ASSOCIATION OF BLOOD LIPID AND GLUCOSE LEVELS WITH CAROTID INTIMA MEDIA THICKNESS

Syed Aown Raza Shah Bokhari[1], Sikandar Hayat Khan[2], Muhammad Shahzad Hanif[3], Mariam Hassan[4], Naila Azam[5]

ABSTRACT

Objective: *To measure the differences in CIMT across groups based upon normal and higher levels of fasting glucose and lipids.*

Methodology: *This cross sectional study was carried out between January to June 2011 at department of radiology and pathology, PNS Rahat hospital Karachi. From a target population of patients presenting for fasting blood glucose measurement, a total 0f 201 subjects were shortlisted and consented after various exclusion. These patients were sampled for glucose and lipids after brief clinical evaluation. Later subjects underwent CIMT measurement in radiology department.*

Results: *Age showed moderate positive correlation with CIMT readings (r=0.493, p=0.000), while BMI (r=0.038, p=0.636), fasting blood glucose (r=0.038, p=0.646), triglyceride (r=0.179, p=0.029), and total cholesterol (r=0.221, p=0.007) showed lesser correlations. Patients with hyperglycemia had higher CIMT [{Group-1, Normolycemia, FBG≤5.5mmol/L = 0.667±0.137cm} {Group-2, Hyperglycemia, FBG>5.5mmol/L = 0.7180±0.147cm}(p=0.028)]. Mean CIMT values among subjects with hypertriglyceridemia and hypercholesterolemia were higher than patients with normal triglycerides and cholesterol [(triglyceride: p=0.040) (total cholesterol: p=0.055)].*

Conclusion: *The carotid intima medial layers were found to be thicker in subjects having higher blood levels of fasting blood glucose, triglycerides and total cholesterol.*

Key Words: *Carotid intima media thickness (CIMT), Fasting blood glucose, Triglycerides, Total cholesterol, Atherosclerosis.*

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INTRODUCTION

Today's world is plagued by the rise of several diseases of metabolism, including the diabetes mellitus, hypertension and dyslipidemias[1]. The common end point to almost all of these disorders includes accelerated atherosclerosis, leading to narrowing in vasculature across several body organ[2]. The narrowing in vasculature due to atherosclerosis leads to stroke, myocardial infarction and other ischemia related complications[3]. In this regard the available literature search identifies measures of carotid intima media thickness as a surrogate measure of ongoing atherosclerosis[4]. The thickness of carotid intima media is a non-invasive, cost-effective and easy to measure and interpret radiological investigation which in theory can estimate the degree of underlying atherosclerosis[5]. Moreover, the investigation has also been utilized as the marker for showing response to treatments targeted against the cardiovascular diseases[6].

Theoretically, the idea of measuring the severity of atherosclerosis seems straightforward by using carotid intima media thickness (CIMT) in carotid arteries[4,5]. However, the literatures search through pubmed highlights following: Firstly, not all authors advocate the presence of significant differences between various cardiovascular risk factors and measures of atherosclerosis including CIMT[7, 8]. Secondly, the available literature has also highlighted racial and ethnic variations in the

[1-5]Department of Radiology, PNS Rahat Hospital, Karachi - Pakistan

[5]Department of Pathology, PNS Rahat Hospital, Karachi - Pakistan

[5]PNS Rahat Hospital, Karachi - Pakistan

Address for Correspondence:
Dr. Sikandar Hayat Khan,
Department of Pathology, PNS Rahat Hospital, Karachi - Pakistan
E-mail: sik_cpsp@yahoo.com

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measures of carotid vessels and their dimensions leading to variable vessel's intima media thickness readings[9,10]. Finally local data yields limited literature regarding CIMT measures. Whatever, data is available do not directly address the association of intima media thickness of carotid wall thickness with lipids and glycemia[11].

Keeping in view the variable findings on literature search relating cardiovascular risk factors and carotid intima media thickness measures and lack of local data on the subject it was planned to measure the differences of carotid intima media thickness across groups based upon normal and higher levels of fasting glucose and lipids.

