

Original Research Article

Prevalence and study of lipid abnormalities in nephrotic syndrome attending a tertiary hospital, Nepal

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Received: 29 July 2018

Accepted: 26 September 2018

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ABSTRACT

Background: The nephrotic syndrome is a common presentation of adult or pediatric kidney diseases characterized by proteinuria, dyslipidemia, edema and hypoalbuminemia. Mainly, two types of dyslipidemia are observed: elevated serum cholesterol alone (hypercholesterolemia) and elevation of serum cholesterol along with triglyceride (combined hyperlipidemia). Therefore, majority of patients could predispose for the development of coronary artery disease and other related complications.

Methods: This was the prospective hospital-based study conducted in Tribhuvan University Teaching Hospital (TUTH), Nepal. Total sixty patients who meet the inclusive criteria were selected and enrolled from Nephrology outpatient department (OPD) and ward, attending from May 2009 till August 2010.

Results: In this study, total sixty patients were enrolled who was diagnosis as primary nephrotic syndrome that was established by clinical parameters supported by renal biopsy. Minimal change glomerulonephritis was common diagnosis by renal biopsy followed by Focal segmental glomerulosclerosis (FSGS). The total serum cholesterol, TG and HDL was normal in 25%, 15%, 83.3% whereas, it is high among 75%, 85% and 1.7% of the study populations. Similarly, 24hour urinary protein was >3.5gm/day in all patients. Total serum protein and albumin was normal in 18.3% and 8.3% respectively whereas, rest of the patients had low serum protein and albumin levels. TC/HDLc ratios were and among them, 70% had moderate to high risk value. Similarly, in this study, the serum cholesterol, TG and TC/HDL level was inversely correlated with low protein and albumin.

Conclusions: Majority of patients have derangement of lipid profile among nephrotic syndrome patients, which could also predispose for the development of coronary artery disease.

Keywords: Adults, Dyslipidemia, Hypoalbuminemia, Nephrotic Syndrome, Proteinuria

INTRODUCTION

The nephrotic syndrome is one of the best known presentations of adult or pediatric kidney disease.¹ The prevalence of the syndrome depends largely on the

underlying causes and varies significantly by age of onset.² Nephrotic syndrome results from increased urinary protein excretion and is characterized by altered plasma protein composition. This altered composition results not only from urinary loss of proteins yielding

decreased concentrations, but also from increased hepatic secretion of a group of proteins.³ Nephrotic syndrome is characterized by certain abnormalities, i.e. proteinuria exceeding 3.5g/24 hr per 1.73m² of body-surface area per day, hyperlipidemia, edema, hypoalbuminemia and among others, lipiduria and hypercoagulability.⁴ Although pathophysiological aspects of hyperlipidemia have not been completely identified, hypoalbuminemia, increased lipoprotein synthesis and decreased lipoprotein lipase activity are described by various workers.⁵ Two types of dyslipidemia are mainly hypercholesterolemia, and combined hyperlipidemia.⁶ The mechanisms responsible for raised lipid concentrations in the nephrotic syndrome are not fully understood. However, it has been proposed that hypoalbuminemia induces the over synthesis of lipoproteins.⁷ Increased hepatic lipoprotein synthesis, in response to low plasma oncotic pressure, as a consequence of the urinary loss of an as-yet unidentified regulatory substance, or both, is thought to play a key pathogenetic part.⁸ The concentration and composition of most classes of lipoproteins are affected, resulting in the accumulation of lipoproteins rich in cholesterol and phospholipids. Hyperlipidemia is found in almost all patients with nephrotic syndrome. High cholesterol level is a risk factor for atherosclerosis and is well documented.⁹ The present study was designed to study the derangement of serum lipids along with prevalence of nephrotic syndrome.

METHODS

This was the prospective hospital-based study conducted in Tribhuvan University Teaching Hospital (TUTH), Nepal. The study period was May 2009 to August 2010. The sample collected from Nephrology outpatient department (OPD) and admitted patients in medical ward and laboratory analysis was performed at Department of Biochemistry, TUTH, Nepal.

