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ASSESSMENT OF LIPID PROFILE INPATIENTS WITH NEPHROTIC SYNDROME IN KANO METROPOLIS

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ABSTRACT

Nephrotic syndrome (NS) is a complex kidney disease associated with numerous complications which can subsequently lead to cardiovascular disease among others. This study was aimed at assessing the lipid profile, serum and urinary proteins of patients with Nephrotic syndrome (NS) in Kano metropolis. A total of 50 NS patients and 25 apparently healthy volunteers(controls) were recruited for the study, made up of 32 males and 18 females with the age range of 4-70 years. Blood and urine sample were collected from the participants. Serum urea and creatinine were determined using urease berthelot's reaction and Alkaline picrate methods. Serum total protein and albumin were assayed using Biuret and bromocresol green binding method through the manual colorimetrictechnique. Serum lipid profile were measured by an enzymatic spectrophotomeric method and the precipitation enzymatic method was specifically used for evaluating the levels of high-density lipoprotein cholesterol (HDL-C). Urine protein was determined using sulphur salicylic acid test. SPSS software package version 21 was used for the analysis of data. High frequency of NS of 40(80%) was observed in patients of <18 years while patient of >46 years had a lower frequency of 4(8%). Males recorded higher frequency of 32(64%) and the frequency of NS among females was 18(36%), thus the male to female ratio for NS was 1.78:1. The mean values of serum creatinine, urea, urinary protein (UP), total cholesterol (T.C), triglyceride (TG), low density lipoprotein cholesterol (LDL-C), T.C/HDL-C, TG/HDL-C, LDL/HDL-C ratio were significantly higher ($p<0.05$) in patients with NS than the healthy volunteers. Total protein (TP), albumin (Alb), globulin, HDL-C ratio were significantly lower ($p<0.05$) in NS when compared to healthy volunteers. There was positive correlation between UP and TC, TG and LDL, however, negative correlation was observed between UP and HDL-C with no statistical significance. Dyslipidemia, decreased serum protein and increase serum creatinine, Urea as well as UP were associated with NS. In conclusion, lipid profile and UP analysis may be a useful tool for diagnosis of NS and early diagnosis can reduce the disease morbidity.

Key words: Creatinine, Dyslipidemia, Lipoprotein, Nephrotic syndrome, Protein, Urea

INTRODUCTION

Nephrotic syndrome (NS) is a kidney disease associated with increased glomerular permeability, large proteinuria, hypoalbuminemia, dyslipidaemia and hypercoagulability (Adekoye*et al.*, 2011; Adu, 2013). It is usually accompanied with water and sodium retention and the degree to which this can manifest can vary from mild edema of the eyelids that decreases during the day - edema that affect the lower limbs - generalized body swelling (anasarca) (Behrman *et al.,* 2008). NS patients usually have proteinuria of greater than 3g/day and the common primary and secondary causes of NS include minimal-change nephropathy, focal glomerulosclerosis, membranous nephropathy and systemic diseases such as diabetes mellitus, lupus

erythematosus and amyloidosis (Behrman *et al.,*2008; Chan, 2008; Adu, 2013).Thus, in NS, the epithelial cell of the glomerulus and the tubularepithelium suffer a putative damage possibly as a result of traffic of macromolecules through them and prolonged proteinuria with its associated dyslipideamia and hypercoagulability (Agrawal *et al*., 2018; Basile*et al.,* 2012).Congenital and hereditary focal glomerulosclerosis can result from genetic mutations that code for podocyte proteins, including nephrine, podocin or cation channel protein 6,environmental causes of NS include drug abuse such as heroin (Behrman *et al.,* 2008).

Lipid profile is a panel of lipoproteins which usually includes Total cholesterol (TC), High-density lipoprotein cholesterol (HDL-C), Triglycerides (TG), and the calculated Low-density lipoprotein 'cholesterol (LDL-C) (Rosenson, 2020). Lipoproteins have a number of physiological uses such as regulation of energy metabolism, storage of adipose in tissue cells, contribute to structural components of cells as well as numerous important roles in different metabolic pathways (Isah *et al*, 2019). The levels of lipoproteins in bio fluids are used clinically for the diagnosis of cardiovascular disease and various lipid related disease, it also plays an important role in predicting the rate of the progression of glomerular dysfunction (Adu, 2013; Upadhyay, 2015; Rosenson, 2020).