METHODOLOGY

This Cross-sectional study was carried out at the departments of radiology and pathology, PNS Rahat hospital Karachi from January to June 2011. The target population included adult subjects who presented at the department of pathology for measurement of fasting blood glucose. These subjects were initially interviewed for inclusion into the study. Diagnosed diabetics, pregnant ladies, not observing exact medical fasting status or having a chronic infectious disease process were excluded from the study. Finally selected subjects (201) were consented by signing the data collection document, and evaluated by brief history and clinical examination. The clinical examination included were measuring the height ($\pm$ 2cm) and weight ($\pm$1kg). The Body mass indexes (BMI) of subjects were later calculated. Subjects were then sampled for fasting blood glucose, serum triglycerides and total cholesterol. Post phlebotomy subjects were sent to radiology department for evaluation of their carotid intima media thickness. Subjects who had not completed the complete sequence including consenting for radiological examination, or were lost to follow up were also excluded from the study. Samples showing hemolysis, massive hypertriglyceridemia (>6.0 mmol/L) or hypercholesterolemia (>10.0 mmol/L) were also excluded from the study. CIMT were measured by B-Mode high frequency (7.5 Hz) ultrasound probe of ultrasound machine (Sonoline ADARA). After explaining the patients mean CIMT were measured in prone position with neck semi-extended and shoulders resting on soft pillow[12]. Fasting blood glucose was measured by hexokinase method, triglyceride by GPO-PAT, and total cholesterol by CHOD-PAP. All measurement were made on Hitachi-902(Clinical chemistry analyzer). Subjects were divided into groups as per their glycemic status as Group-1 with Normoglycemia (Fasting blood glucose <5.6 mmol/L) and Group-2: Hyperglycemia (Fasting blood glucose >5.5mmol/L). Individuals were grouped into two as per their triglyceride results :Group-1: Normotriglyceridemia (Fasting triglyceridemia <2.3mmol/L) and Group-2: Hypertriglyceridemia (Fasting triglyceridemia >2.2mmol/L). As per the subject's total cholesterol results, 2 groups were made as Normocholesterolemia (Total cholesterol < 5.2 mmol/L) and Hypercholesterolemia (Total cholesterol >5.1 mmol/L).

All data were entered into SPSS version-15. Descriptive data was measured for age and gender. Data was compared between the group with subjects demonstrating normal levels with group of subjects demonstrating higher levels of fasting blood glucose, triglycerides, and total cholesterol for carotid intima media thickness. This was done by "Independent sample t-test". Correlation between CIMT values in cm and age, fasting blood glucose, BMI, triglycerides and total cholesterol were measured by using pearson's correlation. Finally, linear regression for estimating intercept and slope was measured by keeping CIMT as dependent factor. Age, BMI, fasting blood glucose, triglycerides and total cholesterol were considered as independent factors.

RESULTS

Mean age among our data subjects was 40.02$\pm$10.52 years. Males tend to have higher carotid intima media thickness and body mass indices in comparison to females (Table 1). Age showed moderate correlation with CIMT, while fasting blood glucose, BMI, fasting triglycerides and total cholesterol showed minimal correlations with CIMT readings (Table 2). The linear regression analysis after keeping the CIMT values as a dependent factor showed an increase of 0.007 cm, 0.001cm, 0.003 cm, 0.023 cm and 0.037 cm increase in CIMT readings after one unit increase in age, BMI, fasting blood glucose, fasting triglycerides and total cholesterol (Table 2). Mean CIMT in subjects with glucose dysregulation was higher than subjects with patients with normal fasting blood glucose [{Group-1, Normolycemia, FBG$\leq$5.5mmol/L=0.667$\pm$0.137cm}{Group-2, Hyperglycemia, FBG>5.5mmol/L=0.718$\pm$0.147cm} (p=0.028)] as shown in Figure 1. Figure 2 shows mean CIMT values among subjects with or without hypertriglyceridemia. [{Group-1, Normotriglyceridemia, Triglycerides $\leq$2.2mmol/L =0.665$\pm$0.154cm} {Group-2, Hypertriglyceridemia, triglycerides >2.2mmol/L = 0.714$\pm$0.133cm} (p=0.040)]. The intimal medial thickness values in carotid arteries (CIMT) were higher in subjects with hypercholesterolemia than subjects demonstrating normal cholesterol level. [{Group-1, Normocholesterolemia, Total cholesterol $\leq$5.1mmol/L=0.677$\pm$0.141cm}{Group-2,

Table 1: Gender differences for CIMT, BMI, Fasting blood glucose, Triglycerides, total Cholesterol and age among our data (n=201)

