalence of self reported hearing impairment using HHIE-S is lower compared to the gold-standard PTA. The study shows that HHIE-S under-detects hearing impairment due to the fact that it may be accepted as a normal part of ageing process. The HHIE-S performed better at higher cut of value, hence is a relatively good tool for screening of moderate hearing impairment however it may not be a better alternative compared to PTA especially in detecting the mild hearing impairment. There is good prospect of further research and discovery of new innovations for a more cost effective, physician friendly and easily available hearing assessment tool for screening in the future.

Acknowledgement

The authors of this study wish to thank Universiti Kebangsaan Malaysia for funding this project.

REFERRENCES

1. Sim OF. Aging in Malaysia: A review of national policies and programmes, in David R Philips and Alfred Chan Cheung-Ming (eds); Aging and long-term care: National policies in the Asia Pacific, IRDC, available from URL htpp://web.idrc.ca/en/ev-28476-201-1-DO_TOPIC.html (accessed 03.01.11)
2. Tambs K. Moderate Effect of Hearing Loss on Mental Health and Subjective Well-Being: results from the Nord-Trøndelag Hearing Loss Study. Psychosom Med 2004; 66:776-782.
3. Mullin G, Campbell KCM. Pure-tone audiometry Pure Tone Testing. E-medicine Audiology 2006. Available from URL http://emedicine medscape.com/article. /1822962-overview
4. Dalton DS, Cruickshanks KJ, Klein BE, Klein R, Wiley TL, Nondahl DM. The Impact of Hearing Loss on Quality of Life in Older Adults. Gerontologist 2003; 43:661-8.
5. Bagai A, Thavendiranathan P, Detsky AS. Does this patient have hearing impairment? JAMA 2006; 295:416–428.
6. Demers K. Hearing Screening. Dermatology Nursing 2004; 16:199-200.
7. World Health Organization fact sheet: Deafness and hearing impairment. In: W.H. Organization, Editor, World Health Fact Sheet (#300 ed.), World Health Organization, Geneva (2006).
8. Sangster JF, Gerace TM, Seewald RC, Golding M, Newwall P, Hartly D. 1991. Hearing loss in elderly patients in a family practice. CMAJ 1991; 144:981-984.
9. Sindhusake D, Mitchell P, Smith W, Golding M, Newall P, Hartley D et al: Validation of Self-Reported Hearing Loss. Int J Epidemiol 2001; 30:1371-1378.
10. Gates GA, Murphy M, Rees TS, Fraher A. Screening for handicapping hearing loss in the elderly. J Fam Pract 2003; 52:56-62.
11. Jupiter T, Palagonia CL. The Hearing Handicap Inventory for the elderly screening version adapted for use with elderly Chinese American individuals. Am J Audiol 2001; 10:99-103.
12. Noor Hassim I, Rampal KG. Prevalence of Hearing Loss and Hearing Impairment among Rural Males in Selangor. Med J Malaysia 1994; 49:78-85.
13. Walsh RM, Bath AP, Bance ML, Keller A, Rutka JA. Consequences to hearing during the conservative management of vestibular schwannomas. Laryngoscope 2000; 110:250-5.

The New Iraqi Journal of Medicine

Original Article

Laparoscopic Surgery

Comparison between laparoscopic and mini-cholecystectomy in Al-kadhmiya teaching hospital

Husam Abdul Kareem Ahmed *, Qahtan Adnan Mahdi**, Adel Khdair Abbas***

Abstract

Aim: To compare laparoscopic cholecystectomy with mini – cholecystectomy, taking into account several parameters that used for comparison between two therapies including operative time, complications, need for analgesia and assessment of postoperative pain, mortality, and postoperative hospital stay.

Patients and methods: In this prospective study, the outcome of 54 patients with symptomatic cholelithiasis were randomized to undergo open cholecystectomy using small – incision technique (minilaparotomy cholecystectomy), from November 2008 to November 2009 was compared with that of 33 patients treated by laparoscopic cholecystectomy within the same period in Al – Kadhmiyia teaching hospital. The two groups of patients were similar in age, weight, risk factors and history of previous operations.

Results: Laparoscopic cholecystectomy required more operative time to perform than minicholecystectomy (77 min. versus 48 min.). Postoperative assessment of pain by verbal rating score of pain (VRS) and the use of narcotic analgesics was markedly less after the laparoscopic procedure. In addition, hospital stay was shorter for laparoscopic cholecystectomy (mean of 2.4 day) than minicholecystectomy (mean of 3.5 day). The incidence of complication after laparoscopic cholecystectomy (23.3%) was higher than minicholecystectomy (15.5%).

Conclusions: Both laparoscopic and minicholecystectomy provide a safe and effective treatment for most patients with symptomatic gall stones.

The N Iraqi J Med, April 2011; 7(3):78-87

***Keywords**: Cholecystectomy, Laparoscopic cholecystectomy, Minicholecystectomy*

INTRODUCTION

Gallstone disease affects 10 – 12% of the population. The prevalence is higher in women, old patients, in association with multiple pregnancies, obesity, rapid weight loss, certain ethnic groups [Native American (Pima Indian), Scandinavian], certain drugs (postmenopausal estrogens, total parenteral nutrition) as well as ileal disease or resection. [1] Most patients with gallstones are asymptomatic and only 1 – 4% of those will develops symptoms or complications. [2] The consequences of gallstones vary and ranging from brief episodes of biliary pain to potentially serious complications as acute cholecystitis, CBD stones with or without cholangitis, gallstones ileus, pancreatitis and rarely gallbladder malignancies (1 per 1000 patients per year). [2]

The therapeutic options:

A) Non surgical treatment:

1. Oral dissolution therapy:

2. Contact dissolution therapy:

3. Extracorpreal shock wave lithotripsy (ESWL):

B) Surgical treatment:

1. Cholecystectomy:

2. Conventional open cholecystectomy:

Associated Professor (F.R.C.S.), Supervisor for post graduate center Iraqi Board Dept. of Surgery, College of Medicine, Al-Nahrain University, Baghdad – Iraq
E-mail: dr_husam44@yahoo.com

3. Minicholecystectomy:

4. Laparoscopic cholecystectomy:

The indications for laparoscopic cholecystectomy:

The indications for laparoscopic cholecystectomy are the same as those for conventional open method which are mentioned above. [7]

The contraindications of laparoscopic cholecystectomy:

There are absolute and relative contraindications to laparoscopic cholecystectomy. The absolute contraindications include unable to tolerate general anesthesia, refractory coagulopathy, suspicion of gallbladder carcinoma, cholangitis, and diffuse peritonitis, while relative contraindications include previous upper abdominal surgery, cirrhosis and/or portal hypertension, chronic obstructive pulmonary disease, cholecystoenteric fistula, morbid obesity and pregnancy.[7] Complications of laparoscopic cholecystectomy:

There are primary complications that occur during the operation and 1st two days after the operation such as vascular injury, perforation of hallow viscus, biliary leak and injury, problems of CO2 pneumoperitoneum and spillage of gallstones and secondary complications that occur after the first two postoperative days and within the first two post – operative weeks as injury and stricture of CBD, infection, hernia through the port openings. [13]

Complications of laparoscopic cholecystectomy can be classified into general complications, pneumoperitoneum related complications and trocar related complications. [7]

The general complications include hemorrhage, bile duct injury, bile leak, retained stones, pancreatitis, wound infection and incisional hernia. Pneumoperitoneum related complications include CO_2 embolism, vaso-vagal reflex, cardiac arrhythmia and hypercarbic acidosis while trocar related complications include abdominal wall bleeding and hematoma, visceral injury and vascular injury. [7]

Sometimes laparoscopic or minicholecystectomy need to be converted to the standard method. The conversion may be done due to "necessity" as uncontrollable bleeding; CBD injury detected during injury or other reasons, or the conversion may be for "safety" as the presence of dense adhesion around the gallbladder or unclear anatomy [13]. Such conversions are not regarded as a complication of the procedure and should be considered a sound surgical judgment. [2]

Advantages and disadvantages of laparoscopic cholecystectomy:

Advantages and disadvantages of laparoscopic cholecystectomy in comparison with conventional method are shown in table (1). [7]

Advantages	Disadvantages
Less pain	Lack of depth perception
Smaller incisions	View controlled by camera operator
Better cosmesis	More difficult to control hemorrhage
Shorter hospitalization	Decreased tactile discrimination (haptics)
Earlier return to full activity	Potential CO_2 insufflation complications
Decreased total costs	Adhesions/inflammation limit use
	Slight increase in bile duct injuries

Table (1): Advantages and disadvantages of LC compared to OC

AIM OF THE STUDY

To compare laparoscopic cholecystectomy with mini – cholecystectomy, taking into account several parameters that used for comparison between two therapies including operative time, complications, need for analgesia and assessment of postoperative pain, mortality, postoperative hospital stay.

PATIENTS AND METHODS

In this randomized prospective study, we compared data from thirty – three patients that underwent laparoscopic cholecystectomy from November 2008 to November 2009 with fifty- Four patients who underwent small- incision cholecystectomy within the same period.

All patients in both groups underwent elective cholecystectomy for symptomatic cholelithiasis. Patients with acute cholecystitis as evidenced by preoperative fever, leucocytosis, peritoneal signs, patients with history of upper abdominal procedure or patients with simultaneous surgical procedure done with the cholecystectomy and finally patients who were suspected to have malignancy of the GB were all excluded from both groups.

All patients had symptoms consistent with biliary colic and other symptoms of chronic cholecystitis. Data have been taken from the history like age, gender, presentation, history of previous surgery. Clinical examination and investigations like liver function test, hematocrit, and abdominal ultrasound were done to all patients preoperatively, the latter to assess the GB size, thickness of the wall, presence of stones, location and number of the stones, and diameter of the CBD. For some patients we needed to do upper oesophage-gastroduodenoscopy, prothrombin time (PT) and partial thromboplastin time (PTT).

