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General Medicine

A STUDY ON CAROTID INTIMA MEDIA THICKNESS IN SUBCLINICAL HYPOTHYROIDISM AND CORRELATION WITH METABOLIC PARAMETERS

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ABSTRACT **Aim of the Study:** To measure carotid artery intima thickness in subclinical hypothyroidism patients and compare with euthyroid subjects. Material & Methods: 100 Cases and 100 Controls of the present study seen subclinical hypothyroidism patients attending medical OPD at tertiary care hospital. Results: Out for 200 subjects (100 cases & 100 controls). Mean CIMT in cases and controls is calculated and compared. CIMT in cases is correlated with TSH and other metabolic parameters. Continuous variables are represented as mean and standard deviation where data follows normal distribution, otherwise as median with range. Categorical variables are represented as frequencies and percentages. The significance in the difference in the outcome of variables between the groups was found through Chi- Square test, Fisher exact test, t test. Significance is defined by p value ≤ 0.05. Pearson Correlation test was used to assess correlation between variables. All statistical analyses were performed using SPSS (Statistical package for social sciences) software for windows. **Conclusion:** This study suggests that CIMT is positively correlated with metabolic parameters like LDL, triglycerides, total cholesterol, VLDL, hypertension, BMI and waist circumference.

KEYWORDS : Carotid Intima Media Thickness; Low Density Lipoproteins; High Density Lipoproteins; Very Low Density Lipoproteins

Introduction

Subclinical hypothyroidism is defined as a biochemical evidence of thyroid hormone deficiency with few or no apparent clinical features of hypothyroidism. Subclinical hypothyroidism is characterized by normal serum free thyroxine (fT4) and normal serum free Triiodothyronine (fT3) and elevated levels of serum Thyroid Stimulating Hormone (TSH)[1].

Subclinical hypothyroidism is a common disorder with a prevalence of 2.8 – 4.4% in males and 7.5 – 8.5% in females worldwide[2].

Overt hypothyroidism has been associated with abnormal lipid profile and atherosclerosis thereby increasing cardiovascular mortality and morbidity[3]. Association of atherosclerosis and overt hypothyroidism has been well existed for long and is a well-known fact[4].

Studies conducted to establish the relationship between subclinical hypothyroidism and development of atherosclerosis have produced conflicting results[5]. Some studies have established a significant relationship between subclinical hypothyroidism and metabolic parameters thereby increased risk of cardiovascular diseases.

Atherosclerosis is a clinical condition that eventually leads to various complications like coronary artery disease (CAD), stroke, increase in blood pressure. The carotid intima media thickness (CIMT) measurement directly correlates with atherosclerosis[6].

In clinical studies, the C-IMT measurement parallels the significance of traditional cardiovascular risk factors, thus highlighting the utility and consistency of using non-invasive measurements to assess risk factors based on vessel wall biology. Accordingly, the clinical application of C-IMT represents a powerful, non-invasive surrogate marker of atherosclerosis, providing a meaningful end point measurement for clinical trials[7]. Many epidemiological studies and clinical trials proved that carotid intima media thickness is an indicator of subclinical atherosclerosis along with coronary atherosclerosis.

The effects of overt hypothyroidism on lipid parameters has been extensively studied. However the studies relating the association between the subclinical hypothyroidism and the lipid parameters are few. In the Indian clinical scenario such studies are lacking.

Subclinical hypothyroidism having been diagnosed with greater frequency in recent times particularly among the women population, it has become necessary to study extensively the relation between subclinical hypothyroidism and cardiovascular risk related to altered carotid intimal media thickness and deranged metabolic parameters.

AIM OF THE STUDY

1) To measure carotid artery intima thickness in subclinical hypothyroidism patients and compare with euthyroid subjects.
2) Measuring carotid artery intima media thickness in subclinical hypothyroidism and to find relation with dyslipidemia, arterial hypertension and obesity.
3) Establish or differ subclinical hypothyroidism as a risk factor for atherosclerosis.

