Original Research Paper



Internal Medicine

A STUDY OF CAROTID INTIMA MEDIA THICKNESS AS A MARKER OF ATHEROSCLEROSIS IN CLINICAL VS SUBCLINICAL HYPOTHYROIDISM

Dr. Shivani A.Patel
Associate Professor, Department of General Medicine, CHA.

Dr. Yash S. Shah Second year resident, Department of General Medicine, CHA.

Dr. Brij B. Patel* Second year resident, Department of General Medicine, CHA. *Corresponding Author

Dr.Khantil K. Shah Second year resident, Department of General Medicine, CHA.

ABSTRACT Introduction: Hypothyroidism increases the risk of atherosclerosis, which in turn increases the cardiovascular disease risk. Carotid intima media thickness (CIMT)>1 mm is used as a non invasive marker of atherosclerosis.

Aim: To find the prevalence of atherosclerosis in patients with clinical vs subclinical hypothyroidism using CIMT as a marker for atherosclerosis **Methods:** Type of study: Prospective observational study. 100 patients of clinical or subclinical hypothyroidism of age more than 12 years, were included in the study. Theyunderwent laboratory and radiological investigations (CIMT-Carotid Intima Media thickness). Data analysis was carried out using statistical package for social sciences.

Result:54.55% of clinical hypothyroid patients had CIMT>1 mm as compared to 17.86% of subclinical hypothyroidism.

Elevated total cholesterol, triglycerides and LDL in clinical hypothyroid patients were 45.46%,68.18% and 40.90% respectively, As compared to subclinical hypothyroidism which had 3.58%, 39.29%, 21.43% respectively. Markers of inflammation CRP>3.0 mg/dl, ESR>30 mm and TLC>10,000 were also significantly higher in patients with clinical as compared to subclinical hypothyroid patients. (40.91%,50% and 40.91% respectively) suggesting possibility of active atherogenesis being significantly higher in clinical hypothyroidism as compared to subclinical hypothyroidism.

KEYWORDS: Atherogenesis, CIMT, Inflammatory markers

INTRODUCTION:

Primary hypothyroidism is the condition resulting from the inherent inability of the thyroid gland to supply a sufficient amount of the hormone. The association of thyroid disease with atherosclerotic cardiovascular disease may in part be explained by thyroid hormones regulation of lipid metabolism and its effect on blood pressure (BP). As hypothyroidism is associated with parameters like obesity, hypertension, decreased HDL and elevated triglycerides, it may be associated with metabolic syndrome^[1]. Studies reveal that free T4 was significantly related to four of five components of the metabolic syndrome (abdominal obesity, triglycerides, high- 2 density lipoprotein cholesterol, and blood pressure), independent of insulin resistance^[2]. CIMT more than 1 mmwas associated with risk of stroke, myocardial infarction, and death from coronary disease in several large observational studies^[3]. Coronary artery atherosclerosis is twice as common in patients with hypothyroidism compared with sex and age-matched controls, and adequate thyroid hormone replacement therapy may protect against the progression. Patients with subclinical hypothyroidism who are not started on levothyroxine as well as those withdelayed diagnosis of hypothyroidism may have increased risk of metabolic syndrome and hence atherosclerotic events.

MATERIALS AND METHODS:

Clinical hypothyroidism is increase in serum TSH level with reduced free thyroid hormones fraction while subclinical hypothyroidism by elevated serum TSH with normal free thyroid hormones level. 100 patients of clinical or subclinical hypothyroidism of age more than 12 years attending general medicine OPD or admitted in medical ward, were included in study for the period from July 2020to September 2021. Details of medical history, vital signs and clinical examination of each patient were recorded.Radiologically - carotid intimal medial thickness was assessed by doppler ultrasound. Laboratory investigations like lipid profile (Total cholesterol, HDL, Triglyce rides), ESR,CRP were done enzymatically on XL-300 ERBA fully automated clinical chemistry analyser. Thyroid hormone assay was done by Radio-ImmunoAssay(RIA) or Indirect radioimmunoassay (IRMA) using ADVIA centaur Bayer Healthcare.

OBSERVATION

Table 1 Carotid Intimal Medial Thickness In Hypothyroid Patients As A Marker Of Atherosclerosis

CIMT SUBCLINICAL CLINICAL HYPOTHYROIDISM NO. OF PATIENTS NO. OF PATIENTS
--

<1 mm	46 (82.14%)	20 (45.45%)
>1 mm	10 (17.86%)	24 (54.55%)
Total patients	56 (100%)	44 (100%)

Note: CIMT>1 mm has been considered as a marker of atherosclerosis as per American society of echocardiography guidelines.

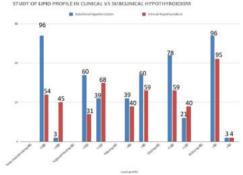
In the present study, CIMT Was >1mm in \sim 55% patients of clinical hypothyroidism as compared to \sim 18% patients of subclinical hypothyroidism. Mean value of CIMT in clinical hypothyroidism (1.02) in present study was comparable withmean CIMT value of Valentina et al. (0.98). Similar results were observed by Mariana tudoran et al. in their study.