The study population was from patients visiting and admitted in nephrology outpatient department (OPD) and medical ward with newly diagnosis of primary nephrotic syndrome were studied. The diagnosis of primary nephrotic syndrome was established with 24hrs urinary proteinuria (>3.5g/day), peripheral edema, hyperlipidemia, hypoalbuminemia and supported by renal biopsy. Hyperlipidemia was classified according to National Cholesterol Education Program Adult Treatment Panel III.

Informed consent was taken from all patients. Study was conducted after the approval from Institutional review board TUTH.

Inclusion criteria

Patients with diagnosis of idiopathic glomerulonephritis with nephrotic syndrome irrespective of age and duration of illness.

Exclusion criteria

- Diagnosis inconclusive
- Pregnancy
- Systemic lupus erythematosus (SLE)
- Amyloidosis
- Henoch schlein purpura (HSP)
- Multiple myeloma
- Nephritic syndrome
- Secondary hyperlipidemia
- Chronic liver disease
- Other causes of hypoproteinemia-diabetic patients
- Along with patients with lipid lowering drugs.

Sample collection and processing

5ml of blood was drawn after an overnight fast (8 - 12hours) by veni puncture and a routine urine sample was also collected. The samples were coded and then separated within half an hour, by centrifugation at 1500 - 3000rpm for 5min. The tests for blood glucose, serum urea, creatinine, uric acid, serum sodium, potassium, calcium, phosphorus, HDL-cholesterol, LDL cholesterol, total cholesterol and TG were performed with standard methods. The 24hr urine sample was processed and estimated by dipstick for albumin and sugar. 24 hour urinary protein was estimated by Pyrogallol method. Internal quality control sera, both normal and pathological, were also run foreach lot for the validation of the results.

Sample size

Total sixty newly diagnosed cases of idiopathic primary nephrotic syndrome were enrolled in this study. All the biochemical parameters were analyzed in fully automated auto analyzer in clinical chemistry department

RESULTS

Total sixty patients with diagnosis of primary nephrotic syndrome were enrolled in this study.

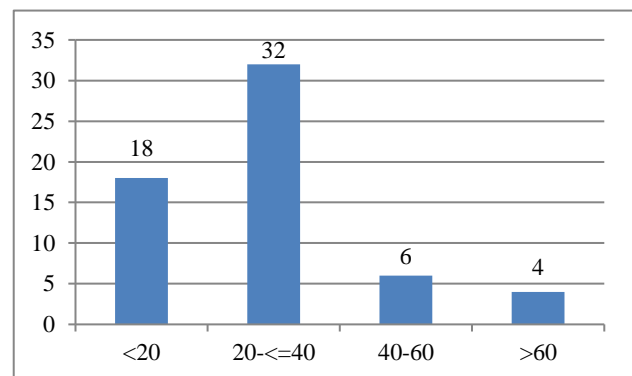


Figure 1: Age distribution.

The mean age of the study participants was 29.90±13.7(15-73) years with male (53.3%) to female (46.7%) ratio of 1.14:1. As shown in Figure 1 and 2 respectively.

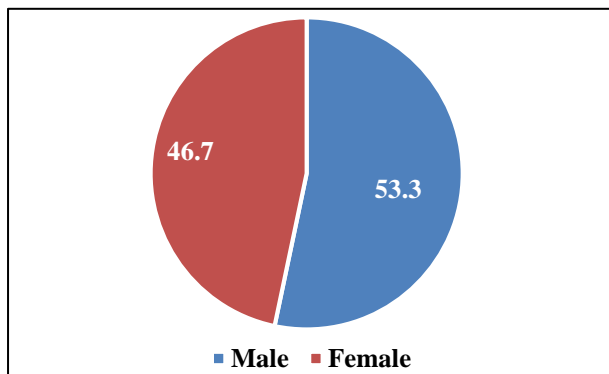


Figure 2: Sex distribution.

