Section: Pediatrics

Original Research Article

DETERMINATION OF CAROTID INTIMA-MEDIA THICKNESS IN CHILDREN WITH NEPHROTIC SYNDROME-A CASE-CONTROL STUDY

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Abstract

Background: Idiopathic Nephrotic Syndrome (NS) is the most common glomerular disorder among children. Carotid intima-media thickness is an indirect marker of atherosclerosis and targets adult organ damage. This study aimed to estimate carotid intima-media thickness in children with nephrotic syndrome and compare it with age- and sex-matched controls. **Material and Methods:** Children with nephrotic syndrome who were admitted to the government of Rajaji Hospital, Madurai. Patient details were collected regarding nephrotic syndrome, including the age of onset, number of relapses, response to steroids, need for steroid-sparing agents or other drugs, total cholesterol levels, body mass index, presence or absence of hypertension, and carotid intima-media thickness. The combined thickness of the carotid intima and media was measured sonographically, which indicated increased atherosclerotic plaque formation. **Results:** Fifty children were studied: 25 cases and 25 controls. The most studied age group was 6–10 years. No statistically significant correlation was found between the sex of the patient and carotid intima-media thickness. In addition, there was no significant correlation between sex and carotid intima-media thickness. Serum cholesterol levels were significantly positively correlated with carotid intima-media thickness in patients and controls with nephrotic syndrome. The age of onset, body mass index, and blood pressure of patients with nephrotic syndrome had a significant positive correlation with carotid intima-media thickness. **Conclusion:** We conclude that the thickness of the CIMT was higher in nephrotic syndrome. CIMT was positively correlated with age, BMI, hypertension, disease duration, and serum cholesterol level.

INTRODUCTION

Idiopathic Nephrotic Syndrome (NS) is the most common glomerular disorder in children. Risk factors for developing arterial wall lesions in children with nephrotic syndrome may be associated with NS per se and with drugs used for treatment.[1] The remaining nature of NS is linked with multiple biochemical alterations that affect the structure of arterial vessel walls. Clinical and metabolic risk factors that contribute to atherosclerosis in NS include hyperlipidemia, hypertension, nephrotic proteinuria, and drugs used for treatment.[2,3]

Carotid intima-media thickness is an indirect marker of atherosclerosis and targets adult organ damage.[4,5] Its value in children is still under debate, but there are increasing numbers of studies among children with risk factors for vascular damage.[6] Few studies have reported persisting lipid abnormalities during remission and severe persistent proteinuria as risk factors for the later development of atherosclerosis.[7,8]

Currently, increased carotid intima-media thickness (CIMT) has been accepted as a reliable marker for atherosclerosis and its complications, such as cardiovascular disease, coronary artery disease, myocardial infarction, and stroke.[9] Increased CIMT in children is also associated with other cardiovascular risk factors, such as familial hypercholesterolemia, diabetes, and other arteriopathy diseases, such as Kawasaki disease.[10] There are nearly fivefold increased chances of stroke or heart attack rates with increased CIMT.[11] This work has been planned to study CIMT in children, its correlation with dyslipidemia, and other risk factors that influence CIMT in the pediatric age group.

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Aim

This study aimed to estimate carotid intima-media thickness in children with nephrotic syndrome and compare it with age- and sex-matched controls.

MATERIALS AND METHODS

This case-control study was conducted on 50 children with nephrotic syndrome aged 1–12 years admitted to Government Rajaji Hospital, Madurai, from January 2021 to December 2022. The study was approved by the institutional ethics committee before initiation, and informed consent was obtained from all patients.

Inclusion Criteria

All children with nephrotic syndrome in the age group of 1 to 12 years and age- and sex-matched controls who had normal body mass index and were normotensive were included.

Exclusion Criteria

Children with nephrotic syndrome who were defaulters and children with nephrotic syndrome who were treated with cyclosporine were excluded.

The combined thickness of the carotid intima and media was measured sonographically, which indicated increased atherosclerotic plaque formation. Measurements were performed using B-mode ultrasound in the common carotid and internal carotid arteries from the thickest area along the course using a Samsung HS70A, an ultrasound machine with a linear probe with a frequency of 10-12hz.

Patient details were collected regarding nephrotic syndrome, including the age of onset, number of relapses, response to steroids, need for steroid-sparing agents or other drugs, total cholesterol levels, body mass index, presence or absence of hypertension, and carotid intima-media thickness. To highlight the increased carotid intima and media thickness in children with nephrotic syndrome compared within that the normal population, indicating early atherosclerosis.

Statistical Analysis

Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) for MS Windows. The obtained data were entered into MS Excel. Data were analysed using descriptive statistics and chi-squared tests.

