

Original Research Article

Prevention of Infective Endocarditis, Should Developing Country have Concern with the Guidelines?

Atif H. Alzahrani¹, Mona A. Kholeif¹, Abeer Al Shukairi², Areej Mufti³ and Abdulhalim Jamal Kinsara^{1*}

Abstract

¹Department of cardiology, Ministry of National Guard health Affair, Jeddah, Saudi Arabia. King Abdullah International medical research center, King Saud Bin Abdulaziz University for Health Sciences, COM-WR

²Infectious Diseases Department- King Faisal Specialist Hospital and Research Center,

³Microbiology Division, Department of Pathology and Laboratory Medicine, At King Saud bin Abdulaziz University for Health Sciences, COM-J. King Abdul Aziz Medical City-WR.

*Corresponding Author's Email: kinsaraaj@ngha.med.sa
Tel 966-12-2266666, ext. 25797

The published guidelines of Infective endocarditis (IE) markedly restricting the use of antibiotic prophylaxis for prevention of IE resulted in some controversy. The aim of this study is to attempt to answer the question – Should the developing country have a concern of rising incidence of IE with the current guidelines? Retrospective analysis of all reported cases of definitive IE based on modified Duke Criteria in tertiary hospital over a 5-year period. 20 reported cases of IE, 9 males (45%) and 11 females, mean age 36 years (12 days- 72 years); one patient had history of rheumatic heart disease, 4 patients (20%) had congenital heart disease. 14 patients (70%) had history of a prior procedure. Blood cultures were positive in 16 patients (80%), with culture-negative IE in 4 patients. The most common organisms were *Staphylococcus* spp. In 9 patients (45%), *Enterococcus* spp. Was isolated in 2 patients (10%), Gram negative bacilli isolated in 2 patients, one *Enterobacter* and one *Acinetobacter* *baumannii*. There was one case of streptococcal IE, the usual target for prophylactic antibiotics and the patient had received prophylactic antibiotics peri-procedurally. Most organisms were acquired nosocomially and/or after procedures which did not require prophylactic antibiotics under any previous or current guidelines. IE is uncommon disease in our practice representing only 0.017% of total admissions and complicating only one dental procedure out of 101,825. The current guidelines for IE antibiotic prophylaxis did not carry extra risk in developing country, but preferably we may continue to collect relevant data.

Keywords: Infective Endocarditis, developing country, Antibiotic Prophylaxis

INTRODUCTION

Although Infective Endocarditis (IE) is a relatively rare disease worldwide, with an estimated incidence between 3 and 10 cases per 100 000 per year, mortality and morbidity of patients with this disease belong to the highest in cardiology (Que and Moreillon, 2011; Connaughton and Rivett, 2010). Despite recent advances in the diagnosis including transeosophageal echocardiography, serology and molecular assays, as well as progress in therapeutic methods – medical and surgical

management – the prognosis still remains poor, with a one-year mortality of 20 – 25%, reaching 50% at 10 years (Que and Moreillon, 2011; Connaughton and Rivett, Provide year). Incidence of IE has not declined over recent years, but the patterns of predisposing and precipitating conditions, as well as its microbiology, have changed (Connaughton and Rivett, 2010; Murdoch et al., 2009; Tornos et al., 2011). This has resulted in extensive reviews of IE and the development

of guideline recommendations limiting the use of prophylactic antibiotics for its prevention (Que and Moreillon, 2011; Connaughton and Rivett, 2010; Murdoch et al., 2009; Tornos et al., 2011; Martin et al., 2018).

A recent article had examined the impact of the guideline of antibiotic prophylaxis prescribing against infective endocarditis. It noted that it was fell among all risk groups, with a significant increase in IE incidence among high-risk individuals, a borderline significant increase in moderate-risk individuals, and no change for those at low/unknown risk. Data do not establish a cause-effect relationship but warrants further investigation (Thornhill et al., 2018).

