Assessment of CXCL-16 Chemokine and Body Mass Index in Patients with Renal Impairment Attending Aminu Kano Teaching Hospital Kano.

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Abstract

Background: Renal impairment and its various complications are associated with enormous economic burden, increased morbidity and mortality as such; obtaining an early biomarker for this disease is crucial. The aim of this study was to assess the serum levels of CXCL-16 and Body Mass Index in patients with renal impairment attending Aminu Kano Teaching Hospital, Kano. **Materials and Methods:** A total of 111 patients with renal impairment (64 males and 47 females) and 56 apparently healthy controls with age between 4-70 years were used for the study. Blood samples were collected from the participants and serum urea and creatinine were determined using Urease Berthelot's reaction and Alkaline picrate methods respectively, while serum CXCL-16 was determined using quantitative enzyme linked immunosorbent assay technique and BMI was calculated using the weight and height of the subjects using standard techniques. **Results:** This study reveals that, higher frequency of 51.4 % was observed in patients within the range of 18-45 years while lower frequency of 9.9% was observed in patients age<18 years. Males recorded higher frequency of 57.7% while females recorded a frequency of 42.3% with the ratio of 1.36:1 and higher frequencies of 60.4% was observed in BMI of 18- 24.9 kg/m^2. The mean serum urea, creatinine and CXCL-16 were significantly ($p = 0.00$) higher in patients group compared with controls., while BMI was significantly ($p < 0.000$) lower in patients group compared with controls. A significant positive (p=0.00) correlation was established between serum creatinine and urea ($r = 0.95$, p=0.00) and between CXCL-16 with creatinine and urea ($r = 0.99$, p=0.00 and $r = 0.98$, $p = 0.00$respectively). **Conclusion:** The result revealed significantly higher level of serum urea, creatinine and CXCL-16 chemokine with lower in BMI in patients with renal impairment. Hence, patients who present with symptoms of this condition may be recommended for CXCL-16 chemokine analysis, which may serve as an early biomarker for the diagnosis of kidney disease.

Key words: CXCL-16 Chemokine, Urea, Creatinine, Renal Impairment, inflammation**.**

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INTRODUCTION

Renal impairment is the inability of the kidney to exert an excretory function which leads to the retention of nitrogenous waste in the blood (1).Kidney is recognized as one of the most common target organs of toxicity and urinary tract diseases that induce a slow and gradual decrease in kidney function, reinforced by several factors including infections, autoimmune diseases, diabetes and other endocrine disorders, cancer and toxic chemicals (2). Mortality from kidney disease in the form of nephritis is the eighth leading cause of death, and hypertensive kidney failure is not far behind, ranking 13th among the most common causes of death and morbidity (3).It is associated with numerous disorders such as anaemia, mineral and bone disorders, cardiovascular risk, renal haemodynamic changes among others (4).

CXCL-16 is a pro-inflammatory cytokine that belongs to the CXC chemokine subfamily (5)CXCL-16, which was originally described as a receptor for phosphatidylserine and low density oxidized lipoproteins (oxLDL), promotes the adhesion of cells expressing its related receptor, CXCR6 (6).In humans, the CXCL-16 gene is found on chromosome 17p13, in a locus separate from all other known chemokines (5).CXCL-16 has been reported to be expressed in immune cells such as dendritic cells, macrophages, B cells, T cells, smooth muscle cells, endothelial cells and platelets (7,8,9).In the kidney, CXCL-16 is expressed constitutively by human mesangial cells, podocytes and tubular cells, mainly distal tubular cells and main cells of the collecting duct and is weakly expressed in the thick ascending loop of Henle (10,11).The infiltration of inflammatory cells into the kidney intervenes in the appearance and progression of damage by direct cytotoxicity, the secretion of soluble factors such as cytokines or chemokines by the induction of the immune response (12).CXCL-16 in the kidney causes chemotaxis of kidney immune cells following injury and may cause kidney failure leading to increased morbidity and mortality in this group of patients (13).

Body mass index (BMI), is the relationship between weight and height (kg / m^2), it is a common indicator for measuring obesity or low weight in adults (14).A high or low BMI may be associated with kidney failure, but a high BMI is linked to multiple metabolic disorders which may act as a risk factor (15).The rational of this study is to assess theCXCL-16 chemokine and BMI in patients with renal impairment attending Aminu Kano teaching hospital Kano.

MATERIALS AND METHODS

The study was a case control study evaluating concentration of CXCL-16 chemokine in patients with renal impairment attending Aminu Kano Teaching Hospital (AKTH), Kano. The subjects comprised of 111patients with renal impairment that were referred from Nephrology Units of Departments of internal Medicine and Paediatrics, AKTH, Kano. Fifty-six (56) apparently healthy volunteers were used as controls, participant's age range was between 4-70 years. Serum CXCL-16 Chemokines was measured by ELISA technique using reagents supplied by Kuancheng District, Changchun Jilin Province, China. Urea was measured by Urease-Berthelot method using test kit procured from Randox Laboratories, England (16, 17) and creatinine using Jaffe:s method (18).Body Mass Indexwas determined using standard technique as described by WHO (19).