The patients have been admitted a day before operation and all patients had endotracheal intubation and general anesthesia. Nasogastric tube was put in stomach at the time of operation especially for the laparoscopic group to deflate the stomach.

The laparoscopic cholecystectomy was done by four trocar technique after CO_2 insufflation, two tocar openings one cm. in diameter and two half cm. in diameter. End viewing laparoscope equipped with a video camera used. Monopolar electrocautery was used. The minicholecystectomy was done by small incision 5 – 8 cm. either subcostal or high small transverse incision. The insertion of postoperative intraperitoneal drain or nasogastric tube depended on the surgeon's preference and opinion. Parameters were collected and analyzed.

The operative time, the time taken from skin incision to skin closure i.e. after induction of anesthesia and insufflations of CO_2 in the case of laparoscopic cholecystectomy, was measured and analyzed.

The post operative pain was evaluated by measuring the dose and recording the type of analgesia required postoperatively and by monitoring the postoperative pain using verbal rating pain score VRS as follow: [14]

VRS 1: no pain

VRS 2: mild pain

VRS 3: moderate pain

VRS 4: severe pain.

The conversion rate, the complication rate and postoperative hospitalization rate were measured and analyzed.

RESULTS

Eighty seven patients were initially included in this study. Fifty – four were operated on as minicholecystectomy and thirty – three as laparoscopic cholecystectomy.

There was no difference in the base line characteristics between patients in either group.

Table (2) shows that in the laparoscopic group patients, there were 23 (69.9%) female, 10 (30.3%) males with mean age of 42 years (15-65 y.) while in the minicholecystectomy group; there were 41 (75.9%) female, 13 (24.7%) males with mean age of 43 y (22-60 y.).

The incidence of risk factors for the patients in both groups were nearly the same 7 (21.2%) in laparoscopic group, 14 (25.9%) in minicholecystectomy group as shown in table 3.

Patients of the laparoscopic group who got previous lower abdominal surgery were 4 (12.1%) compared with 7 (12.9%) of the minicholecystectomy group.

Patients who were diagnosed as calculus cholecystitis in laparoscopic group were 1 (3.03%) versus non in minicholecystectomy group.

Characteristic	LC (n=33)	MC (n=54)
Female%	**23 (69.6%)**	**41 (75.9%)**
Male%	**10 (30.3%)**	**13 (24.7%)**
Age (mean)	**42 y.**	**43 y.**
(Range)	**25-65**	**22- 60**
Risk factors (%)	**7 (21.2%)**	**14 (25.9%)**
Previous surgery %	**4 (12%)**	**7 (12.9%)**
A calculus cholecystitis	**1 (3.03%)**	**0**

Table (2): The baseline characteristics between patients in both groups

LC = laparoscopic cholecystectomy

MC = Minicholecystectomy

n = number

LC was accomplished successfully in thirty patients of the thirty- three patients; three have been converted to the conventional open method. Conversion rate of 9.09%, two because of sever adhesions and one was due to variable unclear anatomy.

We arbitrarily considered 8 cm or less incision line in minicholecystectomy as indicating that the procedure was successfully completed. Nine patients, conversion rate of 16.6% of the minicholecystectomy group required extension of the incision line. Five of them were due to dense adhesions and obesity, three due to unclear and variable anatomy and one was due to excessive bleeding.

Table-3 shows that the mean operative time in laparoscopic cholecystectomy was 77 min. (45 – 170 min.) versus 48 min. in mini-cholecystectomy (35 – 70 min.)

Duration of Surgery	LC		MC		P Value
	Mean	Range	Mean	Range	
Operative Time (min.)	77	45-170	48	35-70	< 0.05

Table (3): Comparison between the operating times in the two methods

n= number, min. = minutes, Operative time = from skin incision to skin closure in minicholecystectomy group, the mean abdominal incision length was 6.4 cm (5-8 cm.). In the laparoscopic cholecystectomy, there were 4 abdominal ports openings of 0.5cm.-1.5 cm. extension of the openings were needed in 6 patients (20%), usually the upper port opening due to difficulty of extraction of the GB. Nasogastric tube was left after the operations in 23.3% of patients of laparoscopic group and in 31 (68.8%) patients with minicholecystectomy group with a mean insertion time of 15 h. for the former group and 28 h. for the later (see Table 5).

A tube drain was left in the sub-hepatic space at the end of the procedure in 8 (26.6%) patients in laparoscopic cholecystectomy with a mean insertion time of 35 h. versus 37 patients (82.2%) in minicholecystectomy group with a mean time of insertion of 52 h. (see Table 5).

Table (4) shows that Patients underwent laparoscopic cholecystectomy started oral fluid of a mean time 16 h. compared with 28 h. for the minicholecystectomy group.

Characteristic	LC (n=30)	MC (n=45)
Abdominal Drain		
- Number of patients (%)	8 (26.6%)	37 (82.2 %)
- Meantime of insertion (hours)	35 hr.	52 h.
Nasogastric tube		
- Number of patients (%)	7 (23.3 %)	31 (68. 8 %)
- Meantime of insertion (hours)	15 h.	28 h.
Time of the first oral Fluid intake (hours)		
- Mean	16 h.	28 h.
- Range	8- 30 h.)	20- 48 h.

Table (4) Comparison between the use of abdominal drains and nasogastric tubes and mean time of their insertion, time to the first oral fluid intake in both groups.

The post operative pain was assessed by VRS pain score, in the 1st 24 hours, the majority of patients in laparoscopic group (28, 93.3%) were assigned as score 2 and 3, where as 38 patients (83.3%) of the MC group lying in score 3 and 4. In the 2nd 24 h., 28 patients (93.3%) with laparoscopic cholecystectomy were in score 1 and 2 while for minicholecystectomy group, 23 patients (51.1%) were in score 3 and 5 patients (11.1%) still in score 4 (Table 6).

Of the laparoscopic patients, 7 patients (23.3%) required only acetaminophen in 1st 24 hours as analgesia, 14 patients (46.6%) required NSAID including Diclofenac injection and 9 patients (30%) required narcotic analgesics while in the minicholecystectomy group, 6 patients (13.3%) needed only NSAID, 28 patients (62.2%) required one dose of narcotics, and 11 patients (24.4%) required two doses. This is shown in table (5). There was no mortality in either group.

For the postoperative complications, Table (7) shows that it was 23.3% (7 patients) in laparoscopic group which was little more than that of mini-cholecystectomy group (15.5%, 7 patients).These complications don't carry the same degree of importance and some of them are specific and some are general. Biliary injury and biliary leak reported in 3 cases of laparoscopic group (10%). One of them managed by re-exploration, CBD was seen to be injured, T-tube was inserted and a drain was put and patient discharged after 16 days in a stable condition. The other one underwent re-exploration and multiple extra-hepatic biliary tract injuries were found and managed by drainage and the patient discharge after 14 days. The remaining one managed conservatively. For the minicholecystectomy group, only one patient (2.2%) reported to get biliary leak from the drain that stopped after 10 days and patient discharged well after 14 days.

Table (5): Postoperative pain and analgesia

VRS = Verbal rating score, VRS 1 = no pain, VRS2 = mild pain, VRS3 = moderate pain, VRS4 = Severe pain

Characteristic Severity of post operative pain according to VRS pain score		LC n = 30				MC n =45			
1st 24 h. post op.	VRS	1	2	3	4	1	2	3	4
	No. (%)	0	21 (70%)	7 (23.3%)	2 (6.5%)	0	7 (15.5%)	16 (34.5%)	22 (48.8%)
2nd 24 h. post op.	VRS	1	2	3	4	1	2	3	4
	No. (%)	7 (23.3%)	21 (70%)	1 (3.3%)	1 (3.3%)	2 (4.4%)	15 (33.3%)	23 (51.1%)	5 (11.1%)
Analgesics in the first 24 h. post op.									
No analgesics no (%)			0				0		
Acetaminophen no (%)			7 (23.3%)				0		
NSAID no. (%)			14 (46.6%)				6 (13.3)		
Narcotics in the first 24 h. post op.		One Dose	Two	> 2		One Dose	Two	> 2	
		9 (30.0%)	0	0		28 (62.2%)	11 (24.4%)	0	

LC= Laparoscopic cholecystectomy, MC= Minicholecystectomy.

Complications	LC n =30		MC n= 45	
	No.	%	No.	%
Wound Infections	1	3.3	3	6.6
Pulmonary Infection	1	3.3	2	4.4
Ischemic Chest Pain	0	0	1	2.2
Biliary Injury and Biliary Leak	3	10	1	2.2
Spillage of Gallstones to the Peritoneal cavity	2	6.6	0	0
Total	7	23.3	7	15.5

Table (6): The comparison of the complications of both methods

Spillage of stones occurred in 2 (6.6%) of patients with laparoscopic cholecystectomy to the peritoneal cavity especially during extrusion of the gallbladder through the port opening while it's not reported in minicholecystectomy. Other complications are shown in table-6.

The mean postoperative stay in the hospital was 2.4 day for laparoscopic cholecystectomy versus 3.5 d. for the minicholecystectomy group. (Table 7).