In another study, IE risk in some 'moderate-risk' patients noted to be similar to that of several 'high-risk' conditions and higher than repaired congenital heart conditions (Wilson et al., 2007).

Classically, Streptococci have been the main causative microorganisms of IE but recently, *Staphylococcus aureus* has been detected more frequently, in accordance with the growing numbers of hospital procedures and IV Drug Abuse cases and has become the dominant pathogen in many countries (Que and Moreillon, 2011; Connaughton and Rivett, 2010; Murdoch et al., 2009; Tornos et al., 2011). After echocardiography was incorporated into the diagnostic criteria, culture negative IE has also been recognized as an important subset (Durack et al., 1994). The current patterns of IE in developing countries are not clearly defined, making it difficult to decide on the most appropriate course of action with regards to current recommendations on antibiotic prophylaxis for its prevention. The aim of this retrospective study is to evaluate the microbiology of IE in addition to the risk factors (predisposing cardiac conditions and precipitating procedures) for developing IE in our institution over 5 years.

METHODS

This retrospective study was conducted at tertiary hospital in Jeddah, Saudi Arabia, and covered last 5-year period. The study received approval from the Hospital Research Committee. We conducted a search for definite IE by 2 methods. Firstly, we identified cases with a discharge diagnosis of IE from a hospital computer database and hand-searched the files. Secondly, we identified all cases of bacteremia involving organisms' known to cause IE from a laboratory database, and then reviewed the echocardiography studies conducted within 4 weeks from the time of the positive culture. We then reviewed the files of all patients who had both bacteremia and echocardiographic criteria consistent with IE. The modified Duke criteria were used in the diagnosis of IE in

our series. Only patients who met the Duke "definitive" criteria for IE were included. The data collected included age, sex, predisposing factors, precipitating procedures, causative organism, and cardiac involvement on echocardiogram, treatment and outcome.

RESULTS

We identified 20 patients with IE admitted to the hospital. This represents 0.017% of total admissions of 115152 patients to the hospital. The total number of patients who visited the Dental OPD during the same period was 101825 patients. We identified only one case of IE, which may have been precipitated by dental procedure. Patient characteristics: The male to female ratio was 1:1.2; 9 males and 11 females. The mean age was 36.02 years (range 12 days –72 years). Predisposing conditions: 4 patients (20%) have congenital heart disease (1 VSD, 1 PDA, 1 PFO, 1 common atrium). One patient had known Rheumatic Heart Disease. 15 patients (75%) had no predisposing cardiac conditions

Precipitating procedures: Table 1 summarizes the precipitating procedures. 5 patients (25%) are oncology patients having Porta Cath or Hickman catheter, 3 patients (15%) had ESRD on hemodialysis through temporary central lines or permcath, 3 patients (15%) are NICU preterm with central lines and one patient (5%) had bladder cancer with bilateral nephrostomy tubes. One patient had history of dental extraction one month before developing IE (this patient also had history of rheumatic heart disease and poor oral hygiene). Another patient had necrotizing pancreatitis post-laparotomy with 2 abdominal drains complicated later by multiple intra-abdominal abscesses, developing IE 2 weeks later. Other risk factors: One patient was known as IV drug abuser and one patient had sepsis secondary to pneumonia. Microbiology: Blood cultures were positive in 16 patients (80%) and 4 patients had negative cultures. The most commonly isolated organisms were *Staphylococcus* spp. in 9 patients, 7 were *Staph aureus* (5 methicillin sensitive and 2 methicillin-resistant) and 2 were coagulase-negative *Staph. Enterococcus* spp. isolated in 2 patients, one of whom was *Enterococcus faecium*, table 2. *Candida* spp., non-albicans, were isolated in 2 patients both known cases of acute lymphocytic leukemia. Other isolates were two gram negative bacilli (10%) (1 *Enterobacter* and 1 *Acinetobacter* *Bummani*) and 1 *streptococcus viridans* (5%). Aortic valve was more affected, details cardiac involvement identified on echocardiography summarized in Table 3. 4 patients died in hospital and *Staph. Aureus* (MSSA) was responsible for mortality in 2 patients (Table 4). *Enterococcus*.spp was responsible for one death. 14 patients (70%) had history of procedure 11 patients (55%) had central line either temporary or permanent. 3 of the 11 patients were