Table 2 correlation Of Lipid Profile With Cimt Value

Lipids	CIMT		T value	P value
	< 1 mm	> 1 mm		
Total cholesterol	177.21 <u>+</u> 47.03	177.94 <u>+</u> 45.82	1.14812	0.0466
triglycerides	156 <u>+</u> 45.15	156.0 <u>+</u> 46.60	1.72467	0.0415
HDL	50.39 <u>+</u> 19.33	50.39 <u>+</u> 19.09	3.27282	0.0019
LDL	117.60 <u>+</u> 43.86	<u>1</u> 17.60 <u>+</u> 44.19	5.38341	< 0.00001

Association of the total cholesterol with CIMT>1 mm was statistically significant with p value of 0.0466. Likewise other parameters of lipid profile such as Triglycerides and LDL(except HDL) had a positive association with CIMT of more than 1 mm.

Lipid Profile Of The Hypothyroid Patients Studied, No. Of Patients: 100



Out of 56 patients having subclinical hypothyroidism, only 3.58%

patients (n=2) had total cholesterol >200 while out of 44 patients with clinical hypothyroidism45.46% (n=20)had total cholesterol>200. Triglycerides(>150 mg/dl) and LDL(>130 mg/dl) values were higher (68.18% and 40.90 % respectively) in clinical hypothyroidism as compared to subclinical hypothyroid patients (39.29% and 21.43% respectively). Higher HDL values(>40 mg/dl) were observed among subclinical hypothyroidism (60.71%) compared to clinical hypothyroidism (59.10%)

Table 3 Association Of Thyroid Profile With Atherosclerotic Inflammatorymarkers

ATHEROSCLERO	SUBCLINICAL	CLINICAL
TIC	HYPOTHYROIDISM	HYPOTHYROIDISM
INFLAMMATORY	NO. OF PATIENTS	NO. OF PATIENTS
MARKERS		
CRP		
< 0.5	36 (64.28%)	8(18.18%)
0.5-3.0	16 (28.57%)	18 (40.91%)
>3.0	4 (7.15%)	18 (40.91%)
ESR		
<10	12 (21.42%)	0 (0%)
10-30	38 (67.85%)	22 (50%)
>30	6 (10.72%)	22 (50%)
TOTAL COUNT		
4000-10,000	44 (78.57%)	26 (59.09%)
>10,000	12(21.43%)	18 (40.91%)

CRP>3 was noted in 40.91% patients of clinical hypothyroidism whereas it was noted in 7.15% of subclinical hypothyroidism. Likewise, higher ESR (>30)and TOTAL COUNTS (>10,000) were noted moreamong clinical hypothyroid patients (50% and 40.91% respectively) as compared to subclinical hypothyroid patients (10.72% and 21.43% respectively).

DISCUSSION

Hypothyroidism is associated with atherosclerotic cardiovascular disease which can be explained by thyroid hormones regulation of lipid metabolism and its effect on blood pressure (BP). Hypothyroidism is associated with parameters like obesity, hypertension, decreased HDL and elevated triglycerides, and hence with metabolic syndrome. Few studies have suggested the role of hypothyroidism as an independent risk factor for atherosclerosis even in subclinical hypothyroidism^[4]. Clinical hypothyroidism is associated with increased risk of atherosclerosis as these subjects share the potential atherogenic factors such as higher total and LDL cholesterol, increased high sensitivity C-reactive protein (CRP), hyper homocysteinemia, altered coagulation profile, increased arterial stiffness, and endothelial dysfunction.

Along with this, thyroid hormones have a substantial influence on theperipheral vasculature, and thyroid hormone receptors have also been identified in human vascular smooth muscle cells^[5]. So, the role of these cells in the development of atherosclerosis raises the hypothesis that thyroid hormone deficiency and higher levels of TSH may be associated with atherosclerosis as an independent factor. Low-grade inflammation may also cause endothelial dysfunction and impaired nitric oxide availability. Patients with Hashimoto's thyroiditis, which is a leading cause of hypothyroidism, can have more of the underlying inflammation hastening the progression of atherosclerosis.

Carotid intima-media thickness (CIMT) testing via B-mode ultrasound is a safe, simple, and inexpensive method for evaluating CV risk by measuring the combined thickness of the intimal and medial layers of the arterial wall. According to large studies, such as The Atherosclerosis Risk in Communities (ARIC) study, The Cardiovascular Health Study (CHS), and The Rotterdam study, a correlation between CIMT measurements and risk of cardiovascular events has been established. The advantage of measuring the CIMT by high resolution B-mode ultrasonography lies in its rapidly applicable and available, non-invasive and cost-effective nature. Progression of CIMT is therefore an attractive method for use in research as it can be easily assessed to study vascular risk or the therapeutic effects of a specific treatment.