Post operative hospital stay (days)	LC		MC	
	Mean	Range	Range	Mean
	2.4	1 – 16	3.5	1 – 14

Table (7) Comparison between the recovery periods in the hospital for the both groups

DISCUSSION

Any new procedure must be shown in general to have one or more of the following possible advantages: safer, easier, quicker, speedier recovery, shorter hospital stay, lower cost and more cosmetic; these are not equally important and need to be weighed for a balanced conclusion to be reached. [25]
The differences of laparoscopic cholecystectomy from the conventional method is likely, from the first principle, a smaller incision and a smaller trauma and the smaller the incision used for the conventional method the less the difference is likely to be.[16]
The length of the incision was taken arbitrarly as 8 cm. because there's no fixed definition for the length of incision of minilaparotomy cholecystectomy in the references; some regarded it less than 5 cm.[17], some regarded it less than 10 cm.[18], some measuring it according to the body mass index BMI (incision length = 0.2 cm. for each unit increase in BMI) and the range of their incision was 4-18 cm. and we thought 18 cm. is to much for regarding it as a minicholecystectomy incision. Many references regard the length of incision of minicholecystectomy less than 8 cm, and we took it as such. [19, 20, 21]

Operating time

It was longer in laparoscopic cholecystectomy (mean = 77 min.) than minicholecystectomy procedures (mean = 48 min.).
Our laparoscopic operative time was shorter than some studies as McGill group from Canada 86 min.[22], Southampton study 24 min.[20], study in Sweden 100 min.[23] and study in Mumbai 110 min. [12] but longer than some European studies (35 – 60 min.) [24] and Fredrick study in general teaching hospital in Netherland (71.9 min.)[25].

For our mean operative time of minicholecystectomy (48 min), it is comparable with Sheffield group (45 min.) [26] and seems shorter than Glasgow study (57 min.) [19], Sweden study (85 min.) [23], Mumbai study (94 min.) [12] and Fredrik study in Netherland (60.4 min.) [25].
There are other studies showed longer operative time in laparoscopic cholecystectomy than minicholecystectomy which was similar to that obtained by our study such as study in Mary's hospital in London (82 min. for laparoscopic cholecystectomy versus 65 min. for minicholecystectomy) [11], study in Greece [27], and study in Mayo hospital in Lahore [28] but there are studies showed no significant difference in the operative time between both groups as study in New York hospital in Brooklyn (79 min. for laparoscopic cholecystectomy versus 71 min. for minicholecystectomy) [10] and keus study in Netherland [29].

Hospital stay

In our study it's longer for minicholecystectomy (mean 3.5 d.) than laparoscopic cholecystectomy (mean 2.4 days). For minicholecystectomy, it's comparable with that of McMahon (4 d.) [19], Majeed (3.5 d.) [26], McGill (4 d.) [22] and Mumbai study (3.3 d.) [12].
For LC group, it's more comparable with European studies because of the concern about post operative complications, Cuschieri (3.2 d.) [30], Sheffield study (3.5 d.) [26], McMahon (2 d.) [19] and Mumbai study (3.3 d.) [12], while for American studies Toronto group (1 d.) [31], Southern Surgeon Club (also 1 day) [32] and Sweden study (2 d.) [23].
Other studies also showed less hospital stay in laparoscopic cholecystectomy in comparison with minicholecystectomy such as keus study in Netherland [29] and Mayo hospital study in Lahore [28] while other studies showed no significant difference in both groups as in New York hospital in Brooklyn (2.1 d. for laparoscopic group versus 2.3 d. for minicholecystectomy group) [10] and Mary's hospital in London (2 d. for both groups) [11].
Our hospital stay was longer because of the social condition that the patients belong to and the development of post operative complications. In cases of conversion and complications, hospital stay is longer.

Post- operative oral feeding

The resumption of an oral fluid diet was faster after laparoscopic cholecystectomy (mean 16 h.) than minicholecystectomy (22 h.). This is started according to the presence of bowel sounds which indicates the resolution of postoperative ileus which is affected by bowel manipulation during operation and peritoneal stretching; both are less in laparoscopic cholecystectomy.
It's less than McGill study (1.1 d. versus 1.7 d. for minicholecystectomy) [22] while a study in Greece showed no significant difference between both groups [27].

Postoperative pain and discomfort

Pain was less after laparoscopic cholecystectomy especially in the first 24 h. as assessed by the requirement for analgesics and narcotics and by assessment of the severity of pain by the patients themselves using pain score, though pain score can be difficult to interpret since individual patients vary in their pain perception, but they clearly show the difference in the pain severity between the two groups. This was expected because of the less operative trauma in laparoscopic cholecystectomy and it's the same results of other studies, but they have relatively more patients in the

LC group who required no analgesia, this is because they use post operative 0.5% bupivacaine infilteration to the laparoscopic incision and the liver capsule during the procedure. [19, 26, 33]
However, there are studies showed no significant difference regarding the dosage of analgesia required for both groups such as studies in Greece and Brooklyn. [10, 27]

Complications

The incidence of biliary injury and biliary leak were more in laparoscopic cholecystectomy (3, "10 %") than in minicholecystectomy (1, "2.2 %"). These figures seem significantly higher than some studies as a study from Europe revealed CBD injury ranging from 0.3 - 0.6 % [13], or 1% in Sheffield study [26], and 0.7% in Glasgow study [20].

This is explained to the relative small number of patients in our trial in comparison to these studies who's patients are ranging from 200 [19] to 3200 [13], this large volume of patients also means more surgeons experience and less complication with the time since it's shown that the complication rate of laparoscopic surgery correlate closely to the number of operations done by surgeon yearly and therefore to the experience of the surgeon [34]. Other factor that explains the high complication rate of laparoscopic cholecystectomy in our study was the fact that some of the cases were done by surgeons and residents in their training phase.
Our results are comparable to the results of other studies which showed higher complication rate in laparoscopic cholecystectomy than minicholecystectomy as Brooklyn study [10], Sweden study [23] and Lahore study [28].
However, there were studies showed no significant difference between both groups as Fredriks study in Netherland [25], Mumbai study [12] and a study in Mary's hospital in London [11].
Regarding other complications, the incidence of pulmonary infections were comparable between both groups while wound infections were more in minicholecystectomy (3, "6.6"%) than laparoscopic cholecystectomy (1, "3.3 %"). This is explained by the larger incision and further manipulation in open method than laparoscopic cholecystectomy.

Conversion

Our conversion rate from laparoscopic cholecystectomy to the conventional method (9.09%) is lower than Sheffield study (20%) [19], Glasgow study (10%) [26], a study from California (14%) [15] and more than southern surgeon Club (4.7%) [32]. Conversion rate vary widely in published work and the decision to convert is a matter of the type of pathology and surgeons opinion and experience. We have always felt that early conversion is better than long potentially dangerous dissection.
Our conversion rate from laparoscopic cholecystectomy to conventional method (9.09%) was higher than the conversion rate of minicholecystectomy to the conventional method (2.2%). There were studies showed no significant difference in the conversion rate between both groups as Fredriks study in Netherland [25] and Mumbai study [12]. In the comparison between the two methods, the value of diagnostic exploration through the laparoscope is well- known [35] and such benefit cannot be neglected and it offers the advantage of an extensive and complete examination of the hepato - biliary region and the whole abdomen, a matter which is of great difficulty to be done properly through the small-incision procedure.

CONCLUSIONS

Both laparoscopic and minicholecystectomy provide a safe and effective treatment for most patients with symptomatic gall stones.

The operating time is significantly less in minicholecystectomy than laparoscopic one.

RECOMMENDATIONS

During laparoscopic or minicholecystectomy, when the anatomy is obscure or any problem arise, the operation should be converted to the conventional method which reflects a sound judgment and should not be considered a complication of the procedure.
Adequate training in laparoscopic surgery is required in order to reduce the rate of complications.

REFERRENCES

1. Charles F Bellows, David H Berger, Richard A. Crass. Management of gallstones. American family physician: August 15, 2005: 476 – 9.
2. National institutes of health Consensus development. Conferences statement on gallstones and laparoscopic cholecystectomy. The Amer. Jour. Of surgery. 1993; 165: 390 – 6.
3. Steven M Strasberg. Overview of the therapeutic modalities for gallstones diseases. The Amer. Jour. Of surgery, 1993; 165: 420 – 6.
4. Aljaz Ahmed, Ramsey C. Chenng and Emmet B. Keeffe. Management of gallstones and their complications. American family physicians; March 15, 2000: 167 – 171.
5. Laslie J Schoen Field, Jay Mark. Oral and contact dissolution of gallstones. The Amer. Jour. Of surgery, 1993; 165: 427 – 30.
6. David L Natherwold. Gallstones Lithotripsy. The Amer. Jour. Of surgery. 1993; 165: 431 – 4.
7. Michael J Zinner and Stanley W. Ashley. Maingot's abdominal operations. The McGraw Hill companies. 11th edition. 2007: 847 – 864.
8. Ganey JB, Johnson P. A, Pillaman P. E. cholecystectomy: clinical experience with a large series. The Amer. Jour. Of surgery, 1999; 151: 352 – 7.
9. Douglas O. Osken, St. Louis. Laparoscopic general surgery: past, present and future. Surgery, 1995; 133: 1 – 3.
10. Oyogoaso, Komenaka, Ilkhani R. and Wisel. Mini – laparotomy cholecystectomy in the era of laparoscopic cholecystectomy: a community based hospital perspective. Am. Surg. 2003 Jul.; 69 (7): 604 – 7.
11. Sanjay Puskaystha, Henry S Tinly, Paris P. Tekkis and Ara W. Darzi. Laparoscopic cholecystectomy versus mini – laparotomy cholecystectomy: a meta – analysis of randomized control trails. Surgical endoscopy; volume 21(8), Aug. 2008: 1294 – 1300.
12. Supe A N, Bapat V N, Pandya S V, Dalvi A N., and Bapat R D. laparoscopic versus mini – laparotomy cholecystectomy for gallstone disease. Indian J. Gastroenterol. 1997; Jul; 15 (3): 94 – 6.
13. Jacques Perissat, France. Laparoscopic cholecystectomy: The European experience. The Amer. Jour. Of surgery, 1993; 165: 444 – 9.
14. RM. Kirk, Averil O. Mansfield. Clinical surgery in general RCS course manual: The management of postoperative pain. 2nd ed. 1996.
15. Jeffery H Peter and others. Reasons for conversion from laparoscopic cholecystectomy to open cholecystectomy in urban teaching hospital. The Amer. Jour. Of surgery, 1996; 168: 54 – 6.
16. Angusto Paulino. A review of 391 selected open cholecystectomies for comparison with laparoscopic cholecystectomy. The Amer. Jour. Of surgery, 1996; 166: 71 – 3.
17. O'Dwyer, Murphy JJ, O'Higgins NJ. Cholecystectomy through 5 – cm subcostal incision. Br. J. of surgery. 1994; 77: 1189 – 90.
18. Goso IR. Mini – cholecystectomy and early discharge. South Med. J. 1993; 81: 161 – 3.
19. Andrew J McMahor, Russel IT, Baxter. Laparoscopic versus mini – laparotomy cholecystectomy: a randomized trial. Lancet 1997; 343: 135 – 8.
20. McGinn FP and colleagues. Randomized trail of laparoscopic cholecystectomy versus mini – cholecystectomy. Br. J. of surg. 1999; 82: 1374 – 7.
21. Reddick EJ, Olsen DA. Comparison with mini – laparotomy cholecystectomy. Surg. Endosc. 1994; 3: 131 – 3.
22. Barkun JJ, Barkun A N and the McGill gallstone treatment group. Lancet 1994; 340: 1116 – 19.
23. Ros A, Gustafsson L, Krook H, Nordgren CE, Thorell A, Wallin C,