Parameter	Gender		p-Value
	Male	Female	
CIMT (cm)	0.71 ± 0.12	0.66 ± 0.15	0.041
Body mass index (BMI)	25.92 ± 4.21	27.45 ±5.95	0.034
Fasting blood glucose (mmo/L)	5.88 ± 1.87	5.69 ± 1.09	0.435
Total cholesterol (mmol/L)	4.84 ± 0.87	4.69 ± 0.76	0.232
Fasting triglycerides (mmol/L)	2.29 ± 1.16	1.77 ± 0.76	0.001
Age (years)	42.34 ± 10.20	41.56 ± 11.01	0.605

Table 2: Correlation Co-efficient, Slope and intercept between CIMT and age, BMI, Fasting blood glucose, total cholesterol, & Serum triglycerides (n=201)

Parameter	Correlation co-efficient [r] with CIMT	Slope	Intercept	p-Value
Age (years)	0.493	0.007	0.405	0.000
BMI	0.038	0.001	0.665	0.636
Fasting blood glucose (mmol/L)	0.038	0.003	0.675	0.646
Fasting triglycerides (mmol/L)	0.179	0.023	0.643	0.029
Total cholesterol (mmol/L)	0.221	0.037	0.514	0.007

Figure 1: CIMT differences in subjects with Group-1: normoglycemia (≤ 5.5 mmol/L) and Group-2: hyperglycemia (>5.5 mmol/L), [p= 0.028]

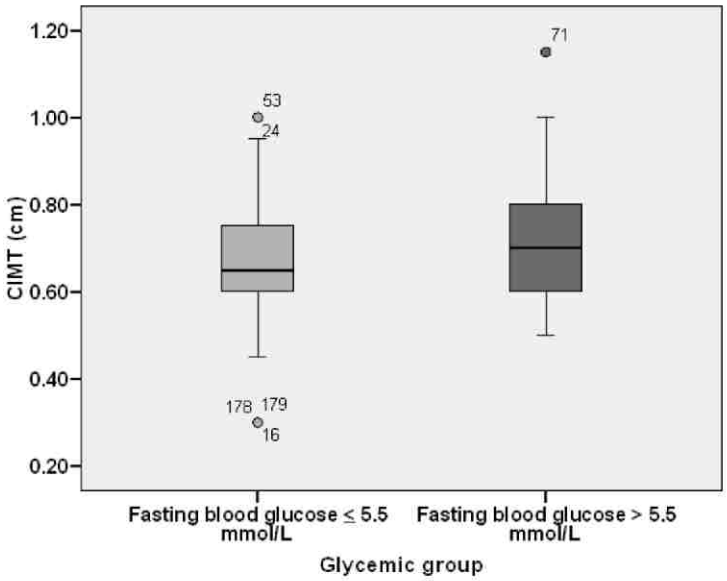


Figure 2: CIMT differences in subjects with normotriglyceridemia (≤ 2.2 mmol/L) and hypertriglyceridemia (> 2.2 mmol/L), [p= 0.040]

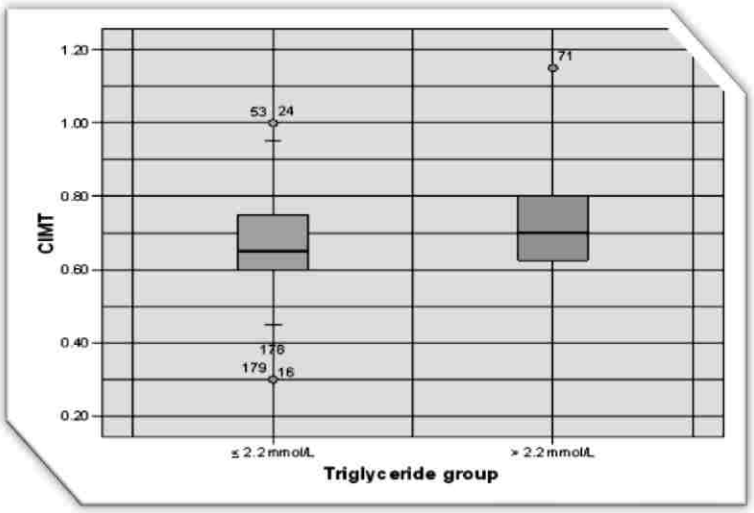
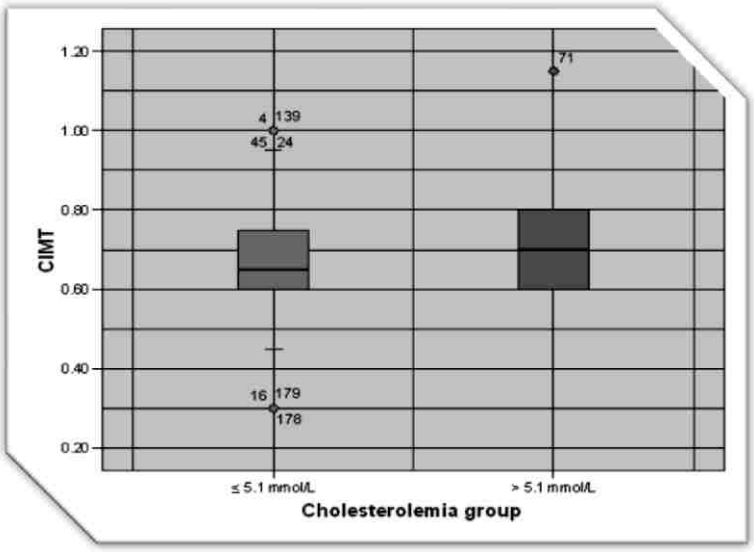