Diagnosis of the nephrotic syndrome was established by clinical parameters supported by renal biopsy which was done in only 53 patients and no renal biopsy was done for 7 patients. Minimal change glomerulonephritis (MCD) was the most common diagnosis by renal biopsy (45%) followed by focal segmental glomerulosclerosis (FSGS) 34%, Membranous glomerulonephritis (MGN) 11%, and Membranoproliferative glomerulonephritis (MPGN) 8% and other glomerular diseases (Mesangial proliferative glomerulonephritis) were 2%. Figure 3 shows the detail information of renal diagnosis.

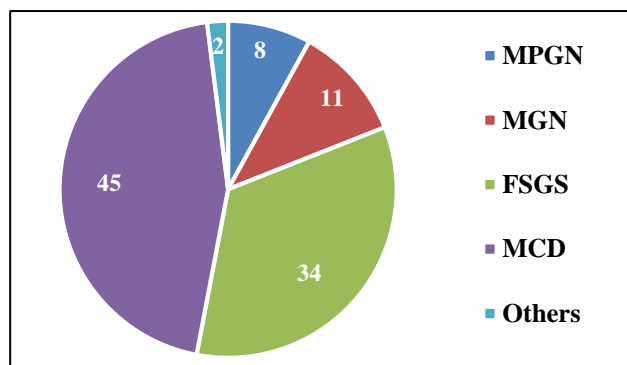


Figure 3: Diagnosis by renal biopsy.

Total serum cholesterol was normal in 25% (n=15) cases while 25% patients had total cholesterol range >6.5-8.5mmol/l, 8.33% of them had >8.5-10.5mmol/l, 20% had >10.5-12.5mmol/l, 21.7% had more than 12.5 mmol/l respectively. The mean cholesterol level was 9.54±4.60 (3.10-20.5mmol/l) and the mean values of cholesterol components were; HDLc=0.90±.21 (0.10-1.70mmol/l), and TG = 2.80±1.34(0.70-8.8), HDL was normal in 50 (83.3%), low in 15% and high in 1.7% patients.

TG was normal in 15% (9/60) patients while 46.7% had >1.8-2.8 mmol/l, 20% had >2.8-3.8 and 18.3% had more than 3.8mmol/L. TC/HDLc ratios were elevated with

Mean±SD:11.6±8.2(2.5-54) and 70% had moderate to high risk (Table 1).

Table 1: Biochemical parameters studied in the participants.

Parameters	Mean±SD	Range
Serum urea	7.35±3.9	2.20-12.00mmol/L
Serum creatinine	139.7±88.5	52.00-240.00µmol/L
Serum uric acid	314.4±151.1	77.00-1016.00µmol/L
Serum sodium	137.8±4.35	130.00-149.00meq/L
Serum potassium	3.83±0.58	2.50-5.00meq/L
Serum calcium	1.95±0.32	1.40-3.80mmol/L
Serum phosphorous	3.91±1.13	2.60-5.0 mg/dl
24hrs urinary proteins	6.30±2.77	3.50-17.90gm/day
Total serum protein	46.13±6.14	31-62gm/L
Serum albumin	21.71±8.46	10.0-40.0gm/L
Cholesterol	9.54±4.6	3.10-20.50mmol/L
HDLc	0.90±.21	0.10-1.60mmol/L
TG	2.8±1.34	0.70-8.80mmol/L
TC/HDL	11.6±8.2	2.5-54

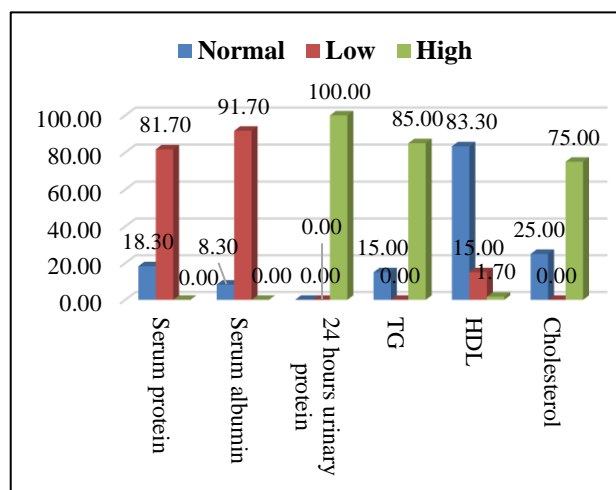


Figure 4: Serum lipid and protein abnormalities.

