Correlation between Serum Cholesterol and Serum Albumin Level in Childhood Nephrotic Syndrome

Abstract

Background: Hypercholesterolemia, a common secondary laboratory abnormality, is very prevalent in children with nephrotic syndrome.

Objective: The aim of this study was to evaluate the direct relationship between serum cholesterol and serum albumin in childhood nephrotic syndrome.

Patients and method: This cross sectional comparative study was performed on 60 children with the age of 2 years to 8 years with nephrotic syndrome in Department of Pediatric Nephrology, Comilla Medical College Hospital from January 2013 to December 2013. Serum albumin and serum cholesterol was measured by enzymatic colorimetric method. The relationship between serum cholesterol and serum albumin was measured by Pearson’s correlation.

Results: The mean cholesterol level in cases was 240(±07) mg/dl. And mean serum albumin level of cases was (1.88±.37)mg/dl. Pearson’s correlation test between serum cholesterol and serum albumin level of cases were significant (p<0.05).

Conclusion: These results suggest that in the childhood nephrotic syndrome, there is a negative correlation between serum cholesterol level and serum albumin level.

Introduction

Nephrotic syndrome is the clinical manifestation of glomerular diseases associated with heavy (nephrotic-range) proteinuria. The triad of clinical findings associated with nephrotic syndrome arising from the large urinary losses of protein are hypoaalbuminemia (<2.5g/dl), edema, hyperlipidemia (cholesterol>200mg/dl) [1]. It consists of clinical and laboratories abnormalities common to several primary and secondary kidney diseases, each characterized by increased permeability of the glomerular capillary wall to circulating plasma proteins, particularly albumin [2]. Nephrotic range of proteinuria is defined as protein excretion of >40mg/m²/hr or a first morning protein: creatinine ratio of >2-3:1. It occurs from 2 to 7 per 100,000 children younger than 18 years of age, and prevalence from 12 to 16 per 100,000 children [3]. It occurs more in children of south east Asia where the condition is primary (idiopathic) in 95% of cases [3,4]. Age at initial presentation also has an important say on the disease distribution frequency. 70% of MCNS patients are younger than 5 years; 20 to 30% of adolescent patients have MCNS [5].

By definition, secondary nephrotic syndrome refers to an etiology extrinsic to the kidney [6,7]. Approximately 90% of children with nephrotic syndrome have idiopathic nephrotic syndrome. Idiopathic nephrotic syndrome is associated with primary glomerular disease without an identifiable causative disease or drug. Idiopathic nephrotic syndrome includes multiple histologic types: minimal change disease, mesangial proliferation, focal segmental glomerulosclerosis, membranous nephropathy, and Membranoproliferative glomerulonephritis [1].

The initiating event that produces proteinuria remains unknown. However, strong evidence suggests that INS, at least in part, has an immune pathogenesis [8]. A circulating factor may play a role in the development of proteinuria in INS [8]. Perhaps the most exciting development in recent years in understanding the pathophysiology of nephrotic syndrome has occurred in the area of podocyte [9,10].

Apart from the podocyte and slit diaphragm, alterations in the glomerular basement membrane also likely play a role in the proteinuria of nephrotic syndrome [11]. The precise cause of the edema and its persistence is uncertain. A complex interplay of various physiologic factors, such as the following, probably contribute [12]: Decreased oncotic pressure, increased activity of aldosterone and vasopressin, diminished atrial natriuretic hormone and activities of various cytokines and physical factors within the vasa recti.

INS is accompanied by disordered lipid metabolism. The traditional explanation for hyperlipidemia in INS was the increased synthesis of lipoproteins that accompany increased hepatic albumin synthesis due to hypoalbuminemia. However, serum cholesterol levels have been shown to be independent of albumin synthesis rates. Decreased plasma oncotic pressure may play a role in increased hepatic lipoprotein synthesis. Also contributing to the dyslipidemia of INS are abnormalities in regulatory enzymes, such as lecithin-cholesterol acyltransferase, lipoprotein lipase, and cholesterol ester transfer protein [12,13].