Figure 3: CIMT differences in subjects with normocholesterolemia (≤ 5.1 mmol/L) and hypercholesterolemia (> 5.1 mmol/L), [p= 0.055]



Hypercholesterolemia, total cholesterol > 5.1 mmol/L = 0.726±0.144cm} (p=0.055)] as depicted in Figure 3. Hypertensive subjects (n=19) in our study were found to have higher CIMT readings (0.767±0.159 cm) than non-hypertensive individual (0.684 ±0.138) [p=0.019].

DISCUSSION

Our study is the first local study which has demonstrated the abnormalities in glucose and lipids in blood in relation with acceleration in atherosclerotic processes by measuring the carotid intima media thickness. Literature search reveals mixed findings in terms of association of CIMT with diabetes mellitus or dyslipidemias, indicating both the associations with glycemia and vice versa[7,13]. Temelkova-Kurktschiev et al has shown that glycemic abnormalities are not related to increased thickness of intima media in carotid vessels[14]. Similarly hyperlipidemias, especially triglyceridemia have not been observed to be associated with measures of atherosclerosis like CIMT[8,15,16]. However, we feel that our observations may be quite significant because: Firstly, some

better controlled trials have identified reduction in CIMT after using statin therapy indicating role of lipidemia with atherosclerosis[17]. Similarly markers of endothelial dysfunction associated with atherosclerosis, have also been found to be significantly different in subjects with diseases of metabolism like diabetes mellitus and control subjects[18]. Secondly, animal studies have also highlighted the predictive role of carotid intima media thickness for underlying atherosclerotic processes[19]. Lastly, a great body of recent evidence now supports the association of dyslipidemias with atherosclerosis, including both the triglyceridemia and hypercholesterolemia[20-22].

Our study has also shown females to have lower thickness of their carotid intima media in comparison to male counterparts. In contrast to our results, studies do highlight non-significant differences between genders[23]. However, this particular study had mean age from 54-56 years, where probably females lose their pre-menopausal protection against the cardiovascular related diseases. Our selected females have a mean age in lower than the above referenced study, which could be the possible reason to the identified differences. Moreover, a study also signifies the presence of significant differences in terms of CIMT readings between male and females supporting our findings[24].

In our study the CIMT correlated weakly with body mass index. Variable literature relationship exists between BMI and carotid intima media thickness. Dogan et al have shown body mass index to be significantly related to intima media thickness measures in carotid arteries[25]. However, others have only reported weaker correlations with carotid intima media thickness[26]. This finding in the opinion of the authors is significant as anthropometric measures include both the body mass indices, which are more dependent upon muscle mass to indices like waist to hip ratios which have been shown to be more representative of fat accumulation inside the body. The latter measures i.e., waist to hip ratio in contrast to BMI have been shown to be associated with various cardiovascular risks in literature[27]. Moreover, insulin resistance in human subjects, which has been shown in literature to be the cause of cardiovascular diseases, has also not been found to be related to body mass indices[28].