and Nillsson E. Laparoscopic cholecystectomy versus mini – laparotomy cholecystectomy. Ann. Surg. 2001 Dec; 234 (6): 741 – 9.

24. Michael Rhodes and colleagues. Randomized trail of laparoscopic cholecystectomy versus small – incision cholecystectomy. The Lancet 1998; 347: 1621 – 4.
25. Fredrik Keus, Johanna E, Hein G. Gooszen, Heuk J. and Cornelis J. Laarhoven. Randomized clinical trail of small incision and laparoscopic cholecystectomy in patients with symptomatic cholecystolithiasis. Arch. Surg. 2008; 143 (4): 371 – 377.
26. A W Majeed et al. A randomized prospective single – blind comparison of laparoscopic versus small – incision cholecystectomy. The Lancet 1996; 347: 989 – 93.
27. Vagenas K, Spyrakopoulos P and others. Mini – laparotomy cholecystectomy versus laparoscopic cholecystectomy: which way to go? Surg. Endosc. Percutan. Tech. 2006 Oct; 16 (5): 321 – 4.
28. Saleem Akhtar, Asim Kamran, Muhammad Nadeem Aslam, Abrar Ashraf Ali, Khalid Massood. A comparative study of laparoscopic versus mini – cholecystectomy. Ann King Edward Med Coll, Apr. – Jun 2001; 5 (2): 159 – 61.
29. Keus F, De Jong JA, Gooszen HG, Van Laarhoven CJ. Laparoscopic versus open cholecystectomy for patients with symptomatic cholecystolithiasis. Arch. Surg. 2007; 118 (4): 235 – 8.
30. Cuschieri A, Dubois F and others. The European experience with laparoscopic versus mini – laparotomy cholecystectomy. The Amer. J. of Surg. 1993; 161: 385 – 7.
31. Jeffrey S Barkun, Alan Barkun, Jonathan L. laparoscopic versus open cholecystectomy: the Canadian experience. The Amer. J. of surg. 1996; 165: 455 – 8.
32. The Souther Surgeons' Club: A prospective analysis for 1518 laparoscopic cholecystectomies. N. Engl. J. Med. 1993; 324: 1973 – 8.
33. National J. Soper, Ralf Clagman. Comparison of early post – operative results for laparoscopic versus open cholecystectomy. Surgery – Gynaecology and Obstetrics, 1995; 174: 114 – 7.
34. Rhodes M, Fenn N, Rees G J, Lawrie B. comparative complication rates from laparoscopic cholecystectomy. Surg. Endosc. 1999; 10: 256.
35. Vargas C, Jeffers L J. Diagnostic Laparoscopy: a 5 years experience in hepatology training program. The Amer. J. of Gastroenterol. 1997; 90: 1258 – 62.

The New Iraqi Journal of Medicine | **Review Article**

Advances in surgery: laparoscopic surgery

Ahmed Al Mamar *

The N Iraqi J Med, December 2011; 7(3):88-90

Laparoscopic surgery, also called minimally invasive surgery (MIS), bandaid surgery, keyhole surgery is a modern surgical technique in which operations in the abdomen are performed through small incisions (usually 0.5–1.5 cm) as compared to the larger incisions needed in laparotomy.Keyhole surgery uses images displayed on TV monitors for magnification of the surgical elements. Laparoscopic surgery includes operations within the abdominal or pelvic cavities, whereas keyhole surgery performed on the thoracic or chest cavity is called thoracoscopic surgery. Laparoscopic and thoracoscopic surgery belong to the broader field of endoscopy.There are a number of advantages to the patient with laparoscopic surgery versus an open procedure. These include reduced pain due to smaller incisions and hemorrhaging, and shorter recovery time.

The key element in laparoscopic surgery is the use of a laparoscope. There are two types: [1] a telescopic rod lens system, that is usually connected to a video camera (single chip or three chip), or [2] a digital laparoscope where the charge-coupled device is placed at the end of the laparoscope, eliminating the rod lens system. Also attached is a fiber optic cable system connected to a 'cold' light source (halogen or xenon), to illuminate the operative field, inserted through a 5 mm or 10 mm cannula or trocar to view the operative field. The abdomen is usually insufflated, or essentially blown up like a balloon, with carbon dioxide gas. This elevates the abdominal wall above the internal organs like a dome to create a working and viewing space. CO_2 is used because it is common to the human body and can be absorbed by tissue and removed by the respiratory system. It is also non-flammable, which is important because electrosurgical devices are commonly used in laparoscopic procedures [1].

Phillip Bozzini is credited with developing the first cystoscope, although it was never used in humans. In 1805, he developed a system of candles and mirrors to examine canine bladders [2–4] During the 19th century, lenses, light sources, and endoscopes evolved, and surgeons and internists performed cystoscopy, proctoscopy, laryngoscopy, and esophagogastroscopy.3 In 1901, German surgeon George Kelling used a cystoscope through the abdominal wall to evaluate the effect of pneumoperitoneum in dogs, inventing the technique of "celioscopy."[2–6] After enduring harsh criticisms from the medical community, he later applied his technique to humans, publishing his results in 1910.

In 1910, Hans Christian Jacobaeus of Sweden reported the first laparoscopic operation in humans. He was credited with coining the term "laparoscopy" ("laparothorakoskopie") [5] He began his animal experiments in 1901, inserting cystoscopes without pneumoperitoneum.4 He subsequently reported his clinical experience with 17 laparoscopies using pneumoperitoneum, and 2 thoracoscopies in 1910. He also was subjected to criticism [7].

A German gastroenterologist, Heinz Kalk, developed a superior laparoscope with improved lenses and the first forward viewing scope in 1929, earning him the title "Father of Modern Laparoscopy."[3] Kalk pioneered in many diagnostic techniques, including a safe technique for laparoscopic liver biopsy.

In the 1930s, internist John Ruddock popularized laparoscopy in the United States. Using a forward-viewing scope similar to Kalk's, he extolled the virtues of diagnostic laparoscopy as a safer, less-invasive alternative to laparotomy.The goal of minimally invasive surgery (MIS) was clearly

* *General Surgeon , United Arab Emirat*
E-mail: mamar_66@yahoo.com

identified. In 1933, gynecologist Karl Fervers described laparoscopic lysis of adhesions using cautery[4,5,8].Three years later, Boesch, a Swiss gynecologist, performed the first laparoscopic sterilization by electro coagulation of the fallopian tubes[2,3,7]. These breakthroughs paved the way for operative laparoscopy, but progress was very slow [3, 8].

During the mid-1960s and 1970s, gynecologist Kurt Semm in Kiel, Germany, contributed greatly to laparoscopic technology. He perfected many technical refinements, including an automated insufflator, the suction irrigator, safer electrocoagulation instruments, intracorporeal and extracorporeal knot tying, and an electrical morcellator for myomas [2, 4]. In 1971, gynecologist and SLS past president Harrith Hasson contributed to the safety of laparoscopy, developing the Hasson trocar with the open entry technique. In 1983, Kurt Semm performed the first laparoscopic appendectomy, bringing him criticism and censor rather than accolades. The German Board of Surgery condemned him [2, 9, 10]. The first surgeon to perform a laparoscopic cholecystectomy met with a similar fate. German surgeon Erich Muhe used his "galloscope," a 3-cm, direct vision laparoscope of his own design to remove a gallbladder. He presented his work at the 1986 Congress of the German Surgical Society. He, too, suffered skepticism and criticism and was ultimately censored by the courts [9, 10, 11].

Over period of decades numerous individuals refined and popularized the approach further for laparoscopy. The start of computer chip television camera was a seminal event in the field of laparoscopy. This technological innovation provided the means to project a magnified view of the operative field onto a monitor and, at the same time, freed both the operating surgeon's hands, thereby facilitating performance of complex laparoscopic procedures. Prior to its conception, laparoscopy was a surgical approach with very limited application, used mainly for purposes of diagnosis and performance of simple procedures in gynecologic applications.

The first publication on Diagnostic Laparoscopy by Raoul Palmer appeared in the early 1950s, followed by the publication of Frangenheim and Semm. Hans Lindermann and Kurt Semm practiced CO2 hysteroscopy during the mid-1970s.