Material & Methods

Subclinical hypothyroidism patients attending medical OPD at tertiary care hospital 100 CASES and 100 CONTROLS from April 2020 to March 2022

Inclusion Criteria

- Newly diagnosed and untreated cases of subclinical cases of hypothyroidism
- Age more than 12 years

Exclusion Criteria

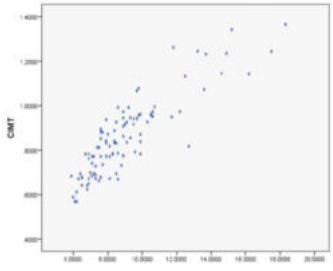
- Previous history of thyroid disease on treatment
- Patients who are on medication that could change thyroid hormone level such as iodine, amiodarone.
- Patients with diabetes, renal failure, hepatic failure
- Patients with known cardiac disease and cerebrovascular disease
- Smoking and alcohol abuse
- Pregnant women

Results

Table: 1 – CIMT IN CASES AND CONTROLS

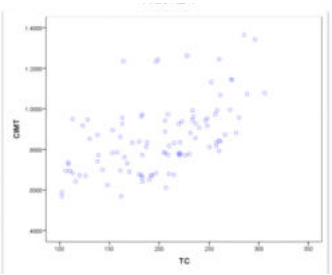
Variable	Case	Control	P-value
CIMT	0.85 + 0.17	0.65 + 0.07	< 0.01

Graph 1: RELATIONSHIP BETWEEN CIMT AND THYROID STIMULATING HORMONE IN CASES



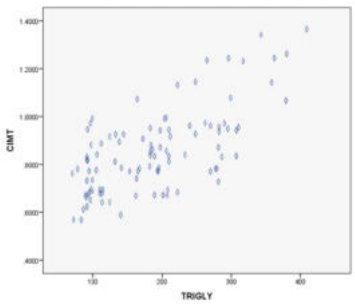
Above graph 1 shows there was positive correlation between CIMT and TSH with Pearson's coefficient of 0.87 which is statistically significant (p value-<0.01).So with increase in TSH, CIMT increases.

Graph 2: RELATIONSHIP BETWEEN CIMT AND TOTAL CHOLESTEROL IN CASES



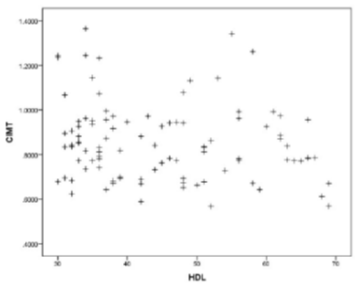
Above graph 2 shows that there was positive correlation between CIMT and total cholesterol value. This was indicated by Pearson's R correlation value of 0.54 with p value of <0.01 which is statistically significant. So CIMT were significantly increased with increased level of total cholesterol

Graph 3: RELATIONSHIP BETWEEN CIMT AND TRIGLYCERIDES IN CASES



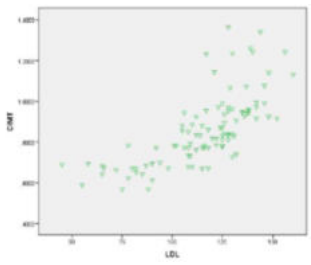
Above graph 3 shows that there was positive correlation between CIMT and triglyceride value .This was indicated by Pearson's R correlation value of 0.68 with p value of <0.01 which is statistically significant. So CIMT was significantly increased with increased level of triglyceride.

Graph 4 : RELATIONSHIP BETWEEN CIMT AND HDL IN CASES



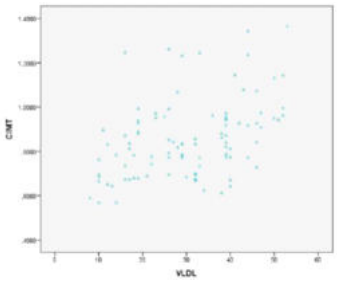
Above graph 4 shows that there was no significant correlation between CIMT and HDL which is indicated by Pearson coefficient of -0.16.P value of 0.11 which indicates that it is statistically insignificant .So with increase in HDL there is no major change in CIMT value.

Graph 5 : Relationship between CIMT and LDL in Cases



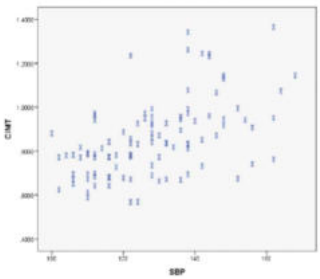
Above graph 5 shows depicts positive correlation correlation between CIMT and LDL which is indicated by Pearson coefficient of 0.71 and is statistically significant (p value - <0.01).So CIMT increases with increase in LDL levels

Graph 6: Relationship between CIMT and VLDL in Cases



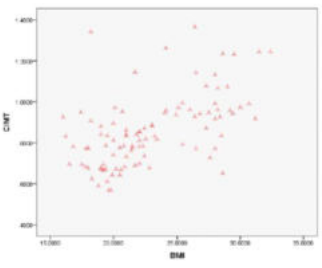
Above graph 6 shows there was positive correlation between CIMT and VLDL which is depicted in the above scatter plot with Pearson's coefficient of 0.43 which is statistically significant (p value- <0.01).So with increase in VLDL, CIMT also increases.