The mechanism for its occurrence is complex and involves a combination of reduced clearance of lipoproteins from
the circulations [14-18] and increased hepatic synthesis of lipoproteins [15,16,19-21].

Most investigators have found a negative correlation between serum albumin concentration and serum cholesterol levels [22,23]. Some degree of correlation between lipids and serum albumin as suggested by Thomas et al. and between lipedema and edema by Peter et al. [24,25] generally, when edema regresses, lipid levels fall but some cases, it may continue to persist even after the edema has disappeared. Hyperlipidemia usually observed during the active phase of the disease and disappears with the resolution of proteinuria. Hyperlipidemia may contribute to renal injury. Therefore, this study was conducted to determine the lipid abnormalities and to know any correlation exist between serum lipid and serum albumin levels in nephrotic syndrome.

Ethical Issue

Ethical issue was addressed duly by taking informed written consent of parents/guardians of each patient before enrollment and taking permission of ethical committee of Comilla Medical College.

Patients and Method

The objective of this study was to estimate the serum cholesterol and serum albumin and to evaluate the correlation between serum cholesterol and serum albumin in children with idiopathic nephrotic syndrome. It was a cross sectional study carried out in the Department of Pediatric Nephrology, Comilla Medical College Hospital, and Comilla during January 2013 to December 2013. A total of 60 cases were enrolled by simple random sampling in this study. Study population was all children aging from 2 years to 8 years irrespective of sex with the following inclusion and exclusion criteria.

Inclusion criteria

- i. Nephrotic syndrome age from 2 years to 8 years.
- ii. Child and parents were willing to give consent and blood sample.

Exclusion criteria

- I. Age less than 2 years and more than 8 years.
- II. Those who had taken blood/fresh frozen plasma/albumin transfusion.
- III. Patient with liver disease.
- IV. Patient with severe malnutrition.

Procedures

Nephrotic syndrome was diagnosed by history who had generalized edema, scanty micturition, massive proteinuria, hypoalbuminemia and hypercholesterolemia. Massive proteinuria was diagnosed who had morning spot urinary protein creatinine ratio more than 2, hypoalbuminemia was diagnosed who had serum albumin level less than 2.5 gm/dl and hypercholesterolemia was considered who had serum cholesterol more than 220 mg/dl. Every case satisfying the selection criteria was enrolled in the study. With all aseptic precaution, blood was taken both from cases and controls. Serum albumin and serum cholesterol were measured by enzymatic colorimetric method. Data were collected by a preformed structured questionnaire.

Data analysis and interpretation

Data were processed, calculated and analyzed using computer software. Pearson’s correlation test done see the relation between serum cholesterol and serum albumin. The statistical analysis was performed using the Statistical Product and Service Solutions version 16.0 for Windows (Figure 1).

Results

A total of 60 nephrotic syndrome children were recruited to this study. The mean albumin level in was 1.88(±.37) g/dl. The mean cholesterol level was 240(±07) mg/dl.

Interpretation: Negative correlation (r = -0.27) and since p-value=0.03 <0.05, at 5% level of sig. the test is significant. So we can say significant correlation exist between albumin and cholesterol of NS Children.

Discussion

The primary pathologic process that occurs in the nephrotic syndrome is a change in the permselectivity of the glomerular basement membrane allowing the passage into the urine of macromolecules that are normally excluded from glomerular ultrafiltrate. Other processes that occur should result from that loss or from the homeostatic responses to it. In order to determine what relationship, if any, the various interdependent processes may have on serum lipid concentration, it is necessary to examine the relationship between them and plasma albumin concentration will decrease if net albumin availability resulting from increased synthesis, decreased catalysis or both does not occur.

There were total 60 children enrolled in the study out of these 41 males and 19 female children in the study group. In our study, we found the inverse relation of serum total cholesterol
with serum albumin. All studied patients had a relatively high value of serum total cholesterol 240(±07) mg/dl and low value of serum total albumin values 1.88(±.37)mg/dl. Comparatively male patient with NS was more common than female which was correlated with other workers as shown in the Table 1.