There is scarcity of documented information on the pattern of lipid profile in this population of patients in Kano state. However, earlier studies have reported the lipid profile in NS from other populations (Anaja and Isah, 2017). The focus of this study was to assess the Lipid profile inpatients with NS in Kano metropolis.

MATERIALS AND METHODS

The study was a comparative cross-sectional study evaluating lipid profile in nephrotic syndrome patients, the research was conducted in Aminu Kano Teaching Hospital, (AKTH), Muhammad Abdullahi Wase Specialist Hospital (MAWSH) and Abubakar Imam Urology Centre. The study participants recruited included fifty (50) nephrotic syndrome (NS) patient and twenty-five (25) apparently healthy volunteers for comparison.

Serum total protein and albumin were assayed using Biuret and bromocresol green (BCG) binding method through the manual colorimetric techniques as described by Randox brand diagnostic test kit (Zheng*et al*., 2017). The level of serum globulin was obtained by subtracting the concentration of serum Albumin from serum the concentration of total protein obtained (Zheng *et al*., 2017). Urinary protein was assayed according to Turbidimetric methods using sulphosalicylic acid as described in the literature (Yalamati*et al*. 2016). Serum urea was measured by Urease-Berthelot method using standardized test kit (Randox Laboratories, England) (Fawcett and Scott, 1960), while creatinine was evaluated using Jaffe's method (Pardue*et al*., 1987). Total cholesterol was measured by the enzymatic colorimetric method, triglycerides by the glycerol phosphate oxidase method, High-density lipoprotein cholesterol (HDL-C) by the enzymatic colorimetric method (Fi-Fletcher, 1969; Lopes *et al*., 1977; Allain *et al*., 1979). The Low-density lipoprotein cholesterol (LDL-C) was calculated using Friedewald formula (Friedewald, *et al*., 1972). Atherogenic indices were defined by TC/HDL-C, TG/HDL-C and LDL-C/HDL-C.

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$\pm$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 the Aminu Kano Teaching Hospital Kano, with a Reference number NHREC/21/08/2008/AKTH/EC/2548 dated 10th July, 2019 and from Ministry of health, Kano state of Nigeria with a Reference number MOH/Off/797/T.I/1385. 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

Table 1 shows distribution of NS patients according to age and gender. The highest frequency 40(80%) of patients were <18years old while patients of >45 years made up only 4(8%) of the entire NS study population. There were more male NS patients 32(64%) when compared to females 18(36%), thus the ratio of male for female was 1.78:1.Table 2 shows the mean levels of serum protein, urea, creatinine and urinary protein in patients and controls. The mean values of total protein, albumin, globulin and urea were statistically significantly lower ($p< 0.05$) in the patient group when compared with the controls.

The mean values of serum creatinine and urinary protein were statistically significantly higher ($p< 0.05$) in the patient group than the control group.

Table 3 represents the mean value of serum lipid profile and androgenic indices in patients and controls. The mean value of HDL-C was statistically significantly lower ($p> 0.05$) in the patient group when compared with the control group. The mean values of TC, TG, LDL-C, TC/HDL-C, TG/HDL-C and LDL/HDL-C were statistically significantly higher ($p> 0.05$) in the patient group when compared to the control group.

The correlation of urinary protein (UP) levels with lipid profile among the study participantswas reported in Table 4.7. There were no statistically significant ($p>0.05$) correlation between UP and T. Chol, HDL-C, TG and LDL-C in both patients and controls groups (Table 4).

Table1: Distribution of Patients according to Age and Gender

Age group (yrs)	Frequency (%)	Gender	Frequency (%)
<18	40(80)	Male	32 (64)
18-45	6(12)	Female	18(36)
>45	4(8)	Male to Female Ratio	1.78:1

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

Table 2: Serum protein, urea, creatinine and urinary protein (Mean±SD) in patients and controls

Parameter n	Patients (50)	Controls (25)	*t-value*	*p-value*
Total Protein(g/l)	52.12±11.32	71.96±8.05	-8.736	0.000*
Albumin(g/l)	28.42±5.04	41.56 ±6.11	-9.298	0.000*
Globulin(g/l)	24.54±6.77	30.68±9.87	-3.163	0.002*
Urea(mmol/L)	2.41±0.81	5.51±2.38	-8.336	0.000*
Creatinine (umol/L)	106.92±20.35	88.32±22.65	3.465	0.001*
Urinary protein(g/l)	2.92±0.41	0.72±0.37	23.459	0.000*