Statistical Analysis

Data was analyzed using SPSS version 21.0 statistical software. The Mean and Standard Deviation were computed and results were expressed as mean±SD. Student t-test was used to compare differences between means. Correlation was performed using Pearson's Correlation Coefficient. Statistical significance was set at $p<0.05$.

Ethical Consideration

This study was approved by the Ethical Committee of Aminu Kano Teaching Hospital Kano, with a Reference number AKTH/MAC/SUB/12A/P-3/VI/2647 dated 10th July, 2019. The purpose and the procedure of the study were explained to all participants and a written informed consent was obtained from the participants before samples were collected.

RESULTS

The results obtained from the present study are presented in Tables 1-4 respectively. Table 1 depicts the distribution of patients according to age and gender. Higher frequency was observed in age range 18 - 45 years with percentage frequency of 51.4 % and lower frequency was observed in those < 18 years with percentage frequency of 9.9%.The male had higher frequency of 64 (57.7%) than the females with frequencyof 47 (42.3%) and with a ratio of 1.36:1.

Table 1: Distribution of Patients according to Age and Gender

Age group (yrs)	Frequency (%)	Gender	Frequency (%)
<18	11(9.9)	Male	64 (57.7)
18-45	57(51.4)	Female	47 (42.3)
>45	43(38.7)	Male to Female Ratio	1.36:1

***Yrs**= Years; **%**=percentage*

Table 2:Distribution of Body Mass Index in Patients and Controls

Variables		Patients (n=111)		Controls (n=56)	
Grade	BMI(kg/m^2)	Frequency	Percentage (%)	Frequency	Percentage (%)
Underweight	<18	7	6.3	2	3.6
Normal	18-24.9	67	60.4	33	58.9
Overweight	25-29.9	32	28.8	12	21.4
Moderate Obesity	30-39.9	5	4.5	9	16.1
Morbid obesity	>40	0	0	0	0

***BMI**= Body Mass Index; **n**= Number; **%**=percentage*

Table 2 shows the distribution of patients and controls groups according to Body Mass Index. Higher frequency was observed in patients and controls with BMI of 18- 24.9 kg/m^2 with percentage frequency of 60.4% and 58.9% respectively while, lower frequency was observed in BMI of >40 with

percentage frequency of 0% in both patients and controls.

Table 3 shows, serum urea, creatinine, CXCL-16 and BMI in patients and controls. The mean± SD of serum urea (18.24±17.54mmol/L), creatinine (494.70±343.44µmol/L) and CXCL-16(62.21±18.89 ng/L) of patients were significantly (p = 0.00) higher compared with controls (3.76±1.20 mmol/L,64.57±18.98µmol/L and 50.22±13.25ng/Lrespectively). The BMI of patients (22.81±3.73 kg/m^2) was significantly (p = 0.03) lower when compared with corresponding values of controls (24.24±4.38kg/m^2).Correlation of serum creatinine, urea and CXCL-16 among participants is shown in Table 4. There was significant positive correlation between serum creatinine and urea(r=0.95, p=0.00) and between serum CXCL-16 with each of creatinine (r=0.99, p=0.00)and urea (r = 0.98, p = 0.00).

Table 3: Serum Urea, Creatinine, CXCL-16 and BMI (Mean±SD) in Patients and Controls

Parameter	**Patients (n=111)**	**Controls (n=56)**	***t-value***	***p-value***
BMI(kg/m^2)	22.81±3.73	24.243±4.38	-2.14	0.03
Urea(mmol/L)	18.24±17.54	3.76±1.20	6.16	0.001*
Creatinine(µmol/L)	494.70±343.44	64.57±18.98	9.35	0.001*
CXCL-16 (ng/L)	62.22±18.89	50.22±13.25	4.25	0.001*

*P≤ 0.05 (significant of t-test) for patient Vs Control for Analysis *; n=Number of Subjects; BMI= Body Mass Index*

Table 4: Correlation of Creatinine, Ureaand CXCL-16among patients

Parameters	**Patients (n=111)**	
	r-value	***p-value#***
Cr & Ur	0.95	0.001
CXCL-16 & Cr	0.99	0.001
CXCL-16 &Ur	0.98	0.001

*#=determined by Pearson's correlation;*P= Correlation is significant at ≤ 0.05 levels (2-tailed); r = strength of correlation; n=Number of Subject; Ur=Urea; Cr=Creatinine;* &= and.