Table 1: Baseline characteristics of cases.

| Characteristics          | NS Children (n=60) |
|--------------------------|--------------------|
| Age                      |                    |
| 2- 4 years (%)           | 29(48)             |
| 5-8 years (%)            | 31(52)             |
| Sex                      |                    |
| Male (%)                 | 41(68)             |
| Female (%)               | 19 (32)            |
| Weight in kg (±SD)       | 17.27(±5.54)       |
| Height in cm(±SD)        | 100.83(±16.00)     |
| Swelling of the Body (%) | 60(100)            |
| Scanty Micturition (%)   | 60(100)            |
| Puffiness of Face (%)    | 60(100)            |
| Generalized edema (%)    | 60(100)            |
| Serum Albumin in gm/dl(±SD) | 1.88(±.37)     |
| Serum cholesterol in gm/dl(±SD) | 240(±07)    |

In this study we have found a negative correlation (r = -0.27 and p-value <0.05). This study is in confrontation of many studies [22,23] So we can say significant negative correlation exist between albumin and cholesterol of NS Children. This means that lower the albumin, higher will be the cholesterol levels (Table 2). Some degree of correlation between lipids and serum albumin and between lipedema and edema general, when edema regress, lipid levels fall but some cases, it may continue to persist even after the edema has disappeared [26,27].

Table 2: Correlation between serum Albumin with serum cholesterol.

| Correlations            | Albumin | Cholesterol |
|-------------------------|---------|-------------|
| Albumin                 |         |             |
| Pearson Correlation     | 1       | -2.71*      |
| Sig. (2-tailed)         | .036    |             |
| N                       | 60      | 60          |
| Cholesterol             |         |             |
| Pearson Correlation     | -2.71*  | 1           |
| Sig. (2-tailed)         | .036    |             |
| N                       | 60      | 60          |

*Correlation is significant at the 0.05 level (2-tailed).

Conclusion

There is a negative correlation between serum cholesterol level and serum albumin level in childhood nephrotic syndrome and this study showed that lower the serum albumin level, higher will be cholesterol level.