In 1972, Clarke invented, published, patented, presented, and recorded on film laparoscopic surgery, with instruments marketed by the Ven Instrument Company of Buffalo, New York, USA [9]

In 1975, Tarasconi, from the Department of Ob-Gyn of the University of Passo Fundo Medical School (Passo Fundo, RS, Brazil), started his experience with organ resection by Laparoscopy (Salpingectomy), first reported in the Third AAGL Meeting, Hyatt Regency Atlanta, November 1976 and later published in The Journal of Reproductive Medicine in 1981[10] This Laparoscopic Surgical Procedure was the first Laparoscopic organ resection reported in the Medical Literature.

In 1981, Semm, from the Universitats Frauenklinik, Kiel, Germany, performed the first Laparoscopic Appendectomy. Following his lecture on Laparoscopic Appendectomy, the President of the German Surgical Society wrote to the Board of Directors of the German Gynecological society suggesting suspension of Semm from medical practice. Subsequently, Semm submitted a paper on Laparoscopic Appendectomy to the American Journal of Obstetrics and Gynecology, at first rejected as unacceptable for publication on the ground that the technique reported on was ' unethical,' but finally published in the Journal Endoscopy[11] . Semm established several standard procedures that were regularly performed, such as ovarian cyst enucleation, myomectomy, treatment of ectopic pregnancy and finally laparoscopic-assisted vaginal hysterectomy (nowadays termed as cervical intra-fascial Semm hysterectomy). He also developed a medical instrument company Wisap in Munich, Germany, which still produces various endoscopic instruments of high quality. In 1985, he constructed the pelvi-trainer = laparo-trainer, a practical surgical model whereby colleagues could practice laparoscopic techniques. Semm published over 1000 papers in various journals. [11] He also produced over 30 endoscopic films and more than 20,000 colored slides to teach and inform interested colleagues about his technique. His first atlas, More Details on Pelviscopy and Hysteroscopy was published in 1976, a slide atlas on pelviscopy, hysteroscopy, and fetoscopy in 1979, and his books on gynecological endoscopic surgery in German, English, and many other languages in 1984, 1987, and 2002.

Prior to 1990, the only specialty performing laparoscopy on a widespread basis was gynecology, mostly for relatively short, simple procedures such as a diagnostic laparoscopy or tubal ligation. The introduction in 1990 of a laparoscopic clip applier with twenty automatically advancing clips (rather than a single load clip applier that would have to be taken out, reloaded and reintroduced for each clip application) made general surgeons more comfortable with making the leap to laparoscopic cholecystectomies (gall bladder removal). On the other hand, some surgeons continue to use the single clip appliers as they save as much as $200 per case for the patient, detract nothing from the quality of the clip ligation, and add only seconds to case lengths.

Laparoscopic cholecystectomy is the most common laparoscopic procedure performed. In this procedure, 5-10mm diameter instruments (graspers, scissors, clip applier) can be introduced by the surgeon into the abdomen through trocars (hollow tubes with a seal to keep the CO_2 from leaking). Dr. Eddie Joe Reddick of Nashville, TN was the pioneer of laparoscopic cholecystectomies in the U.S., and was instrumental in teaching other surgeons the procedure and establishing the technique as the standard of care for gall bladder removal. Over one million cholecystectomies are performed in the U.S. annually, with over 96% of those being performed laparoscopically

REFERRENCES

1.Mastery of Endoscopic and Laparoscopic Surgery W. Stephen, M.D. Eubanks : Steve Eubanks (Editor); Lee L, M.D. Swanstrom (Editor); Nathaniel J. Soper (Editor) Lippincott Williams & Wilkins 2nd Edition 2004

2. Litsky GS. Highlights in the History of Laparoscopy: the Development of Laparoscopic Techniques–a Cumulative Effort of Internists, Gynecologists, and Surgeons. Frankfurt: Barbara Bernert Verlag; 1996

3. Nezhat C, Page B. Let There Be Light: an Historical Analysis of Endoscopy's Ascension Since Antiquity. Available at: http:// laparoscopy.blogs.com/endoscopyhistory. Accessed January 2008.

4. Nezhat F. Triumphs and controversies in laparoscopy: the past, the present, and the future. JSLS. 2003;7:1–5.

5. Vecchio R, Macfayden BV, Palazzo F. History of laparoscopic surgery. Panminerva Med. 2000;42:87–90.

6. Litsky GS, Paolucci V. Origin of laparoscopy: coincidence or surgical interdisciplinary thought. World J Surg. 1998;22:899–902.

7. Litsky GS. Endoscopic surgery: the history, the pioneers.World J Surg. 1999;23:745–753. 8. Kaiser AM, Corman MI. History of laparoscopy. Surg Oncol Clin N Amer. 2001;10:483– 492.

9. Clarke HC . "Laparoscopy—new instruments for suturing and ligation". Fertil. Steril 1972 23 (4): 274–7.

10.Tarasconi JC . "Endoscopic salpingectomy". J Reprod Med 1981; 26 (10): 541–5 11.Semm K . "Endoscopic Appendectomy". Endoscopy 1983 ; 15 (2): 59–64.

The New Iraqi Journal of Medicine | **Review Article**

Therapeutic advances in renal cell carcinoma

Aamir Jalal Al Mosawi*, Hashim Nasir**

Abstract

Renal cell carcinoma (RCC) continues to represent an important proportion of the cancer landscape in many countries. The mainstay of treatment is radical nephrectomy for localized disease, and until recently, the treatment options for patients with either unrespectable or metastatic renal cell carcinoma were limited. Important therapeutic advances in the management of patients with advanced renal cell carcinoma have occurred during the previous decades. Prior to the advent of targeted therapy, the prognosis of patients with metastatic renal cell carcinoma was very poor, with a median survival of one year and a five-year survival of 0%–20%.

The landscape for renal cell carcinoma treatment has changed dramatically in recent years, with the addition of three new FDA-approved agents this year. This brings our arsenal to seven drugs: interleukin-2, the VEGF receptor TKI's sunitinib, sorafenib, and pazopanib, the VEGF neutralizing antibody bevacizumab in combination with interferon, and the mTOR inhibitors temsirolimus and everolimus.The aim of this paper is to briefly review the important therapeutic advances in RCC.

The N Iraqi J Med, April 2011`;7(3):91-95

Keywords: *RCC, new agents, therapeutic advances*

Renal cell carcinoma (RCC) continues to represent an important proportion of the cancer landscape in many countries [1,2,3]. The mainstay of treatment is radical nephrectomy for localized disease, and until recently, the treatment options for patients with either unresectable or metastatic renal cell carcinoma were limited. Important therapeutic advances in the management of patients with advanced renal cell carcinoma have occurred during the previous decades. Prior to the advent of targeted therapy, the prognosis of patients with metastatic renal cell carcinoma was very poor, with a median survival of one year and a five-year survival of 0%–20% [4].

One of the major achievements was the recognition that RCC is not a single disease but a compilation of different histologic types, each caused by different genetic mutations affecting different molecular pathways. In fact, four distinct genes have now been well described as a cause for the different types of RCC. Understanding of these genetic alterations and pathways has resulted in several new medications approved for use in the treatment of metastatic RCC and many more in clinical trials at the present time [5, 13].

The landscape for renal cell carcinoma treatment has changed dramatically in recent years, with the addition of three new FDA-approved agents this year. This brings our arsenal to seven drugs: interleukin-2, the VEGF receptor TKI's sunitinib, sorafenib, and pazopanib, the VEGF neutralizing antibody bevacizumab in combination with interferon, and the mTOR inhibitors temsirolimus and everolimus. Treatment of metastatic renal cell carcinoma involved immunotherapeutic agents such as interferon (IFN-α) or interleukin-2 (IL-2). IFN-α has been shown to provide a benefit in terms of overall survival compared to inactive therapy but with an average response rate between 10%–15%

* *Advisor Doctor, Iraqi Ministry of Health*
E-mail: almosawiaj@yahoo.com
** *General practitioner*

and few durable responses. High dose IL-2 (infusion therapy requiring hospitalization) has a higher overall and complete response (CR) rate compared with low-dose cytokines (subcutaneous, outpatient), with the real benefit realized in the small percentage (5% to 7%) of patients who experience adurable CR. The patient most likely to obtain a durable CR with high-dose IL-2 includes the young, previously untreated patient with clear-cell histology RCC, ECOG performance status 0, and limited volume metastatic disease to lung. The morbidity and lack of applicability of high dose IL-2 to the broad RCC population has dampened enthusiasm for this approach, although it remains a valid treatment option in a very limited subset of patients [14, 15].

Adjuvant and neoadjuvant treatments for RCC represent an important opportunity for reducing the risk of disease recurrence, and potentially expanding the group of patients cured of this cancer. Adjuvant trials of cytokine-based therapies have been disappointing, demonstrating lack of improvement over surgical treatment alone, or in some cases trends toward shortened survival [16, 17]. Recent efforts to implement novel strategies of immune system modulation have been the first to demonstrate a potential for improved outcome. In the 10-year survival analysis of a study of autologous tumor lysate vaccine adjuvant therapy, a trend was showed toward increased survival in all patients, with a statistically significant improvement observed for patients with T3 tumors. In multivariate analysis, the T3 tumor subgroup continued to demonstrate improved survival, HR=1.67, p=0.011 [18]. In a move toward advancing targeted anti-angiogenesis therapy to the adjuvant setting, a small study was performed at MD Anderson Cancer Center exploring the use of adjuvant thalidomide. Forty six patients were enrolled to a randomized study of observation vs. thalidomide 300mg daily for 24 months. The two- and three-year cancer-specific survivals were not improved with treatment, and the thalidomide-treated patients actually had poorer survival at two and three years (47.8% vs. 69.3% and 28.7% vs. 69.3%, respectively; P = .022) [19].