Table 1. Precipitating procedures

Precipitating Procedures	No.	%
Oncology patients with portacath	5	25
ESRD on haemodialysis through temporary central Line or permcath	3	15
Preterm in NICU with central line	3	15
Dental extraction	1	5
Nephrostomy tube	1	5
Laparotomy	1	5
No procedure	6	30

Table 2. Blood culture results in 16 patients with infective endocarditis

Causative Organism	No	%
Staphylococcus aureus	7	43.75
Methicillin-sensitive	5	31.25
Methicillin-resistant	2	12.5
Coagulase-negative staph	2	12.5
Enterococcus spp.	2	12.5
Gram negative bacilli	2	12.5
Streptococcus viridans	1	6.25
Candida spp.	2	12.5

Table 3. Cardiac involvement based on echocardiography findings

Cardiac involvement	No	%
Native valves:	12	60
Aortic valve (AV)	5	25
Mitral valve (MV)	3	15
Both AV & MV	1	5
Tricuspid valve	3	15
Pulmonary valve	0	0
Prosthetic valves	0	0
Right Atrium (RA)	3	15
Junction of Superior Vena Cava & RA	2	10
RA & Left Atrium	1	5
Moderator band in Right Ventricle	1	5
Pacing Wire + RA	1	5

Table 4. Death-related microorganism

Micro-organism	No	%
Staph. aureus (MSSA)	2	50
Enterococcus spp (VRE)	1	25
No organism	1	25

preterm infants and were diagnosed with congenital heart disease during their NICU admission.

DISCUSSION

Our study result showed that IE is an uncommon in our

study with Staph.spp the most common organism 8 patients (88%) acquired Staph.spp nosocomially and 1 patient is IV drug abuse. Only one patient had Strept. viridans IE in this study. Two cases of IE caused by coagulase negative Staphylococci. There is a growing body of evidence that identification of this heterogeneous group up to the species level is demanding for IE cases.

Staphylococcus lugdunensis is a virulent coagulase-negative Staph; well known to cause complicated IE with a considerably rate of mortality. Its identification and antimicrobial sensitivity testing results can be misled owing to the laboratory method used (Oropello and Babu, 2011; Becker et al., 2014). The same is applicable for *Candida-not albicans* where *Candida parapsilosis*, *Candida glabrata*, and *Candida tropicalis* are the most common causes (Peter et al., 2016; Pelemiš et al., 2013). 15 patients (75%) had no predisposing cardiac condition and no previous IE; so, they would not have been eligible for IE prophylaxis under the current guidelines. 6 patients (30%) had no precipitating procedure and one of them is IV drug abuse. Again, such episodes of IE would not have been prevented by adopting any IE prophylaxis protocols. The patient who had Streptococcal IE one month after a dental procedure is the only patient in whom the disease could perhaps have been prevented. However, this patient in fact had received prophylactic antibiotics in keeping with hospital policy at that time.

We identified two previous reviews of IE in Saudi Arabia (Nashmi and Memish, 2007; Al-tawfiq and Sufi, 2009). In both series Staph spp, particularly Staph aureus, were the most commonly identified organisms. Procedures precipitating IE were not clearly outlined, but the fact that Staph spp was the most common organism in both series, suggests that procedures, other than dental or gastroenterology /genitourinary, the targets of previous prophylaxis measures, were involved. Although IE guidelines do not consider differences in the incidence, presentation, priorities and available resources in different countries it should not be a barrier to adopting such guidelines (Elbarbary, 2009).