DISCUSSION

Kidney failure and its various problems are related with a huge financial burden, increased morbidity and mortality (20). It is caused by many kidney and urinary tract diseases that result in a slow and gradual decline in renal function. These diseases

include urinary tract infections, auto immune diseases, cancer, direct effect of toxic chemicals, diabetes and other endocrine disorders (2).Obtaining an early biomarker for this disease is therefore crucial. Cytokines are signalling molecules produced by several immune cells and perform a variety of functions, including immune system mediation and inflammatory responses (21). Assessing the level of CXCL-16 chemokine in the form of a chemotactic cytokine could be of great importance for early detection of renal impairment.

In the current study, high proportion of renal diseases was observed in age range between 18-45 years with percentage frequency of 51.4%, this is similar to the report of Okwuonu et al. (22) in Edo, Nalado et al. (23) in Kano, Nigeria and Zhao et al. (24) in China, but it is at variance with findings of Coresh et al.(25)in USA,where the highest proportion was observed in age >45 years with percentage of 47%. This may be due to increased risk factors for renal impairment such as diabetes, hypertension and cardiovascular diseases (CVD) among this age group (26). From our findings, Males had higher percentage of renal impairement (57.7%) than Females (42.3%). This result is similar to the findings of Nalado et al. (23) in Kano, Nigeria where Males had higher percentage of (83.6%) than Females (16.4%) and Elewa et al.(27) in Madrid, Spain got similar finding with males having higher frequency (68.7%) than the females (31.3%).Contrary to our finding was in the study by Okwuonu et al. (22) in Umuahia, Abia state, where females had higher prevalence of (72%) than males (28%). Also, in the study conducted by Abene et al. (28), females had the higher prevalence of (64.7%) than Males (35.3%).

This may be due to increase in metabolic activities and poor blood pressure control seen more in males which are risk factors for renal impairment (29).The ratio of Male to Female is 1.36:1, which is slightly lower than 1.6:1 reported by Neugarten et al. (30). It is also in disagreement with the report of Oluyombo et al. (31) in Osun, Nigeria where the male to female ratio was 0.8:1. The rationale to this finding may be due to the fact that men have more rapid disease progressionand as age progresses, men tend to have greater chances of developing impaired renal function and increased glomerular sclerosis than women (32).

Our current study indicates that, the mean value of BMI was significantly lower among patients than the controls. This is similar to the reports of Chang et al. (33) in Taiwan and Zaman et al. (15) in Northeast of Thailand.The highest frequency of BMI was observed in normal weight with percentage frequency of 60.4% and the lowest frequency of BMI was observed in Moderate Obesity with percentage frequency of 0%. Our findings disagree with the report of Nalado et al. (23) where they had the highest percentage of 26.7% in overweight patients and lowest percentage of 11% in obese patients. It is also in contrast with the report of Devis et al.(34), in Australia with the highest frequency of 34.8% and lowest frequency of 8.6%.Increased uraemia-associated inflammatory cachexia, reduced nutritional eminence, anorexia, increased energy expenditure, decreased protein stores characterized by a low serum albumin and loss of muscle mass may be infer to our findings (35,36).

In the present study, the mean values of serum Creatinine and Urea were significantly higher in the patient group than the control group. Our finding is in conformity with the findings of Nisha et al. (37) in India and Zhao et al. (24) in China.

There is accumulation of creatinine and urea in the blood circulation due to impairment of kidney function resulting in their reabsorption, poor filtration and decrease Glomerular Filtration Rate (GFR) (38).

Current study revealed that, the mean serum CXCL-16 was significantly higher in the patient group than the control group. This is similar to the findings of Lin et al. (39) and Unal et al.(40) who reported that CXCL-16 concentration increases considerably in chronic kidney disease. This indicates that, CXCL-16 concentration increases considerably in kidney injury. In this finding, significant positive correlation was observed between CXCL-16 with Urea and Creatinine. This agreed with the report of Elewa et al. (27) in Madrid, Spain and Zhao et al. (24) in China. CXCL16 is expressed by injured tubular cells. Increase in serum urea and creatinine due to renal impairment and its associated decrease GFR may explain our findings (27).CXCL-16 molecules being an exceptional chemokine that is synthesized as transmembrane molecules and is known to be constitutively expressed even in the absence of inflammation (41), It promotes the progression of damage from acute inflammation to its progression, leukocyte trafficking control and migration to the site of kidney injury (42,43). Increased concentration of CXCL-16 could be an early indication of renal impairment particularly in patients with renal failure and its related complication such as diabetes mellitus, hypertension among others (43).

CONCLUSIONSAND RECOMMENDATIONS

Based on this study's findings, it can be concluded that, renal impairment is associated with decrease BMI, increase concentrations of serum creatinine, urea and CXCL16. A significant positive correlation was established between serum CXCL-16, creatinine and urea in patients with renal impairment.Further studies should be undertaken with large sample size, wider age range including neonate to augment our finding.CXCL-16 diagnosis and weight loss monitoring at regular intervals may be recommended for patients with renal impairment.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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