Original Article

Serum Low Density Lipoprotein Cholesterol (LDL-C) Level and Its Association with Urinary Total Protein and Serum Albumin Concentration in Adult Nephrotic Syndrome Patients

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Abstract

***Background**: Lipid abnormalities have an important biochemical basis in the disease process of adult nephrotic syndrome patients. Dyslipidemia in nephrotic syndrome involved in the cardiovascular risk and also accelerates the progression of glomerular dysfunction. Higher plasma concentration of low density lipoprotein cholesterol (LDL-C) in nephrotic syndrome is a driving force for atherosclerotic disease as well as the high cardiovascular related mortality. This study is designed to evaluate the association between serum LDL-C level with 24 hour urinary total protein (UTP) and serum albumin concentration. **Materials and Methods**: This cross-sectional anlytical study was carried out in the Department of Biochemistry, Dhaka Medical College, Dhaka during the period of July 2013 to June 2014. A total 50 (fifty) study subjects with age range from 20-50 years of both sexes were enrolled as diagnosed adult nephrotic syndrome patients from the Department of Nephrology, Dhaka Medical College, Dhaka. With baseline information, serum LDL-C level, serum albumin level and 24 hour urinary total protein of study subjects were estimated. Mean values of the variables were determined. Correlation between variables were determined by Pearson's correlation test by using SPSS for windows version 20.0. For all the statistical analysis $p<0.05$ was considered as significant. **Results**: Mean (±SD) value of serum LDL-C, in adult nephrotic syndrome patients was 231.16±34.28 mg/dL. Mean value of 24 hour urinary total protein in study subjects was 5.65±0.54 gm/24 hours. Mean value of serum albumin level in study subjects was 1.87±0.54 gm/dL. Positive correlation was found between 24 hour urinary total protein and LDL-C, ($r=0.444$) ($p<0.05$). Negative correlation was found between serum albumin and LDL-C, ($r= -0.321$) ($p<0.05$). **Conclusion**: Increased level of serum LDL-C in adult nephrotic syndrome, possesses a significant relationship with increased proteinuria and decreased serum albumin concentration, which could predispose abnormalities in lipid metabolism, leading to develop coronary artery disease.*

***Key words**: Nephrotic syndrome; Serum LDL-C; Serum albumin; Proteinuria*

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Introduction

Nephrotic syndrome is a clinical condition with multiple causes characterized by increased glomerular permeability and manifested by massive proteinuria.[1] This disease is represented as urinary total protein excretion more than 3.5 gm/day, low serum albumin level (<2.5 gm/dL) and peripheral edema.[2] Nephrotic syndrome can affect any age.[3] The incidence of nephrotic syndrome is 90-100/million in the Indian subcontinent including Bangladesh.[4] Nephrotic syndrome is a chronic relapsing disease. Relapse is also higher in children of Bangladesh, which is 36.4%. This frequent or infrequent relapse in the nephrotic syndrome may continue even in adult age.[5] Lipid abnormalities are important biochemical findings in nephrotic syndrome. Although pathophysiological aspects of abnormal lipid metabolism have not been completely identified, urinary protein loss resulting in hypoalbuminemia stimulates hepatic overproduction of lipids and decreases lipase activity, which are described as the important causal factors.[6]

Proteinuria in nephrotic syndrome leading to hypoproteinemia may lead to a coordinated increase in the synthesis of albumin and other proteins mainly apoprotein B containing lipoprotein by the liver.[7]

In nephrotic syndrome, generally, when edema regresses, lipid abnormalities tends to being normal but in some cases it may continue after the edema has disappeared. However it may persist in some cases, leading to increased risk of atherosclerosis in later life.[7] The magnitude of the most pronounced secondary changes in lipoprotein metabolism in nephrotic syndrome patients correlates with the severity of the syndrome.[8]

Increased level of serum LDL-C in nephrotic syndrome is not only involved in the cardiovascular risk but also accelerates the progression of glomerular dysfunction.[8] Elevation of serum LDL-C concentrations is an independent risk factor for coronary artery disease and cerebrovascular disease. Lipid levels generally correlate inversely with the serum albumin concentration and plasma oncotic pressure. Very low density lipoproteins (VLDL) and lipoprotein a [Lp(a)] also typically are elevated in nephrotic patients. These abnormalities are believed to result from multiple concurrent mechanisms.[9]

Abnormalities in serum LDL-C level parallels with an increase in the incidence of the disease. Glomerular disease is a common cause of ESRD (end stage renal disease) and comprises 25−45% cases of ESRD in developing nations including Bangladesh.[10] These formidable enemies of health are joining forces to impose a double burden of disease. Till now, limited published data have been found regarding this content, though several studies have been done abroad to establish the relationship of proteinuria and hypoalbuminemia with serum LDL-C levels. The present study was designed in a small group of Bangladeshi population to evaluate the correlation between proteinuria and hypoalbuminemia with serum LDL-C level in adult nephrotic syndrome patients.