RESULTS

The age distribution of the patients among the groups showed a higher number of children in the age group of 8-10 years. Similarly, a very low number of children were observed in the age group of 10-12. The p-value of age distribution was 0.188, which was statistically insignificant. Fifty NS children, 26 male children, and 24 female children were observed, and the chi-square value was 0.0218; the p-value of 0.882 was statistically insignificant.

In the case group, a mean BMI value of 19.28±2.63 kg/m2 was observed. Similarly, in the control group of patients 19.8±2.31 kg/m2. The probability value of the Mean BMI of the patients was 0.219, which was not statistically significant. The mean cholesterol levels of the patients in the case group were 393.36±105.93 mg/dL and in the control group, 105.93±138.9 mg/dL was observed. The p-value of the mean cholesterol level of the patients was <0.001, which was statistically significant. [Table 1]

There was a significant difference in the patient's age, blood pressure, and BMI in CIMT cases ($p<0.05$). There was a statistically insignificant difference in the age of onset and mean albumin level of CIMT cases (p=0.646, p=0.368). The mean cholesterol level of CIMT Cases was 393.36±105.93 mg/dl; with a p-value of 0.022, which was statistically significant. [Table 2 and Figures 1-5]

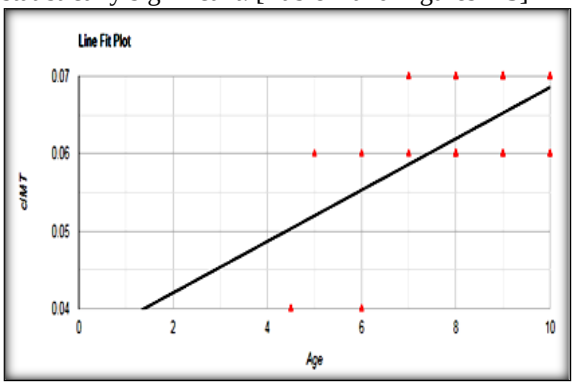

Figure 1: ROC curve on age and blood pressure of CIMT

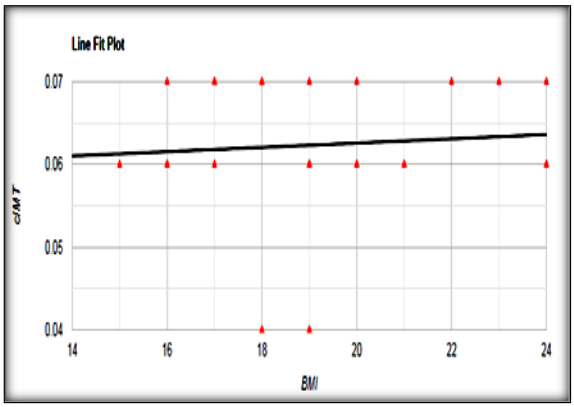

Figure 2: ROC curve on BMI of CIMT

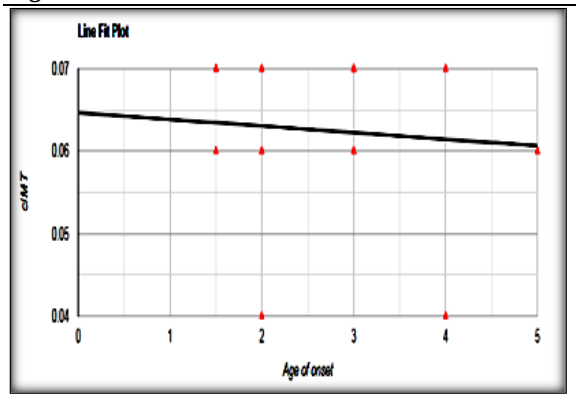

Figure 3: ROC curve age of onset on CIMT

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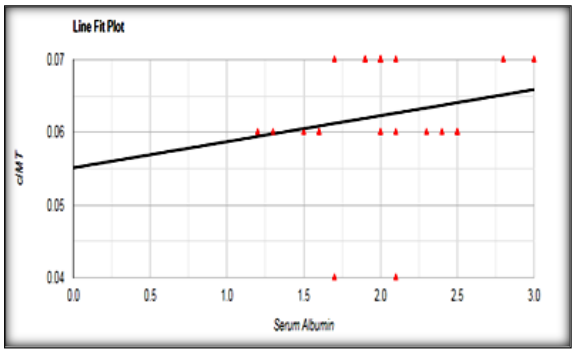