Our study was carried outto find the prevalence of atherosclerosis in patients with clinical vs subclinical hypothyroidism using CIMT as a marker for atherosclerosis. In our study, 54.55% of clinical hypothyroid

patients had CIMT>1 mm as compared to 17.86% of subclinical hypothyroidism.Mean value of CIMTin clinical hypothyroidism in present study was 1.02, whereas mean value of CIMT in Valentina et al. study was 0.98. Thus result in both study were comparable. Similar results were obtained in Mariana Tudoran et al. study.

The total cholesterol was statistically significant with p value of 0.0466in patients with CIMT > 1mm. Similarly other parameters of lipid profile such as Triglycerides and LDL (except HDL) had a positive association with CIMT of more than 1 mm.CIMT had positive correlation with all parameters of lipid profile except for HDL.

Patients having subclinical hypothyroidism, only 3.58% patients had total cholesterol >200 while 45.46% patients clinical hypothyroidi smhad total cholesterol>200. Triglycerides(>150 mg/dl) and LDL(>130 mg/dl) values were higher (68.18% and 40.90 % respectively) in clinical hypothyroidism as compared to subclinical hypothyroid patients (where they were 39.29% and 21.43% respectively). Higher HDL values(>40 mg/dl) were observed among subclinical hypothyroidism (60.71%) compared to clinical hypothyroidism (59.10%). Study by Gupta et al. revealed that elevated total cholesterol(≥ 200mg) in 45.8% and hypertriglyceridemia (≥ 150mg)in28.6%,whereas in our study they were 22% and 52% respectively. Ramachandran et al.in his study found reduced, HDL(<40mg) in 65.5% of patients.whereas our study had 40% patients having HDL<40 mg/dl.

Likewise, CRP>3, higher ESR (>30)and TOTAL COUNTS(>10,000) were noted more commonly among clinically hypothyroid patients compared to subclinical hypothyroid patients, suggesting active accelerated atherogenesis in clinical hypothyroid patients.

CONCLUSION

Prevalence of atherosclerosis is 54.55% and 17.86% in clinical and subclinical hypothyroidism respectivelyin our study, markedly higher in clinical hypothyroidism. Low Free T4 and High TSH are important factors for development of atherosclerosis rather than free T3 Levels. All the markers of atherogenesis like decreased HDL, elevated triglycerides, elevated LDL,CRP,ESR & TLC are substantially increased in Clinical hypothyroidism. CIMT >1 mm is an excellent screening test for early detection of atherosclerosis, and thus Prevention of end organ damage such as cerebrovascular stroke and myocardial infarction. Affordable, accessible health care, health education including diet, exercise and drug compliance may halt the progression ofatherogenesis and hence premature coronary artery disease in hypothyroid patients.

REFERENCES

- Cappola AR et al.; 2003 Hypothyroidism and atherosclerosis. JClinEndocrinolMetab 88:2438–2444.
- Klein I, Ojamaa K;2001 Thyroid hormone and the cardiovascular system. N Engl J Med
- Valentina, Velkoska&Krstevska, Brankica&Srbinovska, Elizabeta&Bosevski, Marijan. (2012). Correlation between thyroid hormone values and carotid intima media thickness in patients with subclinical hypothyroidism.

 Kilic ID, Tanriverdi H, Fenkci S, Akin F, Uslu S, Kaftan A. Noninvasive indicators of
- Although and the Althou
- Rongzhong Huang, Kerry Mills, Julio Romero, Yan Li, Zicheng Hu, Yu Cao, Hua Huang, Yu Xu, Lihong Jiang, Comparative effects of lipid lowering, hypoglycemic, antihypertensive and antiplatelet medications on carotid artery intima-media thickness progression: a network meta-analysis, Cardiovascular Diabetology, 10.1186/s12933-019-0817-1, 18, 1, (2019).
- Tognini S, Polini A, Pasqualetti G, Ursino S, Caraccio N, Ferdeghini M, Monzani F. Age and gender substantially influence the relationship between thyroid status and the lipoprotein profile: results from a large cross-sectional study. Thyroid. 2012 Nov; 22 (11):1096-103. doi: 10.1089/thy.2012.0013. Epub 2012 Oct 10. PMID: 23050788.
- Subhashini Srinivas ,Teena Eugene , Karkuzhali , KhowsalyaSubrajaa Correlation of Subclinical Hypothyroidism and its Relation with Various Inflammatory Markers International Journal of Science and Research (IJSR) (2017): 7.296
- Mookadam F, Moustafa SE, Lester SJ et al. Subclinical atherosclerosis: evolving role of carotid intima-media thickness. PrevCardiol 2010; 13(4):186-97. 113. Dobs AS, Nieto FJ,
- carotia minia-meta mickness. "reve carotia (1947:180-97. 113. Doos AS, Nieto FJ, Szklo M et al. Risk factors for popliteal and carotid wall thicknesses in the Atherosclerosis Risk in Communities (ARIC) Study, Am J Epidemiol 1999; 150 (10): 1055-67. Kumari B, Kumar B, Gupta G, Ganju N FMD and CIMT: surrogate markers of atherosclerosis in subclinical and overt hypothyroidism in sub himalayan region, Indian Journal of Endocrinology and Metabolism 2021, volume 25-issue 3-p 220-225.