The serum cholesterol level was inversely correlated with low total protein levels (r = -0.373; p value=0.003) and albumin level (r=-0.430; p value=0.0001). However, serum cholesterol level did not show significant correlation with 24 hours urinary protein level (r=0.251, p value=0.061). LDL showed significant inverse correlation with total protein (r=-0.372; p=0.003) and albumin (r=-0.354, p=0.006) but did not show significant correlation with 24 hr urinary protein (r=0.175; p=0.182).

The serum TG level had inverse relationships with serum albumin ($p=0.005$). TC/HDL ratio correlated significantly and inversely with total serum protein ($r= -0.370$; $p=0.0001$) and serum albumin ($r= -0.487$; $p=0.0001$) whereas, it was positively correlated with 24-hrs total urinary proteins.

DISCUSSION

The nephrotic syndrome is one of the best-known presentations of adult or paediatric kidney disease. The present study was conducted to evaluate the lipid profile abnormalities in nephrotic syndrome and to correlate with other biochemical abnormalities. Diagnosed cases of nephrotic syndrome aged between 15 to 73 years were included in the study.

Diagnosis of the nephrotic syndrome was established by clinical parameters supported by renal biopsy which was done in only 53 patients (88.3%). The mean age was 29.90 ± 13.7 (15-73) years with male to female ratio of 1.14:1. Several authors reported the age of about 15-80 years, but with mean age of them were 45, 33.6 and 31.4 years but in this study mean ages was 29.9 years with more prevalence in male patients.^{10,11}

Chen H et al, reported almost similar findings as present study, the mean age being 31.4 (ranging from 1 to 78 years), with a male to female ratio of 1.3:1.¹² Ueda Y et al, also reported the mean age between 20 and 50 showed little difference between sexes, the male-to-female ratio is about 1:1.¹³

In present study the mean age ranges from 15-73 year, so all patient above 15 year are classified as adult and more than 60 are classified as elderly. Similarly, Choi IJ et al, had also classified as our classification to find the prevalence of nephrotic syndrome.¹⁴

Minimal change glomerulonephritis was the most common diagnosis by renal biopsy (45%) followed by focal segmental glomerulosclerosis 34%, membranous glomerulonephritis 11%, membranoproliferative glomerulonephritis 8% and other glomerular diseases (mesangial proliferative glomerulonephritis) were 2%.

Minimal change glomerulonephritis is most common biopsy finding in present study followed by focal segmental glomerulosclerosis because the focal sclerosing lesion seen in circumstances outside the apparently primary nephrotic syndrome forms a different group of patients from those with minimal changes and they must share some common expression of injury to generate a lesion, which is morphologically the same as that in primary FSGS which had being reported by Cameron JS.¹⁵

MCD has a variable geographic distribution, being more common in Asia than in North America or Europe. In Korea and Thailand, the MCD comprised 26.6% and

45.8% of total primary glomerular diseases.^{14,16} Choi IJ et al, reported that in adults, MCD comprised 53.3% which is similar to present study which comprised MCD 45% of the total biopsies ($n=53$) out of 60 patients diagnosed with primary nephrotic syndrome.¹⁴

The higher prevalence of minimal changes diseases in present study is difficult to explain. Tse KC et al, had reported that certain cases of FSGS may be misdiagnosed as MCD on initial renal biopsy due to the focal nature of the lesions, relapsing course and older adults with MCD have similar clinical presentations and share similar steroid responsiveness with their younger, but tend to have fewer relapses.¹⁷

Total serum protein was 46.13 ± 6.14 (31-62gm/l). Serum protein was normal in 18.3% and rest of the patients had low protein levels (40-50: 71.7% and <40 in 10%). Serum albumin was normal in 8.3% and rest had low albumin levels (25-35gm/l: 28.3%, <25 gm/l: 41.7%, <15 gm/l: 21.7%) with the mean value of 21.71 ± 8.46 (10-40gm/l).

