

Lipid Profile Abnormalities in Nephrotic Syndrome

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ABSTRACT :

Nephrotic syndrome is a set of indications that include protein in the urine, low blood protein levels, high cholesterol levels, high triglyceride levels, and swelling. Nephrotic syndrome is affected by changed disorders that damage the kidneys. This impairment leads to the release of too much protein in the urine. Hyperlipidemia is a common finding in nephrotic syndrome. There is increased total Cholesterol, LDL, VLDL and low or normal HDL.

It has been noted that certain factors like diet, malnutrition, genetic traits etc., are known to alter the frequency and severity of lipid pattern. The Indian patient has a different dietary, constitutional and genetic background. An attempt was also made to correlate the degree of proteinuria and hypoproteinemia, with the rise in serum lipid values in cases of nephrotic syndrome.

This is a Cross sectional study in which 30 Normal patients and 30 patients with nephrotic syndrome aged 25-65 years old. The Serum Protein & Serum lipid profiles of the admitted patients were evaluated.

There was a significant increase in Total cholesterol, HDL, LDL, VLDC & TG. There was significant decrease in Serum Total Protein, Serum Albumin & Serum globulin in Nephrotic patients when compared to Controls.

The study finding conclude that the serum lipid profile shoed noticeable increase in the nephrotic syndrome in Indian patients. It also observed that nephrotic patients are having hyperlipidaemia. This hyperlipidaemia may progress in to the cardiovascular diseases.

Hence the lipid profile in the nephrotic syndrome must be monitored for better management of the diseases.

Key-words: Lipid profile, Nephrotic syndrome in children, Hyperlipidemia

INTRODUCTION:

Nephrotic syndrome is a general kidney disorder categorized by three signs of disease: large proteinuria, hypoalbuminemia, and edema.[1] Nephrotic syndrome is a group of symptoms that include protein in the urine, low blood protein levels, high cholesterol levels, high triglyceride levels, and swelling. Nephrotic syndrome is caused by different disorders that damage the kidneys. This damage leads to the release of too much protein in the urine.

Common primary causes of nephrotic syndrome include kidney diseases such as minimal-change nephropathy, membranous nephropathy, and focal glomerulosclerosis. Secondary causes include systemic diseases such as diabetes mellitus, lupus erythematosus, and amyloidosis. Congenital and hereditary focal glomerulosclerosis may result from mutations of genes that code for podocyte proteins, including nephrin, podocin, or the cation channel 6 protein. Nephrotic syndrome can result from drugs of abuse, such as heroin.

The proposed mechanisms of membranous nephropathy are as follows:

1. Immune complex deposition from the circulation
2. *In-situ* formation of immune complexes through the reaction of circulating autoantibodies to a native antigen
3. *In-situ* formation of immune complexes with a

non-native (extrinsic) antigen that is bound to the podocytes or glomerular basement membrane

Nephrotic syndrome is usually accompanied by retention of water and sodium. The degree to which this occurs can vary between slight edema in the eyelids that decreases during the day, to affecting the lower limbs, to generalized swelling, to full blown anasarca.[2]

Nephrotic syndrome is characterized by large proteinuria (>3.5 g per 1.73 m² body surface area per day,[3] or > 40 mg per square meter body surface area per hour in children), hypoalbuminemia (< 2.5 g/dl), hyperlipidaemia, and edema (which is generalized and also known as anasarca or dropsy) that begins in the face. Lipiduria (lipids in urine) can also occur, but is not essential for the diagnosis of nephrotic syndrome. Hyponatremia also occurs with a low fractional sodium excretion.

Hyperlipidaemia is caused by two factors:

- Hypoproteinemia stimulates protein synthesis in the liver, resulting in the overproduction of lipoproteins.
- Lipid catabolism is decreased due to lower levels of lipoprotein lipase, the main enzyme involved in lipoprotein breakdown.[4] Cofactors, such as apolipoprotein C2 may also be lost by increased filtration of proteins.

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A few other characteristics seen in nephrotic syndrome are: The most common sign is excess fluid in the body due to the serum hypoalbuminemia. Lower serum oncotic pressure causes fluid to accumulate in the interstitial tissues. Sodium and water retention aggravates the edema. This may take several forms:

- Puffiness around the eyes, characteristically in the morning.
- Pitting edema over the legs.
- Fluid in the pleural cavity causing pleural effusion. More commonly associated with excess fluid is pulmonary edema.
- Fluid in the peritoneal cavity causing ascites.
- Generalized edema throughout the body known as anasarca.
- Most of the patients are normotensive but hypertension (rarely) may also occur.
- Anaemia (iron resistant microcytic hypochromic type) maybe present due to transferrin loss.
- Dyspnea may be present due to pleural effusion or due to diaphragmatic compression with ascites.
- Erythrocyte sedimentation rate is increased due to increased fibrinogen & other plasma contents.

Some patients may notice foamy or frothy urine, due to a lowering of the surface tension by the severe proteinuria. Actual urinary complaints such as haematuria or oliguria are uncommon, though these are seen commonly in nephritic syndrome.

May have features of the underlying cause, such as the rash associated with systemic lupus erythematosus, or the neuropathy associated with diabetes.