Figure 4: ROC of mean albumin on CIMT

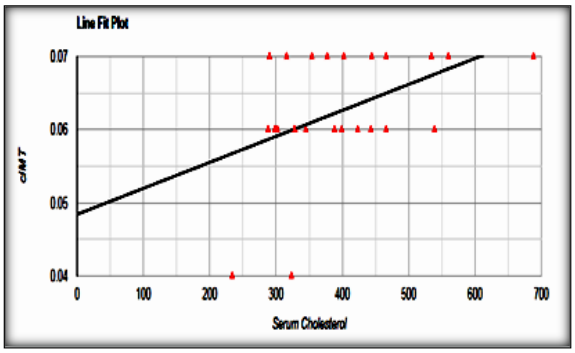

Figure 5: ROC of mean cholesterol on CIMT

Table 1: Demographic data of the study

		Case	Control	P value
Age Distribution (years)	4-6	4	6	0.188
	6-8	9	7	
	8-10	11	10	
	10-12	1	2	
Gender	Male	12	14	0.882
	Female	13	11	
BMI		19.28±2.63	19.8±2.31	0.219
Cholesterol		393.36±105.93	138.9±8.87	<0.001

Table 2: Age, blood pressure, BMI, age of onset, serum albumin and cholesterol between CIMT case

		CIMT Case	r value	P value
Age (years)	4-6	0.05±0.011	0.6031	0.001
	6-8	0.063±0.005		
	8-12	0.065±0.005		
Blood Pressure (mm of Hg)	Normotensive	0.061±0.0085	0.215	0.001
	Hypertensive	0.06±0.0057		
BMI		19.28±2.63	0.082	0.002
Age of onset	1-2	0.062±0.0091	-0.0964	0.646
	3-4	0.063±0.0085		
	5-6	0.06		
S. Albumin	1-2	0.063±0.0081	0.188	0.368
	2-3	0.061±0.0087		
Cholesterol		393.36±105.93	0.4531	0.022

DISCUSSION

A higher number of children was observed in the age group of 8-10 years; similarly, a very low number of children was observed in the age group of 10-12 years. Of the 50 children with NS, 26 were male and 24 were women. Safaei and Maleknejad observed a similar result, but other researchers reported the mean onset age at 7.9 ± 5.1 years.[12]

In our study, 12 males and 13 females were considered as cases, and 14 males and 11 females were used as controls. The mean BMI value of 19.28±2.63 kg/m2 was observed in the case group. Similarly, in the control group of patients, 19.8±2.31 kg/m2 is almost equal and has no statistically significant difference. The mean cholesterol levels of the patients in the case group were 393.36±105.93 mg/dL, and in the control group, 105.93±138.9 mg/dL was observed. Therefore, cholesterol levels were significantly higher in the cases than in the controls, and the p-value <0.001 was statistically significant.

Our study showed a significant correlation between CIMT and BMI; however, Litwin et al. reported a weak positive correlation between them. We found a positive correlation between the CIMT and patient age. In our study, there was a positive correlation between CIMT and blood pressure. However, Anita et al. found no correlation between CIMT and blood pressure. In our study, there was no correlation between the age of onset of the disease and CIMT.[13]

In our study, the serum albumin level was not significantly correlated with CIMT. It has also been discussed elsewhere how hypoalbuminaemia contributes to decreased lipoprotein catabolism in children with NS and, hence, leads to dyslipidaemia. Hypoalbuminaemia also results in endothelial cell oedema, which contributes to an increase in CIMT. Similar results have been reported by other researchers. Anita et al. found no correlation between CIMT and LDL, HDL, triglyceride, or VLDL.[13]

Our study found a positive correlation between serum cholesterol and CIMT. Satish et al. evaluated the intima-media thickness of the carotid artery in children with nephrotic syndrome. CIMT was thicker in nephrotic children, influenced by factors such of CIMT were hyperlipidaemia, hypertension, hypoproteinaemia, and duration of disease.[14] In our

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study, CIMT also has a positive correlation between serum cholesterol and hypertension. Ashraf et al. evaluated carotid intima-media thickness in children with nephrotic syndrome and its relationship to different risk factors. CIMT was positively correlated with disease duration, number of relapses, and BMI.[15]

In line with this study, our study also showed that CIMT positively correlated with BMI, number of relapses, and disease duration. Aleksandra et al. determined that carotid intima-media thickness in children with idiopathic nephrotic syndrome was greater than that in healthy subjects and assessed whether carotid intima-media thickness in children with nephrotic syndrome is associated with clinical (including disease duration, cumulative dose of steroids, and number of relapses) and biochemical parameters. Duration of nephrotic syndrome was the only independent predictor of carotid intima-media thickness.[16]

Finally, in our study, the carotid intima-media thickness in children with nephrotic syndrome and the control group was studied and compared, and the p-value was less than 0.05, making it statistically significant.

CONCLUSION

We conclude that the thickness of the CIMT was higher in nephrotic syndrome. CIMT positively correlated with age, BMI, hypertension, disease duration, and serum cholesterol level. Therefore, this study could provide supportive evidence for further studies on the use of early statins in children with nephrotic syndrome.

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