The study may have certain limitations: Firstly, the observations produced by our study are based upon a smaller sample size, which leaves a chance for type-2 statistical error. Secondly, our sample did not have known diabetics or patients with hyperlipidmeia. So a sample including such cases may show higher degree of differences. Lastly, CIMT measurement technique has also been found to have problems like selection of specific areas of measurements and intra-operator variations have also been observed[29]. However, we utilized the most measured method for CIMT evaluations[12].

The study may have enormous clinical implications. CIMT measurements provide concrete physical evidence to the development of ongoing atherosclerotic processes, which once accelerated in diseases like diabetes mellitus, hyperlipidemias and hypertension results in various micro and macrovascular complications. Measuring CIMT in these disorders may not be invasive and cost-effective, but can also guide physicians' in terms of associated disease complications.

CONCLUSION

The carotid intima media layers were found to be thicker in subjects having higher blood levels of fasting blood glucose, triglycerides and total cholesterol. Age was found to be significantly correlated with the thickness of intima media layers of carotid vessel.

REFERENCES

1. Crawford AG, Cote C, Couto J, Daskiran M, Gunnarsson C, Haas K, et al. Prevalence of obesity, type II diabetes mellitus, hyperlipidemia, and hypertension in the United States: findings from the GE Centricity Electronic Medical Record database. Popul Health Manag 2010;13:151-61.
2. Soor GS, Vukin I, Leong SW, Oreopoulos G, Butany J. Peripheral vascular disease: who gets it and why? A histomorphological analysis of 261 arterial segments from 58 cases. Pathology 2008;40:385-91.
3. Dalager S, Paaske WP, Kristensen IB, Laurberg JM, Falk E. Artery-related differences in atherosclerosis expression: implications for atherogenesis and dynamics in intima-media thickness. Stroke 2007;38:2698-705.
4. Abdelghaffar S, El Amir M, El Hadidi A, El Mougi F. Carotid intima-media thickness: an index for subclinical atherosclerosis in type 1 diabetes. J Trop Pediatr 2006;52:39-45.
5. Sibal L, Agarwal SC, Home PD. Carotid intima-media thickness as a surrogate marker of cardiovascular disease in diabetes. Diabetes Metab Syndr Obes 2011;4:23-34.
6. Taylor AJ, Zhu D, Sullenberger LE, Lee HJ, Lee JK, Grace KA. Relationship between glycemic status and progression of carotid

intima-media thickness during treatment with combined statin and extended-release niacin in ARBITER 2. Vasc Health Risk Manag 2007;3:159-64.