References

1. Priya Pias, Ellis D Avner (2015) Nephrotic Syndrome. Nelson Textbook of Pediatrics. (20th edn), Philadelphia, WB Saunders, USA, pp. 2521-2523.
2. Gowenlock AH, McManur JR, McLauchlan DM (1998) Varley’s Practical Clinical Biochemistry. (5th edn), Heinemann: London, UK, pp. 408-410.
3. Eddy AA, Symons JM (2003) Nephrotic syndrome in childhood. Lancet 362(9384): 629-639.
4. Bagga A, Sriiavastava RN (2005) In: Sriiavastava RN & Bagga A (Eds), Pediatric Nephrology. (4th edn), New Delhi: Jaypee Brothers Medical Publishers Pvt Ltd, India, pp. 159-200.
5. Baqi N, Singh A, Balacchandra S, Ahmed H, Nicastri A, et al. (1998) The paucity of minimal change disease in adolescent with primary nephrotic syndrome. Pediatr Nephrol 12(2): 105-107.
6. International Study of Kidney Disease in Children (ISKDC) (1978) Nephrotic syndrome in children: prediction of histopathology from clinical and laboratory characteristics at time of diagnosis. A report of the International Study of Kidney Disease in Children. Kidney Int 13(2): 159-165.
7. International Study of Kidney Disease in Children (ISKDC) (1981) The primary nephrotic syndrome in children. Identification of patients with minimal change nephrotic syndrome from initial response to prednisone. A report of the International Study of Kidney Disease in Children. J Pediatr 90(4): 561-564.
8. Elie V, Fakhoury M, Deschênes G, Jacqe-Aigrain E (2012) Physiopathology of idiopathic nephrotic syndrome: lessons from glucocorticoids and epigenetic perspectives. Pediatr Nephrol 27(8): 1249-1256.
9. Caridi G, Trivelli A, Sanna-Cherchi S, Perfumo F, Ghiggeri GM (2010) Familial forms of nephrotic syndrome. Pediatr Nephrol 25(2): 241-252.
10. Benoit G, Machuca E, Antignac C (2010) Hereditary nephrotic syndrome: a systematic approach for genetic testing and a review of associated podocyte gene mutations. Pediatr Nephrol 25(9): 1621-1632.
11. Kronenberg F (2011) APOL1 variants and kidney disease. There is no such thing as a free lunch. Nephrol Dial Transplant 26(3): 775-778.
12. Anderson S, Komers R, Brenner BM (2008) Renal and Systemic Manifestations of Glomerular Disease. Brenner BM, Brenner and Rector’s The Kidney. (8th edn), Philadelphia: Saunders Elsvier, USA, pp. 26.
13. Saland JM, Ginsberg H, Fisher EA (2002) Dyslipidemia in pediatric renal disease: epidemiology, pathophysiology, and management. Curr Opin Pediatr 14(2): 197-204.
14. Mckenzie IF, Nestel PJ (1968) Studies on turnover of triglyceride and esterified cholesterol in subjects with the nephrotic syndrome. J Clin Invest 47(7): 1685-1695.
15. Kelki M, Nikkila EA (1971) Plasma triglyceride metabolism in the adult nephrotic syndrome. Eur J Clin Invest 1(5): 345-351.
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16. Chan MK, Persaud JW, Ramdial L, Varghese Z, Seveny P, et al. (1981) Hyperlipidemia in untreated nephrotic syndrome, increased production or decreased removal? Clin Chem Acta 117: 317-323.

17. Garber DW, Gottlieb BA, March JB, Sparks CE (1984) Catabolism of very low density lipoproteins in experimental nephrosis. J Clin Invest 74(4): 1375-1383.

18. Staphrans I, Felts JM (1977) The effect of alpha 1-acid glycoprotein (orosomucoid) on triglyceride metabolism in the nephrotic syndrome. Biochem Biophys Res Comm 79(4): 1272-1278.

19. Marsh JB, Drabkin DL. (1960) Experimental reconstruction of metabolic patterns of lipid nephrosis. Key role of hepatic protein synthesis in hyperlipemia. Metabolism 9: 946-955.

20. Radding CM, Steinberg D (1960) Studies on the synthesis and secretion of serum lipoproteins by rat liver Mslices. J Clin Invest 39: 1560-1568.

21. Marsh JB, Sparks CE (1979) Hepatic secretion of lipoproteins in the rat and the effect of experimental nephrosis. J Clin Invest 64(5): 1229-1237.

22. Sah JP, Pandey R, Jaiswal S, Sharma B, Chaudhary S (2013) Correlation of Hypoproteinemia and Hypoalbuminemia with Hypercholesterolemia with Nephrotic Syndrome. Research & Reviews: A Journal of Health Professions 3(2): 1-7.

23. Kaysen GA, Gambertoglio J, Felts J, Hutchison FN (1987) Albumin synthesis, albuminuria and hyperlipemia in nephrotic patients. Kidney Int 31(6): 1368-1376.

24. Peters JP, Man EB (1943) The inter relationship of serum lipids in patients with diseases of kidney. J Clin Invest 22: 721.

25. Bhandari B, Mandowara SL (1980) Lipoprotein profile in nephrotic syndrome. Indian Pediatr 17(5): 416-419.

26. Beck P, Kurrey VK, Dawale P (2015) To study lipid profile and its correlation with serum albumin level in Nephrotic Syndrome in children. Indian Journal of Applied Research 10(5): 329-330.

27. Dnyanesh DK, Dnyanesh S, Shenoy V (2014) A Serum of Lipids in Nephrotic Syndrome in Children. Journal of Dental and Medical sciences 13(3): 1-6.