CONCLUSION

This study demonstrates that the pattern of IE in developing countries do not varied with the adoption of restricting prophylaxis as per the current guidelines. Efforts and funds may be better directed towards improving antiseptic techniques in relation to insertion of lines and other procedures, as well as improving oral hygiene in general. The number of cases we identified in this study was small. Further surveillance is needed to confirm our findings.

REFERENCES

- Al-tawfiq JA, Sufi I (2009). Infective endocarditis at a hospital in Saudi Arabia: epidemiology, bacterial pathogens, outcome. *Ann Saudi Med.*; 29: 433- 436.
- Becker K, Heilmann C, Peters G (2014). Coagulase-negative staphylococci. *Clin Microbiol Rev.*; 27:870-926.
- Connaughton M, Rivett JG (2010). Easily missed? Infective Endocarditis. *BMJ* 201; 341
- Durack DT, Lukes AS, Bright DK (1994). New criteria for diagnosis of infective endocarditis: Utilization of specific echocardiographic findings: Duke Endocarditis Service. *Am J Med*; 96: 200-209.
- Elbarbary M (2009). International Guidelines: Adoption or adaptation by the Saudi Heart Association? *J Saudi Heart Assoc.* Jul; 21(3): 181-6.
- Lefort A, Chartier L, Sendid B, Wolff M, Mainardi JL, Podglajen et al. (2012). Diagnosis, management and outcome of Candidaendocarditis. *Clinical Microbiology and Infection.* (18): E99-109
- Martin H. Thornhill, Teresa B. Gibson, Eli Cutler, Mark J. Dayer, Vivian H. Chu, Peter B. Lockhart, Patrick T. O'Gara and Larry M (2018). Baddour. Antibiotic Prophylaxis and Incidence of Endocarditis Before and After the 2007 AHA Recommendations. *JACC* (72): 20, DOI: 10.1016/j.jacc.2018.08.2178
- Murdoch DR, Corey GR, Hoen B, Miro JM, Fowler VG Jr, Bayer AS et al. (2009). International Collaboration on Endocarditis – Prospective Cohort Study Investigators. Clinical presentation, etiology, and outcome of infective endocarditis in the 21st century: the International Collaboration on Endocarditis-Prospective Cohort Study. *Arch Intern Med*; 169: 463-73.
- Nashmi A, Memish Z (2007). Infective endocarditis at a tertiary care centre in Saudi Arabia: review of 47 cases over 10 years, *East Mediterr Health J.* 13:64-71.
- Oropello J. babu E (2011). *Staphylococcus lugdunensis*: the coagulase negative staphylococcus you don't want to ignore. *Expert Rev Anti Infect Ther.* 9:901-7.
- Pelemiš M, Stevanović G, Lavadinović L, Matic S, Milošević I, Korać Metal (2013). A rare case of *Candida parapsilosis* endocarditis in a young healthy woman – case report. *J. Cardiothoracic Surgery*; 8:29
- Peter G. Pappas Carol A. Kauffman David R. AndesCornelius J. Clancy Kieren A (2016). Marr Luis et al. Clinical Practice Guideline for the Management of Candidiasis: 2016 Update by the Infectious Diseases Society of America. *Clinical Infectious Diseases.* (62), e1–e50,
- Que YA, Moreillon P (2011). Infective endocarditis. *Nat Rev Cardiol*; 8: 322– 36.
- Thornhill MH, Jones S, Prendergast B, et al. (2018). Quantifying infective endocarditis risk in patients with predisposing cardiac conditions. *Eur Heart J.* 39:586–595.
- Tornos P, Gonzalez-Alujas T, Thuny F, Habib G (2011). Infective endocarditis: the European viewpoint. *Curr Probl Cardiol.* 36: 175-222.
- Wilson W, Taubert KA, Gewitz M, Lockhart PB, Baddour LM, Levison M et al. (2007). Prevention of Infective Endocarditis: Guidelines from the American Heart Association: A Guideline from the American Heart Association Rheumatic Fever, Endocarditis and Kawasaki Disease Committee. *Circulation*; 116: 1736-54.