7. Mete M, Wilson C, Lee ET, Silverman A, Russell M, Stylianou M, et al. Relationship of glycemia control to lipid and blood pressure lowering and atherosclerosis: the SANDS experience. J Diabetes Complications 2011
8. Labreuche J, Touboul PJ, Amarenco P. Plasma triglyceride levels and risk of stroke and carotid atherosclerosis: a systematic review of the epidemiological studies. Atherosclerosis 2009;203:331-45.
9. Breton CV, Wang X, Mack WJ, Berhane K, Lopez M, Islam TS, et al. Carotid artery intima-media thickness in college students: race/ethnicity matters. Atherosclerosis 2011;217:441-6.
10. Wong ND, Lopez VA, Allison M, Detrano RC, Blumenthal RS, Folsom AR, et al. Abdominal aortic calcium and multi-site atherosclerosis: the multiethnic study of atherosclerosis. Atherosclerosis 2011;214:436-41.
11. Najafian J, Fatemi F, Esfahani AM, Najafian A. Relationship between intima-media thickness of carotid arteries and coronary stenosis in angiography. Rawal Med J 2008;33:59-61.
12. Dogan S, Duivenvoorden R, Grobbee DE, Kastelein JJ, Shear CL, Evans GW, et al. Ultrasound protocols to measure carotid intima-media thickness in trials: comparison of reproducibility, rate of progression, and effect of intervention in subjects with familial hypercholesterolemia and subjects with mixed dyslipidemia. Ann Med 2010;42:447-64.
13. Fitch KV, Stavrou E, Looby SE, Hemphill L, Jaff MR, Grinspoon SK. Associations of cardiovascular risk factors with two surrogate markers of subclinical atherosclerosis: endothelial function and carotid intima media thickness. Atherosclerosis 2011;217:437-40.
14. Temelkova-Kurktschiev T, Koehler C, Schaper F, Henkel E, Hahnefeld A, Fuecker K, et al. Relationship between fasting plasma glucose, atherosclerosis risk factors and carotid intima media thickness in non-diabetic individuals. Diabetologia 1998;41:706-12.
15. Riccioni G, Bucciarelli T, D'Orazio N, Palumbo N, di Ilio E, Corradi F, et al. Plasma antioxidants and asymptomatic carotid atherosclerotic disease. Ann Nutr Metab 2008;53:86-90.
16. Magyar MT, Paragh G, Katona E, Valikovics A, Seres I, Csiba L, et al. Serum cholesterols have a more important role than triglycerides in determining intima-media thickness of the common carotid artery in subjects younger than 55 years of age. J Ultrasound Med 2004;23:1161-9.
17. Bedi US, Singh M, Singh PP, Bhuriya R, Bahekar A, Molnar J, et al. Effects of statins on progression of carotid atherosclerosis as measured by carotid intimal--medial thickness: a meta-analysis of randomized controlled trials. J Cardiovasc Pharmacol Ther 2010;15:268-73.
18. Głowińska-Olszewska B, Tołwińska J, Urban M. Interrelationship between endothelial dysfunction, IMT of the carotid arteries and adhesion molecules in obese hypertensive children and adolescents. Pediatr Endocrinol Diabetes Metab 2007;13:7-14.
19. Korshunov VA, Berk BC. Flow-induced vascular remodeling in the mouse: a model for carotid intima-media thickening. Arterioscler Thromb Vasc Biol 2003;23:2185-91.
20. Maki KC, Davidson MH, Dicklin MR, Bell M, Witchger M, Feinstein SB. Predictors of anterior and posterior wall carotid intima media thickness progression in men and women at moderate risk of coronary heart disease. J Clin Lipidol 2011;5:141-51.
21. Yilmazer MM, Tavli V, Carti OU, Mese T, Güven B, Aydin B, et al. Cardiovascular risk factors and noninvasive assessment of arterial structure and function in obese Turkish children. Eur J Pediatr 2010;169:1241-8.
22. Weingärtner O, Pinsdorf T, Rogacev KS, Blömer L, Grenner Y, Gräber S, et al. The relationships of markers of cholesterol homeostasis with carotid intima-media thickness. PLoS One 2010;5:e13467.
23. Youn YJ, Lee NS, Kim JY, Lee JW, Sung JK, Ahn SG, et al. Normative values and correlates of mean common carotid intima-media thickness in the Korean rural middle-aged population: the Atherosclerosis RIsk of Rural Areas iN Korea General Population (ARIRANG) study. J Korean Med Sci 2011;26:365-71.
24. Dengel DR, Jacobs DR, Steinberger J, Moran AM, Sinaiko AR. Gender differences in vascular function and insulin sensitivity in young adults. Clin Sci (Lond) 2011;120:153-60.
25. Dogan S, Duivenvoorden R, Grobbee DE, Kastelein JJ, Shear CL, Evans GW, et al.

Completeness of carotid intima media thickness measurements depends on body composition: the RADIANCE 1 and 2 trials. J Atheroscler Thromb 2010;17:526-35.

26. Yan RT, Yan AT, Anderson TJ, Buithieu J, Charbonneau F, Title L, et al. The differential association between various anthropometric indices of obesity and subclinical atherosclerosis. Atherosclerosis 2009;207:232-8.
27. Elsayed EF, Tighiouart H, Weiner DE, Griffith J, Salem D, Levey AS, et al. Waist-to-hip ratio and body mass index as risk factors for cardiovascular events in CKD. Am J Kidney Dis 2008;52:49-57.
28. Kondaki K, Grammatikaki E, Pavón DJ, Manios Y, González-Gross M, Sjöstrom M, et al. Comparison of several anthropometric indices with insulin resistance proxy measures among European adolescents: The Helena Study. Eur J Pediatr 2011;170:731-9.
29. Freire CM, Ribeiro AL, Barbosa FB, Nogueira AI, de Almeida MC, Barbosa MM, et al. Comparison between automated and manual measurements of carotid intima-media thickness in clinical practice. Vasc Health Risk Manag 2009;5:811-7.

CONTRIBUTORS

SARSB conceived the idea & planned the study. SHK & MSH did laboratory analysis & results compilation. MH helped in radiological examination. NA did data analysis of the study. All the authors contributed significantly to the write up that resulted in the submitted manuscript.