Much attention is being focused on several ongoing studies testing the adjuvant use of VEGF receptor tyrosine kinase inhibitor (TKI) therapy. Despite the failure of thalidomide to demonstrate activity in this venue, evidence from the metastatic disease setting suggests that the VEGF-receptor TKIs are much more potent against RCC. Multiple studies are ongoing and anticipated to complete enrollment in the coming year. These studies include: the ASSURE study, randomizing patients with completely resected clear cell tumor larger than 4cm to 1 year of sunitinib, sorafenib, or placebo, at conventional doses; the SORCE study, randomizing completely resected RCC tumors (any histology) in Europe that are intermediate or high risk according to the Leibovich score [20] to one year or three years of sorafenib at standard dose, or placebo; and finally, a smaller study comparing standard dose sunitinib to placebo (randomized 2:1) . While these studies will take time to fully mature, they will provide immediate demonstration of the acute and longer term side effects of prolonged therapy in otherwise quite healthy individuals, and ultimately represent the most promising avenue of potential risk reduction for patients facing high risk for recurrence.

With drugs that can induce initial tumor shrinkage, it has become relevant to determine whether implementation of pre-operative treatment can impact primary tumors to reduce tumor bulk prior to surgery. Such an intervention may permit less invasive surgical approaches, or render “unresectable” disease “resectable,” or provide an opportunity to gain control of systemic disease prior to removal of the primary mass. Several studies have begun to evaluate these approaches. The use of bevacizumab was investigated in the pre-operative setting for patients undergoing cytoreductive nephrectomy. This study of 50 patients showed responses in the primary tumor, but led to wound dehiscence in three patients, likely due to the long half life of the antibody [21]. Retrospective studies of a variety of VEGF pathway targeted agents with widely varied durations of therapy prior to surgery showed the approach was feasible [22, 23]. Sunitinib treatment until best response was employed in 19 patients with inoperable tumors, with four proceeding to nephrectomy without encountering any unexpected surgical morbidity [24]. A prospective study using sorafenib in a 4–8 week window prior to surgery and continuing to within 48 hours of surgery defined the safety risks, which were minimal, and showed a response in the primary tumor similar to that observed for systemic disease [25]. This study also highlighted the necessity for pretreatment biopsy, as two of the 30 patients on the study were found at nephrectomy to have non-renal cell primary tumors. Overall, these approaches are rational to consider for selected patients, appear to pose minimal risk for decline in performance status for surgery, and can achieve responses in primary tumors. Further investigation is necessary to determine the patient groups most likely to benefit from neoadjuvant therapy, and whether risk for disease recurrence can be reduced. In addition, the optimal duration of treatment prior to surgery needs to be defined.

Sunitinib has emerged as the current standard of care for first line therapy for patients with good or intermediate risk clear cell RCC. However, sorafenib remains an appropriate first line

choice for selected patients, and recently pazopanib has received FDA approval, adding a third agent in this crowded field. With prolonged experience and exposure to these drugs, cardiac toxicity related to sunitinib has become a concern. Patients with pre-existing hypertension and coronary heart disease compose the group at greatest risk for encountering these effects [26]. Preclinical analysis suggests that sunitinib may be directly toxic to cardiac myocytes [27]. The lasting effects of sunitinib exposure to endothelial and other tissues remain largely unknown. It is concerning that administration of high dose IL-2 after sunitinib failure has showed a high incidence of severe cardiac toxicity, suggesting that damage may remain for some time after TKI therapy is discontinued [28]. Ultimately, what is becoming clear is the need to aggressively manage toxicities in order to maintain patients on optimally dosed therapy and avoid detrimental long-term complications [29, 30].

Effective disease control has been inferred from significant improvements in progression-free survival. Now with more substantial follow up, the front-line study of sunitinib vs. interferon has showed an overall survival benefit (26.4 v 21.8 months, p = 0.51), even in the setting of 65% of the interferon patients crossing over to receive sunitinib or another VEGF pathway targeted agent [31]. This survival benefit is modest, but suggests that additional consideration to questions such as when to initiate therapy (early vs. late) may be important to investigate formally.

RCCs initially responding to treatment with VEGF TKI therapy eventually develops resistance to these drugs is also of considerable impotence. Kinase mutations that cause resistance to drugs like imatinib do not appear to play a role here. Ongoing studies suggest angiogenic escape mechanisms may contribute to this process [32]. One experiment examining xenografts resistant to sorafenib showed that they regain sensitivity when transplanted into new hosts [33].

An alternate mechanism of targeted therapy for RCC is the inhibition of mTOR signaling via disruption of the mTORC1 complex. While the activities of mTOR inhibitors (temsirolimus and everolimus being the only rapalogues approved for RCC) on cancer cells remains an active area of investigation, we have learned how to strategically place them in the treatment of RCC patients. In the front line setting, temsirolimus has continued to be the mainstay for patients with poor risk disease, given the improvement in overall survival and it's good side effect profile [34]. This year everolimus was approved based on a study that evaluated this drug after disease progression on one or both VEGF receptor TKIs [35, 36]. Patients showed a

doubling of progression-free survival. Thus, the mTOR pathway provides an ideal scenario for switching drug classes upon disease progression.

Combining two or more agents has employed two basic approaches. “Vertical inhibition” describes combinations of therapies that target factors working in a linear signaling pathway, as opposed to “Lateral inhibition” which implies inhibiting targets from non-overlapping pathways [37]. The first example of vertical inhibition showed that maximally inhibiting the VEGF signaling pathway with bevacizumab.

inhibition of soluble VEGF ligand in combination with inhibition of VEGF receptor signaling with sorafenib could increase response rate, but at the expense of increased toxicity [38].

Lateral inhibition takes the form of combinations of VEGF targeted agents and mTOR inhibitors. The combination of sunitinib with temsirolimus unfortunately showed unacceptable toxicity, particularly a high incidence of microangiopathic hemolytic anemia [39]. Bevacizumab has been amenable to combinations in many settings, and tolerable doses have been identified for combination with temsirolimus; an ongoing study is evaluating the bevacizumab/temsirolimus combination vs. bevacizumab/interferon.