Graph 7 : Relationship between CIMT and Systolic HTN in Cases



Above graph 7 shows there exists positive correlation between SBP and CIMT which is depicted in the above scatter plot.(figure 9) Pearson's coefficient of 0.53 is obtained in above scatter plot which is statistically significant (p value-0.01).So with increase in SBP, CIMT increases.

Graph 8: Relationship between CIMT and Diastolic Hypertension in Cases



Above graph 8 shows depicts positive correlation between diastolic blood pressure and CIMT which is indicated by Pearson's coefficient of 0.49 which is statistically significant. So with increase in DBP, CIMT increases.

DISCUSSION

In this study of Indian population involving 200 subjects, 100 belong to subclinical hypothyroidism group (cases) and 100 belong to euthyroid group (controls). CIMT was compared between two groups. The result showed CIMT was significantly higher in subclinical hypothyroid cases as compared to euthyroid controls.

In this study the mean age of subclinical hypothyroidism group was 32.03 ± 10.43 and euthyroid group was 32.75 ± 7.29.Out of 100 subjects in both cases group and control group 93% were females and 7% were males. Thus it can be interpreted that subclinical hypothyroidism is more common in females.

In Farhana Rahman et.al8. study, mean age was found to be 30 ± 7.4 and 32 ± 8.7 in subclinical hypothyroidism group and control groups

respectively. Male to female ratio was 3:23 in SCH group and 9:21 in control group which also denotes that subclinical hypothyroidism is more common in females.

In this study showed mean CIMT in subclinical hypothyroidism group was 0.85 ± 0.17 and in euthyroid group was 0.65 ± 0.07 with p value <0.01 which is statistically significant. So this denotes that CIMT was increased in subclinical hypothyroid patients compared to euthyroid group.

Previously many studies were done to know the relation between subclinical hypothyroidism and cardiovascular disease. However contradictory results have been obtained. Some studies determined an increase in cardiovascular risk with subclinical hypothyroidism and some studies revealed no significant association between subclinical hypothyroidism and cardiovascular risk.

Valentina et al9 study reports that patients with subclinical hypothyroidism had significantly greater mean CIMT than control group (0.61 ± 0.1 vs 0.56 ± 0.1 mm, p=0.034). They concluded that SCH is associated with increased CIMT and presence of carotid plaques ,independent of classic risk factors for atherosclerosis.

A recent cross sectional study found a significant positive correlation between TSH and CIMT (r=0.28, p<0.05). In that study mean TSH, fT4, CIMT and max CIMT were 7.9 ± 3.6 Miu/l,14.5 ±2.8 pmol/l,0.61± 0.1 mm and 0.65 ±0.1 mm respectively. However Unsal et al study found no significant association between 2 groups of TSH (one with TSH<7 and other with TSH>7) in terms CIMT value (p>0.05).

In Rahman et al study, SCH group was subdivided into 2 groups with a cut off value of serum TSH at 10 Miu/L, it was found that CIMT was significantly higher in SCH group with TSH above 10mIU/L(right - 0.82 ±0.04 mm, left-0.87± 0.06 mm) than SCH group with TSH<10 Miu/L (0.75 ±0.05 mm).The result was significant with p value<0.05.Pearson's rank correlation test showed CIMT was positively correlated(r=0.478) with TSH values and result was significant(p<0.05).

In this study, Pearson's rank correlation test showed that CIMT was positively correlated with TSH value(r=0.87) and result was significant (p<0.05).It indicates that CIMT values were significantly increased with increased values of TSH.

A recent study by Mohammed Aziz et al10, shows that thyroxine therapy in subjects with subclinical hypothyroidism significantly reduces CIMT secondary to down regulation of TSH.

