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Assessment of lipid profile and serum proteins in children with nephrotic syndrome

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Abstract
Hyperlipidemia is found in almost all patients with nephrotic syndrome. High cholesterol level is a risk factor for atherosclerosis and is well documented in text books. But in India there has been few, if any, studies regarding the levels of different lipoproteins and apolipoproteins in nephrotic syndrome. Thus, this study focuses on the changes in different fractions of lipids and lipoprotein levels as well as apolipoprotein concentrations, so that, if necessary, early treatment can be started to prevent complications of atherosclerosis.
The study was planned on 25 children with nephrotic syndrome and 25 normal children. The Nephrotic cases were selected according to the criteria proposed by International study of kidney diseases in children (ISKDC) that is children with oedema, proteinuria, and hypoproteinemia.
From the above findings and the literature evidence there is increasing risk of atherosclerosis. So it is useful to evaluate the lipid and lipoprotein levels early and treat hyperlipidemia in children who suffered from nephrotic syndrome. There is also risk of the progression of chronic renal failure. Hence care must be taken to early diagnosis and treatment to avoid further complications.

Keywords: nephrotic syndrome, lipids, proteins

Introduction
Kidneys are one of the primary excretory organs of the body and they function by separating out unwanted catabolic wastes and toxins from the body through urine. Tiny structures called glomeruli act as filtering machinery inside the kidney. When these glomeruli fail to function effectively, the filtering mechanism fails.
Nephrotic Syndrome refers to a condition in which the kidneys (glomeruli) fail to filter out the proteins from the blood and excrete it in the urine. The term 'nephrotic syndrome' is used to indicate the condition in which the proteins in the urine are above a certain permissible range. The exact medical condition leading to this phenomenon can be many and a deeper examination is usually required to ascertain the cause.
Childhood nephrotic syndrome is not a disease in itself; rather, it is a group of symptoms that

- Indicate kidney damage particularly damage to the glomeruli, the tiny units within the kidney where blood is filtered
- Result in the release of too much protein from the body into the urine

When the kidneys are damaged, the protein albumin, normally found in the blood, will leak into the urine. Proteins are large, complex molecules that perform a number of important functions in the body.
Nephrotic syndrome in children is classified as primary childhood nephrotic syndrome, secondary childhood nephrotic syndrome, and congenital nephrotic syndrome.

- **Primary nephrotic syndrome**: This type of nephrosis is also called idiopathic nephrotic syndrome and many times the reason behind its occurrence is unknown. Minimal Change Disease, focal segmental glomerulosclerosis, and membranoproliferative glomerulonephritis (MPGN) come under this type of nephrotic syndrome.
- **Secondary nephrotic syndrome**: This subtype of nephrosis is caused by some kind of infection, the overdose of certain medications or an underpinning disease in the body. Diseases like diabetes, hepatitis, lupus, HIV, malaria, streptococcal infection and Henoch-Schönlein purpura are some diseases that are associated with the secondary nephrotic syndrome.
- **Congenital (Finnish-type) nephrotic syndrome**: This is the hereditary form of nephrotic syndrome that is transmitted from one generation to the other through their DNA. Primarily, a genetic variation in the gene *NPHS1*, coding for a key Trans membrane protein called nephrin, causes this syndrome. It is quite rare and manifests as early as three months of age.

For children who present with the classical symptoms of childhood nephrotic syndrome, the doctor usually prescribes the following diagnostic tests:
Urine dipstick test: It is a simple procedure that is performed with the first urine of the day. A dipstick is used to check the urine for the presence of proteins. If the protein concentration is high, it changes the colour of the dye in the dipstick. The concentration of the protein is quantified with the help of a colour coded chart.

Urine test: To gain further clarity on the concentration of excreted protein in the urine the doctor usually prescribes a routine urine test that accurately measures the level of albumin in the urine. A ratio of the albumin and creatinine in the urine is estimated and a high ratio of the two proteins indicates a failure of the kidneys to retain albumin.
Blood test: As a converse, the protein levels in the blood are checked to estimate the extent to which the proteins are lost from the blood. A blood test is also used to decipher the underlying cause of the leakage of essential proteins.
Physical exam: Thorough physical examination was done and visible signs of nephrotic syndrome in the children like swelling of the extremities, fever, distension of the abdomen, etc. Were noted.
Family history: Due to genetic disposition, a thorough understanding of any family history of nephrotic syndrome is essential for the doctor to arrive at a correct diagnosis. Genetic testing is also prescribed in the recent times to find out the exact cause of the syndrome.
Ultrasound of the kidney: If the urine or blood tests are suggestive of a nephrotic syndrome, ultrasound examination of the kidneys documented to visualize the extent of the damage in the glomeruli.
Biopsy: In some rare cases of treatment failure, biopsy test of the kidney tissue to understand the morphology of the kidney was performed. In very young children, biopsy avoided unless and until it is completely necessary [3].
The cause of secondary childhood nephrotic syndrome is an underlying disease or infection. It's this underlying disease or infection that causes changes in the kidney function that can result in secondary childhood nephrotic syndrome. Congenital diseases—diseases that are present at birth—can also cause childhood nephrotic syndrome [4].
Hyperlipidemia is found in almost all patients with nephrotic syndrome. High cholesterol level is a risk factor for atherosclerosis and is well documented in text books. But in India there have been few, if any, studies regarding the levels of different lipoproteins and apolipoproteins in nephrotic syndrome. Thus, this study focuses on the changes in different fractions of lipids and lipoprotein levels as well as apolipoprotein concentrations, so that, if necessary, early treatment can be started to prevent complications of atherosclerosis.