REFERRENCES

1. Cancer Facts and Figures 2009. American Cancer Society, Inc: 10. 2009.
2. Jemal A, Siegel R, Ward E, Hao Y, Xu J, Thun MJ. Cancer Statistics, 2009. *CA Cancer J Clin*. 2009;59(4):225–49.
3.Hollingsworth JM, Miller DC, Daignault S, Hollenbeck BK. Rising incidence of small renal masses: A need to reassess treatment effect. J Natl Cancer Inst 2006;98:1331–1334.
4. Linehan WM, Zbar B, Bates BE, Zelefsky MJ, Yang JC. Cancer of the Kidney and Ureter. In: deVita VT HS, Rosenberg SA, editors. *Cancer Principles and Practice of Oncology, 6th ed*. Philadelphia, PA: Lippincott Williams and Wilkins. 2001:1362–96.
5. Linehan WM, Walther MM, Zbar B. The genetic basis of cancer of the kidney. J Urol 2003;170:2163–2172.
6. Linehan WM. Genetic basis of bilateral renal cancer: Implications for evaluation and management. J Clin Oncol 2009; 27:3731–3733.
7. Bratslavsky G, Sudarshan S, Neckers L, Linehan WM. Pseudohypoxic pathways in renal cell carcinoma. Clin Cancer Res 2007;13:4667–4671.
8. Lopez-Beltran A, Carrasco JC, Cheng L, Scarpelli M, Kirkali Z, Montironi R. 2009 update on the classification of renal epithelial tumors in adults. Int J Urol 2009;16:432–443.
9. Linehan WM, Vasselli J, Srinivasan R, Walther MM, Merino MJ, Choyke P, et al. Genetic basis of cancer of the kidney: Disease-specific approaches to therapy. Clin Cancer Res 2004;
10:6282S–6289S.
10. Rosner I, Bratslavsky G, Pinto PA, Linehan WM. The clinical implications of the genetics of renal cell carcinoma. Urol Oncol 2009;27:131–136.
11. Feldman DR, Motzer RJ. Novel targets and therapies for metastatic renal cell carcinoma. Oncology (Williston Park) 2006;20:1745–1753.
12. Kruck S, Merseburger AS, Gakis G, Kramer MW, Stenzl A, Kuczyk MA. An update on the medical therapy of advanced metastatic renal cell carcinoma. Scand J Urol Nephrol 2008; 42:501–506.
13. Rini BI, Bukowski RM. Targeted therapy for metastatic renal cell carcinoma: A home run or a work in progress? Oncology (Williston Park) 2008;22:388–396.
14. Cohen HT, McGovern FJ. Renal-Cell Carcinoma. *N Engl J Med*. 2005; 353(23):2477–90.
15. Fisher RI RS, Fyfe G. Long-term survival update for high-dose recombinant interleukin-2 in patients with renal cell carcinoma. *Cancer J Sci Am*. 2000; 6 Suppl 1:S55–7.
16. Messing EM, Manola J, Wilding G, Propert K, Fleischmann J, Crawford ED, Pontes JE, Hahn R,Trump D. Phase III study of interferon alfa-NL as adjuvant treatment for resectable renal cell carcinoma: an Eastern Cooperative Oncology Group/Intergroup trial. J Clin Oncol 2003;21:1214–
1222.
17. Clark JI, Atkins MB, Urba WJ, Creech S, Figlin RA, Dutcher JP, Flaherty L, Sosman JA, Logan TF,White R, et al. Adjuvant high-dose bolus interleukin-2 for patients with high-risk renal cellcarcinoma: a cytokine working group randomized trial. J Clin Oncol 2003;21:3133–3140.
18. May M, Brookman-May S, Hoschke B, Gilfrich C, Kendel F, Baxmann S, Wittke S, Kiessig ST, Miller K, Johannsen M. Ten-year survival analysis for renal carcinoma patients treated with an autologous tumour lysate vaccine in an adjuvant setting. Cancer Immunol Immunother. 2009 Oct 30;[Epub ahead of print].
19. Margulis V, Matin SF, Tannir N, Tamboli P, Shen Y, Lozano M, Swanson DA, Jonasch E, Wood CG. Randomized trial of adjuvant thalidomide versus observation in patients with completely resected high-risk renal cell carcinoma. Urology 2009;73:337–341.
20. Leibovich BC, Cheville JC, Lohse CM, Zincke H, Frank I, Kwon ED, Merchan JR, Blute ML. A scoring algorithm to predict survival for patients with metastatic clear cell renal cell carcinoma: a stratification tool for prospective clinical trials. J Urol 2005;174:1759–1763. discussion 1763.
21. Jonasch E, Wood CG, Matin SF, Tu SM, Pagliaro LC, Corn PG, Aparicio A, Tamboli P, MillikanRE, Wang X, et al. Phase II presurgical feasibility study of bevacizumab in untreated patients with metastatic renal cell carcinoma. J Clin Oncol 2009;27:4076–4081. [PubMed: 19636008]
22. Thomas AA, Rini BI, Stephenson AJ, Garcia JA, Fergany A, Krishnamurthi V, Novick AC, Gill IS, Klein EA, Zhou M. Surgical resection of renal cell carcinoma after targeted therapy. J Urol 2009;182:881–886. [PubMed: 19616232]
23. Amin C, Wallen E, Pruthi RS, Calvo BF, Godley PA, Rathmell WK. Preoperative tyrosine kinase inhibition as an adjunct to debulking nephrectomy. Urology 2008;72:864–868. [PubMed: 18684493]
24. Thomas AA, Rini BI, Lane BR, Garcia J, Dreicer R, Klein EA, Novick AC, Campbell SC. Response of the primary tumor to neoadjuvant sunitinib in patients with advanced renal cell carcinoma. J Urol 2009;181:518–523. discussion 523.
25. Cowey CL, Amin C, Pruthi RS, Wallen EM, Nielsen ME, Grigson G, Watkins C, Nance KV, Crane J, Jalkut M, et al. A Neoadjuvant Clinical Trial with Sorafenib for Patients with Stage II or Greater Renal Cell Carcinoma. J Clin Oncol. 2010 In Press.
26. Di Lorenzo G, Autorino R, Bruni G, Carteni G, Ricevuto E, Tudini M, Ficorella C, Romano C, Aieta M, Giordano A, et al. Cardiovascular toxicity following sunitinib therapy in metastatic renal cell carcinoma: a multicenter analysis. Ann Oncol 2009;20:1535–1542. [PubMed: 19474115]
27. Chintalgattu V, Patel SS, Khakoo AY. Cardiovascular effects of tyrosine kinase inhibitors used for gastrointestinal stromal tumors. Hematol Oncol Clin North Am 2009;23:97–107. viii–ix.
28. Cho DC, Puzanov I, Regan MM, Schwarzberg T, Seery V, Lee MY, Liu V, Bhatt R, Koon H, Mier JW, et al. Retrospective analysis of the safety and efficacy of interleukin-2 after prior VEGF-targeted therapy in patients with advanced renal cell carcinoma. J Immunother 2009;32:181–185.
29. Shepard DR, Garcia JA. Toxicity associated with the long-term use of targeted therapies in patients with advanced renal cell carcinoma. Expert Rev Anticancer Ther 2009;9:795–805.
30. Robert C, Mateus C, Spatz A, Wechsler J, Escudier B. Dermatologic symptoms associated with the multikinase inhibitor sorafenib. J Am Acad Dermatol 2009;60:299–305.
31. Motzer RJ, Hutson TE, Tomczak P, Michaelson MD, Bukowski RM, Oudard S, Negrier S, Szczylik

C, Pili R, Bjarnason GA, et al. Overall survival and updated results for sunitinib compared with
interferon alfa in patients with metastatic renal cell carcinoma. J Clin Oncol 2009;27:3584–3590.
32. Rini BI, Atkins MB. Resistance to targeted therapy in renal-cell carcinoma. Lancet Oncol
2009;10:992–1000.
33. Panka D, Kumar M, Schor-Bardach R, Atkins M. Mechanism of acquired resistance to sorafenib in RCC. AACR Proceedings. 2008 2500.
32. Bhatia S, Thompson JA. Temsirolimus in patients with advanced renal cell carcinoma: an overview.Adv Ther 2009;26:55–67.
34. Motzer RJ, Escudier B, Oudard S, Hutson TE, Porta C, Bracarda S, Grunwald V, Thompson JA,Figlin RA, Hollaender N, et al. Efficacy of everolimus in advanced renal cell carcinoma: a doubleblind, randomised, placebo-controlled phase III trial. Lancet 2008;372:449–456.
35. Oudard S, Medioni J, Aylllon J, Barrascourt E, Elaidi RT, Balcaceres J, Scotte F. Everolimus
(RAD001): an mTOR inhibitor for the treatment of metastatic renal cell carcinoma. Expert Rev Anticancer Ther 2009;9:705–717.
36. Sosman JA, Puzanov I, Atkins MB. Opportunities and obstacles to combination targeted therapy in renal cell cancer. Clin Cancer Res 2007;13:764s–769s.
37. Sosman J, Puzanov I. Combination targeted therapy in advanced renal cell carcinoma. Cancer
2009;115:2368–2375. [PubMed: 19402058]
38. Fischer, P, Patel, P,Carducci, MA, McDermott, DF, Hudes, GR, Lubiniecki, GM,Gelder, MS,Senico, P, Curiel, RE,Motzer, RJ. Phase I study combining treatment with temsirolimus andsunitinib malate in patients with advanced renal cell carcinomaP, ASCO Annual Meeting Proceedings, 2008; p. 16020

The New Iraqi Journal of Medicine

Short communication

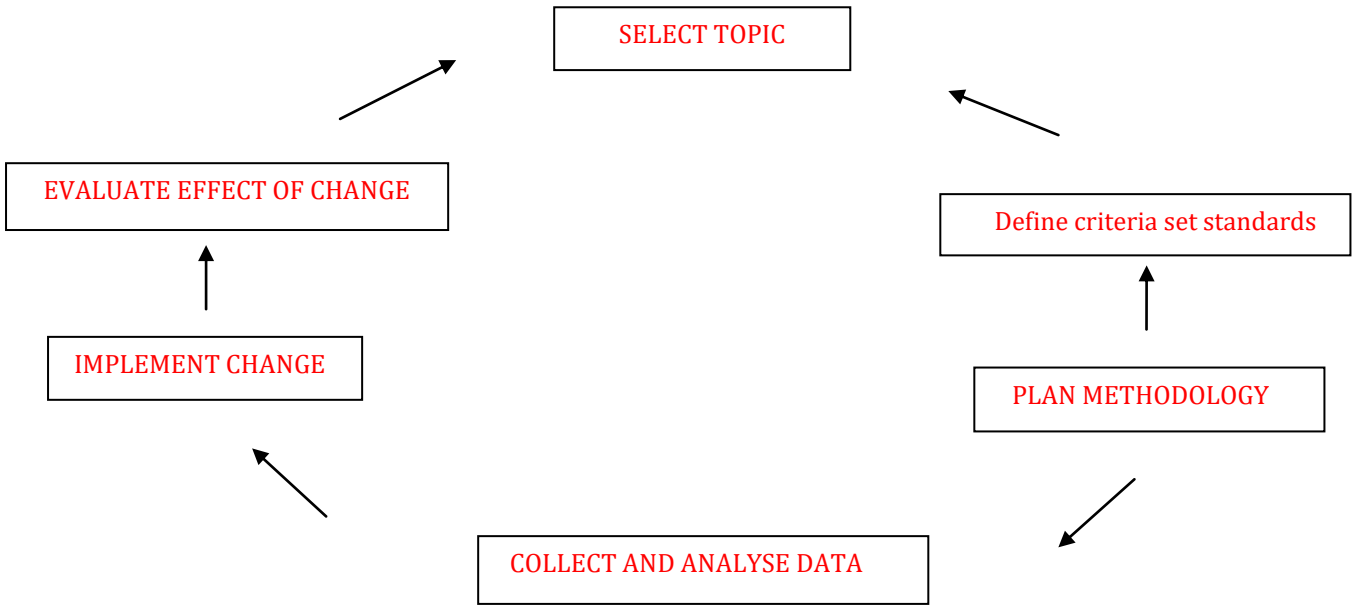
The principle of audit explained

Modhar Mouyed Mahmoud *

The N Iraqi J Med, December 2011; 7(3):96-100

A quality improvement process that seeks to improve patient care and outcome through systematic review of care against explicit criteria and the implementation of change .Aspect of the structure, process and outcomes of care are selected and systematically evaluated against explicit criteria .Where indicated, changes are implemented at an individual, team or service level and further monitoring is used to confirm improvement in health care delivery. (NICE *2003).

The clinical Audit process is known as the audit cycle, this has been diagrammatically displayed as below:



Email: modharmouyed@yahoo.com

Clinical audit is a quality improvement process and therefore benefits of undertaking audit include:

1- Promotes good practice

2- Provides opportunity for training and educations.

3- Increase efficiency by ensuring better use of resources.

4- Improve service outcome by improving professional practice and the quality of service delivered.

Audit versus research

Research aims to establish new knowledge for best practice. Clinical audit tell us if we are following the best practice.

The result of research can be generalised. Clinical audit has local influence on clinical practice.

Research based on hypothesis, while clinical audit measure against standards.

Research is a one off study .Audit is ongoing process.

Research may involve degree of experimentation on patients. Clinical audit never involves anything happening to patient which is different from their normal treatment.