Tarik MH et al, had also reported the mean serum total protein was 48.5 ± 7.8 gm/l and serum albumin was 20.8 ± 6.1 and 24hrs urinary proteinuria 5.2 ± 1.5 mg/d which were similar to present study.⁴ Similar finding was found in Francisco et al, in which 11% had normal total serum protein and low serum albumin level <39 g/l in 48% and <20 g/l in 52% of patients.¹⁸ 24hour urinary protein was high in all patients (3.5-9.5 in 86.7% and >9.5 in 13.3%) with the mean of 6.30 ± 2.77 (3.50-17.9gm/d). However, Obrenovi R et al reported the significant proteinuria with low serum total protein and albumin.¹⁹

Hypercholesterolemia was present in 75% ($n=45$). The mean cholesterol level was 9.54 ± 4.60 (3.10-20.5mmol/l) which is similar to the finding of De Sain-van der Velden et al.²⁰ Similarly, 15% had normal TG level, while 46.7% had >1.8 -2.8mmol/l, 20% had >2.8 -3.8 and 18.3% had more than 3.8mmol/L of serum TG level and the mean value of serum TG was 2.80 ± 1.34 which was similar to De Sain-van der Velden et al. study. However, HDL was normal in 83.3%, low in 15% and high in 1.7%.²⁰ Gerald A et al, had reported that HDL cholesterol have been less consistent, with values ranging from high to low which support to present study.²¹

Joven J et al, had also reported similar finding of mean cholesterol 10.83 ± 4.96 , HDLc= 1.43 ± 0.32 , TG= 3.98 ± 1.12 respectively.²² Francisco AT et al, recognize the strong inverse relationships between proteinuria and serum albumin also between serum albumin and plasma total cholesterol. Such inverse relationships with TC and TG with the serum albumin were also seen in our study. The serum cholesterol level was significantly high in patients with low total protein levels (p value= 0.003), albumin (p value= 0.0001) and A: G ratio (p value= 0.018). However, serum cholesterol level had no

correlation with urinary 24hours protein level (p value=0.061). TC/HDL ratio correlate significantly with low values of total serum protein (p=0.0001), serum albumin (p=0.0001) and positively correlated with 24hrs urinary proteinuria (p=0.038).

The serum TG level had inverse relationships between serum albumin (p=0.005 and A:G ratio (p=0.010). There is no significant correlation with 24hrs urinary protein with LDLc (p=0.18) whereas, there is significant correlation with HDLc (p=0.25).¹⁹ TC/HDLc ratios were elevated and among them 70% had moderate to high risk for developing coronary artery diseases. Similar result had also been reported by Francisco AT et al.¹⁸ In present study, more than half (70% to 83.3%) of nephrotic patients are at moderate to high risk of developing coronary artery disease utilizing TC/HDL-C ratio. Francisco AT et al, had also mention similar findings in his study.¹⁸

The study population was small with only 60 patients and single centre which could not be generalized with major population.

CONCLUSION

Dyslipidemia and hypoalbuminemia are common features of nephrotic syndrome in adults, common in males than in female patients. Minimal change glomerulonephritis was the most common diagnosis by renal biopsy. The patients with low total serum protein and albumin have dyslipidemia more often than patients with normal serum protein and albumin. Similarly, the individual cholesterol components also have significant negative correlation with serum protein and albumin levels. Majority of patients with idiopathic nephrotic syndrome have abnormal lipid profile which could predispose for the development of coronary artery disease.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Baral S, Baral BK, Joshi K, Shrestha S, Raut KB, Jha B. Prevalence and study of lipid abnormalities in nephrotic syndrome attending a tertiary hospital, Nepal. *Int J Res Med Sci* 2018;6: 3576-81.