Examination should also exclude other causes of gross edema—especially the cardiovascular and hepatic system.

A proteinuria of greater than 3.5 g /24 h /1.73 m² (between 3 and 3.5 g/24 h /1.73 m² is considered to be proteinuria in the nephrotic range) or greater than 40 mg/h/m² in children.[4][5] The ratio between urinary concentrations of albumin and creatinin can be used in the absence of a 24-hour urine test for total protein. This coefficient will be greater than 200–400 mg/mmol in nephrotic syndrome. This pronounced loss of proteins is due to an increase in glomerular permeability that allows proteins to pass into the urine instead of being retained in the blood. Under normal conditions a 24-hour urine sample should not exceed 80 milligrams or 10 milligrams per decilitre.[6]

A hypoalbuminemia of less than 2.5 g/dL,[4] that exceeds the hepatic clearance level, that is, protein synthesis in the liver is insufficient to increase the low blood protein levels. Edema is thought to be caused by two mechanisms. The first being hypoalbuminemia which lowers the oncotic pressure within vessels resulting in hypovolemia and subsequent activation of the Renin-angiotensin system and thus retention of sodium and water. Additionally, it is thought that albumin causes a direct effect on the epithelial sodium channel (ENaC) on the principal cell that leads to the reabsorption of sodium and water. Nephrotic syndrome- edema initially appears in parts of the lower body (such as the legs) and in the eyelids. In the advanced stages

it also extends to the pleural cavity and peritoneum (ascites) and can even develop into a generalized anasarca. It has been recently seen that intrarenal sodium handling abnormality is related to Atrial Natriuretic Peptide resistance is associated with decreased abundance and altered subcellular localization of dopamine receptor in renal tubules.[7] Hyperlipidaemia is caused by an increase in the synthesis of low and very low-density lipoproteins in the liver that are responsible for the transport of cholesterol and triglycerides. There is also an increase in the hepatic synthesis of cholesterol.

Thrombophilia, or hypercoagulability, is a greater predisposition for the formation of blood clots that is caused by a decrease in the levels of antithrombin III in the blood due to its loss in urine.

Lipiduria or loss of lipids in the urine is indicative of glomerular pathology due to an increase in the filtration of lipoproteins.[8]

MATERIALS AND METHODS:-

This is a Cross sectional study in which 30 Normal patients and 30 patients with nephrotic syndrome aged 25-65 years old who were referred to Pediatrics Out-Patient Department (OPD) and in-patient department (IPD).

Group I: Normal patients

Group II : Nephrotic syndrome patients

A diagnosis of nephrotic syndrome was confirmed in patients in the presence of the followings.

- Massive proteinuria
- Hypoalbuminaemia
- Oedema
- Hypercholesterolaemia

The samples were analysed for Protein profile (Serum Total protein, serum albumin, serum globulin, A:G ratio, urinary proteins, Blood urea & serum creatinine), Lipid Profile(Total cholesterol, HDL-C, LDLC, VLDL, Non-HDLC, serum phospholipids and triglycerides).

RESULTS AND DISCUSSION:-

The 30 Normal patients & 30 Nephrotic syndrome patients were studied. The age of the patients ranges from 25-65 years. All 50 patients were fresh cases of nephrotic syndrome without any back history of the diseases. The observations were depicted in tabulated form and correlation of serum lipid level with serum albumin level was studied.

Table 1 : Observed Serum Levels of lipo proteins

	Group I: Normal patients	Group II : Nephrotic syndrome patients
Total Cholesterol (mg/dl)	185±30	410±120
High Density Lipids (mg/dl)	47±6	105±8
Low Density Lipids (mg/dl)	123±20	190±40
Very Low Density Lipid (mg/dl)	41±5	53±7
Triglycerides (mg/dl)	98±15	178±20

Table 2 : Observed Serum Levels of Serum Proteins

	Group I: Normal patients	Group II : Nephrotic syndrome patients
Serum Total Protein(g/dl)	7.2±0.40	3.80±0.50
Serum Albumin(g/dl)	4.10±0.30	1.8±0.30
Serum Globulin(g/dl)	3.30±0.25	2.20±0.20

The above data showed significant increase level of the lipo proteins. The level of the cholesterol, HDL, LDL & triglycerides is founds to be markedly increases. The VLDL levels does not showed any marked changes. This concludes that hypercholesterolemia in the nephrotic patients. The hypercholesterolemia is observed is also previously reported in nephrotic syndrome study [9-11]. Krishnaswany D et al, Appel G.B. et al and Alexander J.H et al showed the same findings.

The level of the HDL decrease is also reported in previous studies. Adekoya A.O showed the same results of the decrease in levels of the HDL [12].

The increased LDL can be explained by severe reduction of hepatic LDL receptor protein abundance in nephrotics despite normal LDL receptor mRNA abundance and gene translation rate. [13]

Conclusion:

The study finding conclude that the serum lipid profile shoed noticeable increase in the nephrotic syndrome in Indian patients. It also observed that nephrotic patients are having hyperlipidaemia. This hyperlipidaemia may progress in to the cardiovascular diseases.

Hence the lipid profile in the nephrotic syndrome must be monitored for better management of the diseases.

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