Research deals with complex data, while audit usually involves simple data.

An example of Audit is the central venous catheter audit carried out in Royal Derby Hospital NHS Trust.

Background

. Central venous catheters (CVC's) are commonly used in managing the critically ill and in surgical patients undergoing major procedures .They are inserted for monitoring central venous pressure and for infusing drugs and other fluids .Their use is associated with complications, however, one of which is infection and scrupulous attention to hygiene and aseptic practice is therefore essential to reduce the risk of catheter associated infections**.**

This audit of aseptic practice during central venous catheter insertion was undertaken for three reasons:

1- To assess how closely medical practitioners adhered to the Critical Care guidelines for CVC* insertion, specifically those aspects of the guidelines covering asepsis and hygiene.

2 - To see if there was a difference in practice between the intensive care units and the operating theatres. Microbiological evidence suggested that the number of CVC associated infections appeared to be higher in the step-down unit* than the intensive care units. As most of the step-down patients came directly from theatres and had their lines inserted in theatre a difference in practice might have explained the difference in infection rate.

3) To provide evidence of CVC insertion practice to DHFT's* Infection Control Committee as part of Saving Lives initiative.

Methods

From October to January 2010-2011 medical practitioners were observed during insertion of CVC'S in the ITU*.And the operating theatres of Derby Hospitals NHS foundation trust .Adherence to recommended practice in the CVC insertion guidelines was documented for each 10 criteria during catheter inserted. Observation and documentation were performed by medical and nursing staff and operating department practitioners.

Data Analysis Results

The insertion of 67 CVC'S was observed of which 32 occurred in the operating theatres and 35 in the intensive care units

The 32 theatres CVC's were placed in the following sites (number of catheters in brackets):

Internal jugular (28)

Subclavian (2)

Femoral (1)

Antecubital fossa PICC line (1)

The 35 ICU* CVC's were placed in the following sites:

Internal jugular (27)

Subclavian (4)

Femoral (4)

Standards /Guidelines

The following criteria are recommended in the Critical Care CVC insertion guidelines and a yes /no response was required from the observer for each of these.

1-Medical staff scrubs and wears sterile gown and gloves.

2. Assembling of necessary equipment with full asepsis.

3. Lines aspirated and flushed after insertion.

4. Ensures that an alcohol bases aseptic solution is used.

5. Cleans site using concentric circles moving towards the periphery.

6. User allows the aseptic solution to dry before insertion of line.

7. User maintains a good sterile field around site of insertion.

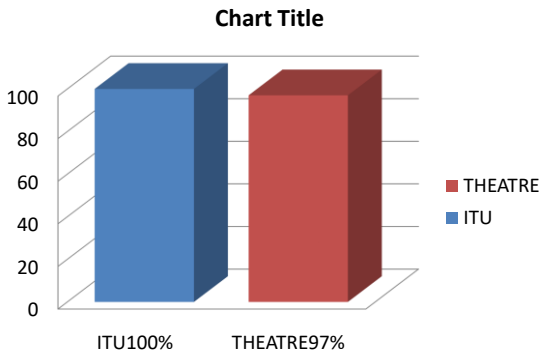
8. Uses a sterile cover for Sonosite (ultrasound) probe.

9. If gel used on skin with Sonosite was it sterile.

10. Does the user cover the site with a sterile, transparent dressing.

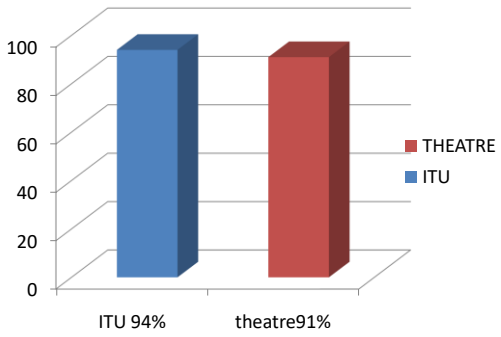
The results for the 10 criteria covered in the audit are displayed in the following bars

ALCOHOL BASED ANTISEPTIC TECHNIQUE

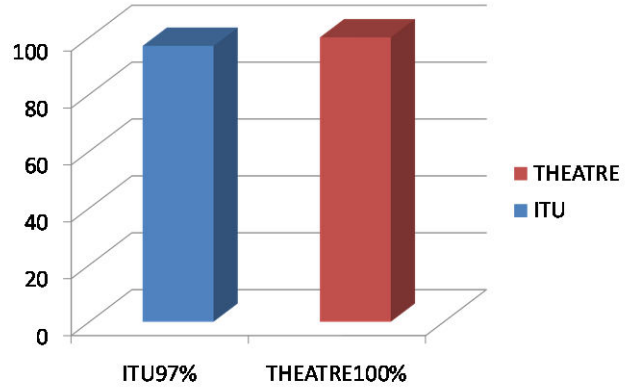


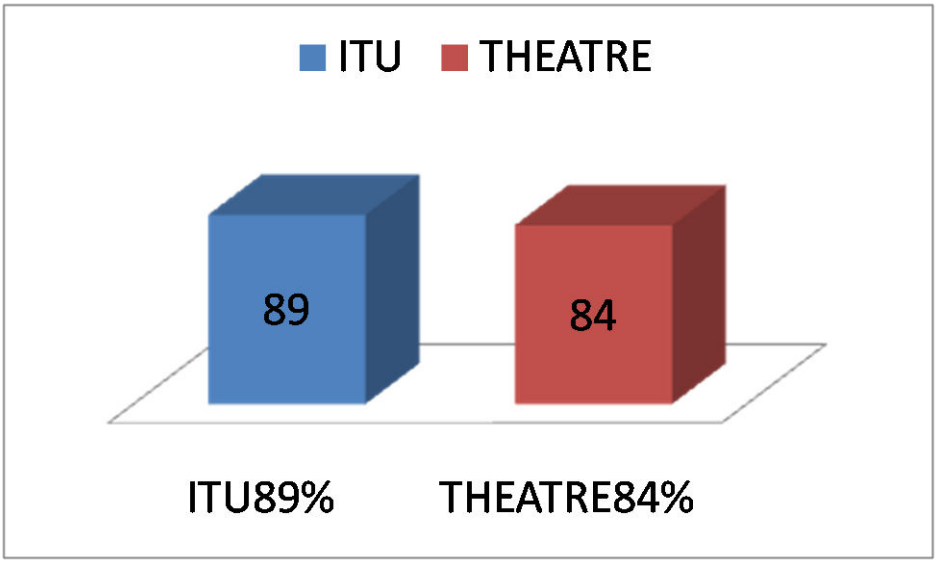
.

- SCRUBS+GOWN+GLOVES



- ASSEMBLES EQUIPMENT WITH FULL ASEPSIS





ALLOWS ANTISEPTIC TO DRY

Criteria	theatre	ITU
Lines aspirated and flushed	94%	97%
Clean using concentric circles	56%	69%
Maintains good antiseptic	94%	97%
Sterile cover of sonosite	97%	97%
Use of sterile gel	96%	94%
Use of sterile dressing	100%	100%

TABLE 1 SHOWING THE RESULTS OF THE ANALYSIS OF OTHER CRITERIA

Conclusion & Recommendation

1) Overall there was good adherence to the guidelines in both the operating theatres and intensive care units .In 8 out of 10 of the selected guideline criteria there was over 90% compliance in both ITU and theatre.

2)The 2 areas where compliance was below 90% were in cleaning the skin using concentric circles moving outwards and in letting the antiseptic dry before inserting the catheter. It is necessary to allow the antiseptic to dry before catheter insertion to ensure maximal disinfection and this point needs to be reinforced during infection control training.

3)There does not appear to be a difference in practice for CVC insertion between ICU and the operating theatres to explain the difference in infection rates between the ICU and step down units.

RE-AUDIT

Good aseptic practice during central venous catheter Insertion is essential to minimise hospital acquired infection and ICU and theatre should be regularly audited. We would recommend that this be done on an annual basis so the next suggested time period would be 2011-2012.

Glossary

NICE (national institute of clinical excellence), CVC (central venous catheter), DHFT (Derby Hospital Foundation Trust), ITU=ICU (intensive therapy (care) unit. Step down unit: is a unit that provides care intermediate between ICU and normal ward

Letter To The Editor

Over diagnosis of typhoid fever: Action is needed

Majid Hameed Jasim

The N Iraqi J Med, April 2012; 7(3):101

Typhoid or enteric fever is one of the communicable diseases that are distributed widely in developing countries and the tropic. Here in my country (Iraq) unfortunately this disease is excessively over diagnosed by many PHC doctors and general practitioner till we reached a situation where thousands of people falsely but strongly believe that they got the disease , some annually and even seasonally in others. Most people attribute irrelevant symptoms like dizziness, mild headache, fatigue and anorexia to typhoid fever despite the absence of fever! And they believe that they must be prescribed an injectable antibiotic to be cured and they crave for even a single injection. These false believe that makes the patient preoccupied by the idea that he has typhoid I called it typhoid neurosis. The reason for this is that some doctors send their patient for Widal test for any symptom and based on this burned out test they erroneously convince their patient with the disease. I consider this as a major health problem in my city. I constantly see at least 10 patients daily in my practice as consultant in internal medicine having this problem and most of them were subjected to a prolonged unnecessary course of antibiotic. To overcome this major health problem we have to work at different levels, first we should target the junior doctors and general practitioners by incorporating them in tutorials about the symptoms, the diagnosis and management of the disease. Secondly we have to target the people through the readable, the heard and the visible media. By solving this problem we are going to reduce the load on doctors, preserve health resources like laboratory materials and expensive broad spectrum antibiotics and protect people from unnecessary exposure to drugs.

* ***AlFao General Hospital***
E-mail: dr_majid79@yahoo.com