*p≤ 0.05 (significant of t-test) for patient Vs Control for Analysis *; n=Number of Subject*

Table 3: Serum lipid profile and androgenic indices (Mean±SD) in patients and controls

Parameter n	Patients (50)	Controls (25)	*t-value*	*p-value*
TC(mmol/L)	7.33±3.18	4.64±0.70	4.170	0.000*
HDL-C(mmol/L)	0.73±0.30	1.02±0.39	-3.335	0.002*
TG(mmol/L)	1.60±0.77	1.16±0.49	2.541	0.013*
LDL-C(mmol/L)	5.76±2.96	3.07±0.58	4.504	0.000*
TC/HDL-C	12.26±7.51	5.46±3.18	4.333	0.000*
TG/HDL-C	2.76±1.91	1.63±2.36	2.090	0.043*
LDL-C/HDL-C	9.37±6.52	3.70±2.32	4.199	0.000*

**p≤ 0.05 (significance of t-test); n=Number of Subject; T.C=Total cholesterol; TG= Triglyceride; HDL-C= High Density Lipoprotein Cholesterol; LDL-C= Low density lipoprotein cholesterol*.

Table 4: Correlation of urinary protein with lipid profile among participants

	Patients n=50		Controls n=25	
Parameters	**R**	***P* Value#**	**r**	***P* Value#**
UP & TC	0.219	0.126	0.331	0.107
UP & HDL-C	-0.140	0.334	0.004	0.985
UP &TG	0.132	0.362	-0.235	0.257
UP &LDL-C	0.191	0.185	0.463	0.060

#P=Level of significance; r = Pearson's correlation*; n=Number of Subject; UP=Urinary Protein; TC=Total cholesterol; TG= Triglyceride; HDL-C= High Density Lipoprotein Cholesterol; LDL-C= Low density lipoprotein cholesterol*.

DISCUSSION

Nephrotic syndrome is a widespread disease that is associated with high morbidity due to its multiple complications associated with an increased risk of atherosclerosis and thromboembolism, which may be related to deregulated lipid metabolism and dyslipidemia (Agrawal *et al*., 2018). It is crucial to know the pattern of lipid profile which is very vital in various metabolic activities such as storing energy, signaling, and serving as structural components of cell membranes (Carvalho and Caramujo, 2018).

Our study reveals that, the highest frequency of 40 was observed in NS patients in<18years and a lower frequency of 4 in NS patients in>45 years. This is similar to the studies of Adedoyin *et al*. (2001); Obiagwu *et al*. (2014).The cause of NS in children may be idiopathic (Niaudet and Boyer, 2009; Vallepu *et al*., 2019), hence, children are more susceptible todiseases that can damage their kidneys, they also easily develop certain types of infections and largely have high effect of certain medications then adult, this may justify our findings (NIDDK, 2010).

In the current study, more males had nephrotic syndrome of (64%) than females (36%). This result was similar to the reports in the other populations (Safaei and Maleknejad, 2009; Desai *et al*., 2017; Anigilaje and Adesina, 2019). It has also been reported in earlier Nigerian studies that NS was more common in men than in women (Asinobi *et al.,* 2005; Anochie *et al.,* 2016; Ladapo*et al.,* 2019). In addition, the male to female ratio of 1.78:1 obtained in the current study was higher, similar and lower to those reported in some earlier studies (Safaei and Maleknejad, 2009; Alhassan *et al*., 2013; Varshney *et al*. 2015; Chang *et al*., 2016). The rationale to our finding may be due to a more rapid disease progression in male children. It may also be due to a higher chance for the deterioration in renal function and increased glomerular sclerosis in men compared to women due to some gender related factors (Schwartzman-Morrisand Putterman, 2012).

Our finding shows that, the mean values of total protein, albumin, globulin and urea were significantly decreased in comparison with control groups respectively, our results were in agreement with the results from the work of Arije *et al.* (1993) in Benin but different from the results of the work of Gherardi *et al.* (1977) in England. The inability of the body to compensate the lost albumin in the urine and also administration of corticosteroid drugs such as prednisone and cortisone may explain our finding (Noone *et al.,* 2018).