Materials and Methods

This cross-sectional study of one year duration from July 2013 to June 2014 was designed to evaluate the association of serum LDL-C with proteinuria and hypoalbuminemia among the adult patients with nephrotic syndrome. The study protocol was approved by the Institutional Ethical Review Board. Informed written consent was obtained from all the study subjects. Study sample consisted of 50 adult nephrotic syndrome patients who were selected as diagnosed and admitted patients in Department of Nephrology of Dhaka Medical College Hospital on the basis of inclusion and exclusion criteria. Both male and female subjects with age range 20−50 years and diagnosed as nephrotic syndrome were included in the study. Patients with history of any acute or chronic systemic illness, patients taking lipid lowering drugs, malignant cases and subjects with pregnancy were excluded.

Along with the baseline information, 3 mL of fasting (at least 12 hours) blood samples were collected and analyzed for serum total cholesterol (Tchol), serum triacylglycerol (TAG) and serum high density lipoprotein cholesterol (HDL-C) along with serum albumin level and the 24-hour urine samples were

analyzed for protein of all participants of the study. Serum Tchol, TAG, HDL-C and serum albumin levels were assayed by semi-automated biochemical analyzer. Serum low-density lipoprotein cholesterol (LDL-C) was estimated by using Friedwald's formula

LDL-C = Tchol - (1/5 TAG + HDL-C)[11]

Statistical analyses were performed by using the SPSS version 20.0 for windows. All data were processed to compute mean and standard deviation and expressed as mean±SD. Pearson's correlation coefficients were used to analyze linear correlation between variables. For all the statistical analyses $p<0.05$ were considered as significant.

Results

Table I shows the distribution of study subjects based on age and sex . The mean ± SD age of nephrotic syndrome patients was 34.62±6.45 years. Among the total study subjects 21 (42%) were male and 29 (58%) were female.

Table I: Distribution of subjects based on age and sex of study subjects (n=50)

Age group (years)	Male (n=21)	Female (n=29)	All patients Number (%)
20−30	07	05	12 (24)
31−40	12	19	31 (62)
41−50	02	05	07 (14)

Estimated mean±SD of serum LDL-C, serum albumin and 24 hour urinary total protein of study subjects were 231.16± 34.28 mg/dL, 1.87±0.54 gm/dL and 5.65 ± 0.54 gm/24 hours respectively (Table II).

Table II: Estimated parameters of the study subjects

Parameters	Adult NS patients (Mean±SD)	Normal range[12-14]
Serum LDL-C (mg/dL)	231.16±34.28 mg/dL	120−200 mg/dL
Serum albumin (gm/dL)	1.87±0.54 gm/dL	3.4 - 5.4 gm/dL
24 hour urinary total protein (gm/24 hours)	5.65 ± 0.54 gm/24 hours	< 100 mg/24 hours

Table III shows the correlation of UTP and serum albumin with serum LDL-C of study subjects. Serum LDL-C maintained positive correlation with UTP ($r= 0.444$) ($p<0.05$) and negative correlation with serum albumin ($r= -0.321$), ($p<0.05$). Fig 1 shows correlation between UTP and LDL-C in cases and Fig 2 shows correlation between serum albumin and LDL-C in cases.

Table III: Correlation of UTP and serum albumin with serum LDL-C (n=50)

Variables		**r values**	**p values**
UTP (gm/24 hours)	LDL-C (mg/dL)	0.444	0.0012*
Serum albumin (mg/dL)	LDL-C (mg/dL)	-0.321	0.0076*