Methodology

The study was planned on 25 children suffering from the nephrotic syndrome and 25 normal children. The Nephrotic cases were selected according to the criteria proposed by International study of kidney diseases in children (ISKDC). That is children with oedema, proteinuria, and hypoproteinemia. Study was conducted in the department of Paediatrics at Anugrah Narayan Magadh Medical College, Gaya, Bihar from a period of November 2017 to September 2018.
Exclusion Criteria: Children with liver disorders, oedema due to Kwashiorkor, oedema due to CCF and Children suffering from kidney diseases other than nephrotic syndrome. The samples were analysed for Lipid and Protein profile.
The approval of the institutional ethic committee had been taken before the study. For all the patients, informed consent was taken. The aim and the objective of the study was conveyed to all patients.

Results & Discussion

Our study shows that in nephrotic syndrome, there is generalized hyperlipidemia and hypoalbuminemia. Although hyperlipidemia is most marked when serum albumin is low, yet no definite correlation can be established between the degree of hypoalbuminemia and rise of lipids. The present study also shows that serum cholesterol level in first episode of nephrotic syndrome reaches normal value at the end of steroid therapy. However in cases of relapses, there is persistent elevation in the cholesterol levels, which may predispose to the development of atherosclerosis and progression of chronic renal failure. Hence there is a rationale for treatment. Further prospective control studies in children evaluating efficacy and safety of lipid lowering drugs are needed.

Table 1: Demographic Details

Age in years	Normal patients	Nephrotic syndrome patients
Below 5 years	12	15
5 to 10 years	10	6
Above 10 years	3	4
Total	25	25
Sex	No of cases	No of cases
Males	18	20
Females	7	5
Total	25	25

Table 2: Observed Serum Levels of Lipid Profile

Type of Patients	Normal patients	Nephrotic syndrome patients
Total Cholesterol	160 - 225 mg/dl	278 - 395 mg/dl
High Density Lipids	42 - 58 mg/dl	44 - 61 mg/dl
Low Density Lipids	108 -151 mg/dl	245 - 336 mg/dl
Very Low Density Lipid	42 - 55 mg/dl	47 - 63 mg/dl
Triglycerides	81 - 115 mg/dl	258 - 291 mg/dl

Table 2: Observed Serum Levels of Serum Proteins

Type of Patients	Normal patients	Nephrotic syndrome patients
Serum Total Protein	6.6 - 7.9 g/dl	3.3 - 4.4 g/dl
Serum Albumin	3.7 - 4.3 g/dl	1.4 - 2.1 g/dl
Serum Globulin	2.9 - 3.7 g/dl	2.2 – 2.7 g/dl

Increased hepatic synthesis of lipoproteins contributes to the development of hyperlipidemia in nephrotic syndrome [5]. Nephrotic hyperlipidemia is the result of a increase in synthesis of apoproteins by the liver [6]. Early experiments with isolated perfused liver slices in rats with nephrotic syndrome demonstrated that lipoprotein synthesis is increased many times [7]. The signal for increased lipoprotein production may be low plasma oncotic pressure, caused by gross albuminuria. Mahmud S *et al*, [8] from his study has concluded that hyperlipidemia in general at remission, specifically serum total cholesterol, may be regarded as predictor of relapse in childhood idiopathic nephrotic syndrome.
In nephrotic syndrome, severity of proteinuria is reported to be correlated well with increase in serum cholesterol and

serum triglyceride concentrations. It has been shown that the loss of albumin or other liporegulatory substances in the urine is more likely to confer the signal for increased lipoprotein production, but the putative liporegulatory substance still awaits final identification [9]. The fact that apolipoprotein synthesis is not increased to the same extent for each apolipoprotein suggests that feedback regulatory mechanisms exist, which are superimposed on the overall stimulation of hepatic synthesis of secretory proteins [10]. The magnitude of the increase in low density lipoproteins (LDL) appears to be related to the degree of hypoalbuminemia [11]. Nevertheless, our current understanding implies that in nephrotic syndrome, increased hepatic synthesis of VLDL leads to accumulation of LDL particles.

Falaschi F *et al*. [12] observed patients with nephrotic range proteinuria (> or=3.5 gm/24 hrs) had a significantly higher carotid intima media wall thickness than did those without patients with nephrotic range proteinuria.

Querfeld [13] suggested that, there is rationale for treatment, since dyslipidemia may contribute to the development of atherosclerosis and the progression of chronic renal failure. However, the benefits of treatment with lipid lowering drugs have not been proven. Short term studies in adults with nephrotic syndrome have documented safety and efficacy of lipid-lowering drugs, including 'Statins', Fabric acids, fish oil and probucol. Statins are the most effective, resulting in a decrease of total cholesterol levels by about 30-40%. Prospective controlled studies in children evaluating efficacy and safety and lipid lowering drugs are needed.

Conclusion

From the above findings and the literature evidence there is increasing risk of atherosclerosis. So it is useful to evaluate the lipid and lipoprotein levels early and treat hyperlipidemia in childrens suffering from nephrotic syndrome. There is also risk of the progression to chronic renal failure. Hence care must be taken to ensure early diagnosis and treatment to avoid further complications.

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