In the present study, the mean values of creatinine and urinary protein were statistically significantly higher in the patient group than the control group. Our reports agreed with Akinsola *et al.* (2017) in Ibadan, Oviasu *et al.* (2016) in Benin and Ifebunandu *et al.* (2012) in Enugu. Our finding is in contrary with the report of Huan *et al.* (2016) in China. The disparity in our finding to that of china may be attributed to racial, lifestyle and geographical locational differences. The reason to our finding may be due to proliferative renal lesion had more severe renal damage or may have been attributed to defects in permeable selectivity of the glomerular filtration barrier to plasma proteins (Kamianowska *et al.,* 2019).

In the current study, the mean values of HDL-Cwere statistically significantly decreased in the patient group when compared with the control group, were TC, LDL-C and TG were significantly increased comparison with control groups respectively. This is in agreement with the reports of Adekoya *et al.* (2011) and Adu *et al.* (2013) in Ibadan. However, it varies with the report of Arije*et al.* (1993) in Benin. lecithin-cholesteryl acyltransferase (LCAT) deficiency caused by urinary losses, elevated plasma cholesterol ester transfer protein levels, hypoalbuminaemia, and reduced expression levels of hepetic HDL docking receptor (SRB1) (Nosratola, 2016),might explained our findings. Linton *et al*. (2019); Agrawal *et al*. (2018), reported that, increasing in TC, LDL-C and TG are highly implicated in Atherosclerosis disease which is one of the hallmarks of NS patients.

In this finding, non-statistically significant positive correlation was observed between urine protein and T.C, TG and LDL-C in both patients and controls groups respectively. This finding is in agreement with the report of Antonio *et al.* (2008). Negative correlation was observed between urine protein and HDL-C also in agreement with the report of Evangelia Dounousi, (2008) in America. The reports of Kibukamusoke *et al.* (2005) in Uganda disagreed with our finding. A plausible explanation for the low level of HDL-C in NS observed in the present study is as a result of the urinary losses of lecithin cholesterol acyltransferase (LCAT) which leads to severe deficiency and limit the HDL-mediated uptake of surplus cholesterol from extra hepatic tissues. This is also compounded by marked reduction of the hepatic HDL-C receptor (Vaziri, 2003).

CONCLUSION AND RECOMMENDATION

it can be concluded that, Nephrotic syndrome is more in patients <18 years and also more of paediatric concern which was more common among males than females. Nephrotic syndrome was associated with increase urinary protein, total cholesterol, low density lipoprotein cholesterol, triglycerides and creatinine. However, decrease in high density lipoprotein cholesterol, total protein, albumin, globulin and urea. Lipid profile, protein profile, urea, creatinine and urinary protein levels should be properly assessed as a guide to early diagnosis of NS. This can putatively reduce the risk of developing atherosclerosis and cardiovascular complication of NS.

Conflict of Interests

There was no any conflict of interest among the authors in whatever form

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Authors Contribution

This work was conducted and approved in collaboration with all the authors, and they take responsibility for its accuracy and integrity. Isah, S.Y, Abubakar, S.L, Danladi, S. B and Gwaram, B. A designed the study; Isah, S.Y, Abubakar, S.L, Danladi, S. B and Gwaram, B. A sourced for funding; Isah, S.Y, Abubakar,S.L, Danladi, S. B Nnodim, J and Okafor, P. Awrote the protocol; Isah, S.Y, Abubakar, S.L, Nnodim, J and Okafor, P. A contributed in literature search; Isah, S.Y, Abubakar, S.L, Danladi, S. B and Okafor, P. Adid Lab experiments; Gwaram, B. A and Akram M did the clinical evaluation. Isah, S.Y, Abubakar, S.L, Danladi, S. B and Nnodim, J did the statistical data analysis; Isah, S.Y, Abubakar, S.L, Danladi, S. B, Gwaram, B. AandAkram M contributed in discussions; Isah, S.Y drafted the manuscript; Isah, S.Y supervised the study; Isah, S.Y wrote the final manuscript; Isah, S.Y, Abubakar ,S.L, Danladi, S. B, Gwaram, B. A, Akram M, Nnodim, J and Okafor, P. A. proof read the final version for publication.

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