* significant

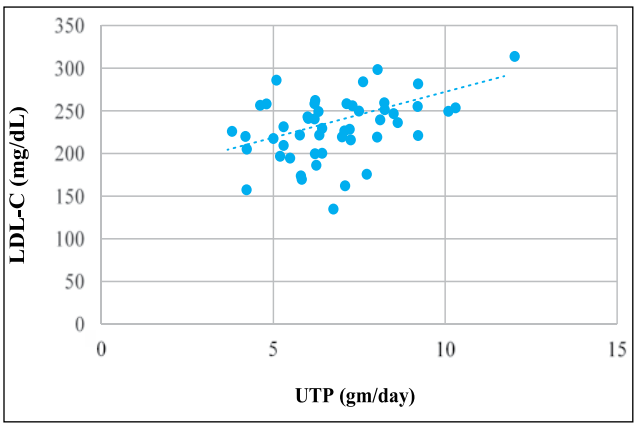

Fig 1. Correlation between UTP and LDL-C in cases

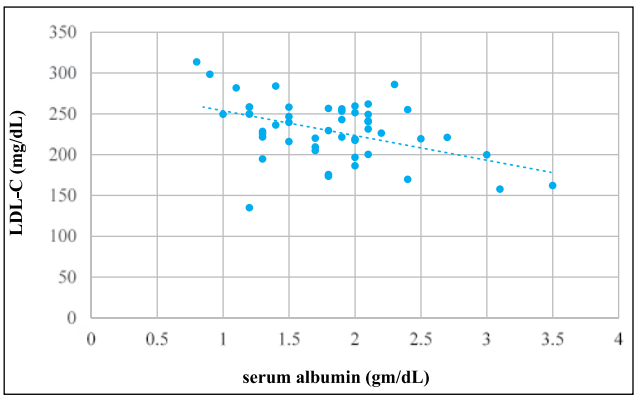

Fig 2. Correlation between serum albumin and LDL-C in cases

Discussion

The present cross-sectional study was designed to observe change of an important biochemical parameters of lipid profile, serum LDL-C in adult nephrotic syndrome patients. In nephrotic syndrome, hypoproteinemia stimulates protein synthesis in the liver, resulting in the overproduction of different types of lioproteins whereas lipid catabolism is decreased due to lower levels of lipase, the main enzyme involved in lipid breakdown. Both these two pathophysiological phenomenon are involved for increased level of LDL-C in adult patients with nephrotic syndrome.[6]

The result of present study showed significant increased level of one of the most important components of lipid profile LDL-C in study subjects (mean±SD: 231.16±34.28). This finding is similar to the result of the study done in Guangxi, China.[15] There were 378 adult patients with nephrotic syndrome and 200 healthy volunteers were recruited in this study. Among cases 273 patients suffered from dyslipidemia with prevalence rate 72.2%, where total cholesterol was significantly ($p<0.05$) higher in the nephrotic patients than in the controls. A case-control study in Nigeria was also conducted[16] on forty-three patients (86%) with nephrotic syndrome, that study showed elevated total cholesterol ($p<0.05$) which is similar to the findings of present study.

Proteinuria in nephrotic syndrome causes progressive reduction of serum albumin level. Proteinuria altered the apolipoprotein content of lipoproteins. Nephrotic syndrome alters the lipoprotein oxylipid composition independently of an increase in total lipoprotein levels which also provides positive feedback mechanism to produce LDL-C predominantly to incorporate lipids in lipoproteins.[16]

The present study found that urinary total protein (UTP) maintained significant ($p<0.05$) positive correlation with serum LDL-C ($r= 0.444$) in adult nephrotic syndrome patients. This result is consistent with the another study done by other researchers of Maharastra, India[11] where there 50 age and sex matched nephrotics were study subjects. They found positive correlation with serum LDL-C and urinary protein excretion ($r=0.381$, $p<0.001$). The present study found negative correlation between serum albumin and serum LDL-C ($r= -0.321$, $p<0.05$) in patients with nephrotic syndrome. This result is also reflected in the other studies. Adu conducted a case control study in Nigeria[1] where high LDL-C in adult nephrotics (242±28 mg/dL) with negative correlation with serum albumin ($r= -0.378$, $p<0.001$) was observed. Prerna et al[7] and Krishnaswamy et al[17] study results are also consistent with this study results.

On the basis of the result of the present study, it can be concluded that increased serum level of LDL-C is associated with nephrotic syndrome in adults. Increased serum LDL-C level is a well-established risk factor for cardiovascular and cerebrovascular diseases. Therefore adult nephrotic syndrome patients should undergo regular screening with lipid profile for the early detection of dyslipidemia and should be treated accordingly to prevent associated complications and better management of patients. The study was single hospital based and conducted with small sample size. We, therefore, suggest further prospective study with large sample to figure out the association of dyslipidemia with individual cause of nephrotic syndrome.

Increased serum level of LDL-C along with positive correlation with proteinuria and negative correlation with serum albumin level in adult nephrotic syndrome patients implies the most important indicator for progression of this disease with atherosclerotic changes. So, the patients with nephrotic syndrome are at higher risk of cardiovascular and cerebrovascular complications.

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