The present study showed that CIMT was positively correlated with the levels of total cholesterol, triglycerides , LDL ,VLDL with r values 0.54, 0.68 ,0.71 ,0.43 respectively which are statistically significant (p<0.05). That indicates increase in total cholesterol, triglycerides, LDL, VLDL is associated with increase in CIMT. This result shows that strong correlation exists between LDL levels, triglyceride levels and CIMT whereas moderate correlation exists between total cholesterol, VLDL levels and CIMT according to Pearson's coefficient values.

This study found that there is no relation between CIMT and HDL levels(r value=-0.16, p=0.11).

Akkoca et al11, also reported that there was an increment of CIMT in clinical and subclinical hypothyroidism resulting from an adverse lipid profile and thyroid hormone replacement might reverse the adverse effects.

Raman k. Marwaha et al12, study shows serum TSH was positively correlated with LDL(r value-0.028), cholesterol (r value- 0.037) and negatively correlated with HDL (r value=0.031).However study conducted by Mallika Biswas et al, (60) showed CIMT was significantly positively correlated with triglycerides TSH,VLDL and HDL.

F.Monzani et al13, study compared 45 subclinical hypothyroid patients with 32 age and sex matched controls, subclinical hypothyroid patients had elevated total cholesterol(r value-0.55), LDL (r value-0.54), triglyceride (r value-0.35)and apo-B levels(r value-0.49) with (p value-0.002,0.0007,0.02 and 0.01 respectively) and higher mean CIMT value (p value<0.0001).

In step wise regression analysis mean CIMT was positively correlated with age, TSH and LDL cholesterol (r^2=0.71, p<0.0001). Levothyroxine replacement significantly reduced both total cholesterol, LDL and mean IMT (p value<0.0001 for all three parameters).

A recent meta-analysis by Gao et al14, reported that SCH was associated with an increase in carotid IMT which may be due to elevated TSH, dyslipidemia and hypertension. Increased CIMT can also be present in patients with serum TSH value of less than 10Miu/L. In this study increase in systolic blood pressure and diastolic blood pressure was associated with increase in CIMT which is statistically significant(p value<0.01).This study showed that there is positive correlation between SBP,DBP and CIMT with Pearson's coefficient value of 0.53 and 0.49 respectively.

Gao N et al study and another study by Cai Y et al found that hypertension has been correlated with CIMT in association with SCH. Possible mechanism which connects hypothyroidism with hypertension is the increased sodium and water re-absorption through the inappropriate secretion of anti-diuretic hormone.

Mohammed Aziz study et al, study shows increase in CIMT with increase in SBP (p value-0.02) and DBP (p value-0.01). Also observed significant decrease in SBP and DBP with thyroxine treatment.

David karasec et al15, study showed that increase in CIMT correlate with increase in SBP (r-0.35,p<0.001), DBP(r-0.21,p<0.01), total cholesterol (r-0.46,p<0.001), LDL cholesterol(r-0.39,p<0.001), triglycerides (r-0.23,p<0.01), apo-B (r-0.36, p<0.001), c peptide (r-0.15,p<0.01), BMI (r-0.23,p<0.01),waist circumference(r-0.29,p<0.01)

This study showed increase in CIMT with increase in body mass index (BMI) with Pearson's coefficient of 0.55 which is statistically significant (p value<0.01).In this study increase in waist circumference was associated with increase in CIMT with Pearson's coefficient of 0.6 which is statistically significant (p value<0.01).

Obesity may contribute independently to carotid structure and function abnormalities. Obesity may modulate CCA diameter and may induce adaptive changes in carotid wall thickness independent of metabolic and atherosclerotic factors.

Lakka et al16 demonstrated that abdominal obesity can be associated with progressive increase in CIMT. Waist circumference as a measure of abdominal obesity is significantly associated with increase in CIMT. De Michele et al17, also found a significant association between waist circumference and carotid wall thickening.

Hala Abd El –Hafez et al17 study also showed increase in CIMT with increase in BMI and waist circumference with r value of 0.40 and 0.54 respectively which is statistically significant (p value-<0.001).

CONCLUSION

- The result of CIMT was significantly higher in SCH group compared to the euthyroid group and the values were also positively correlated with the TSH values.
- This study suggests that subclinical hypothyroidism is associated with elevated cardiac risk as evidenced by CIMT.
- Therefore we may conclude that SCH is an independent risk factor for atherosclerosis in addition to other classic risk factors.
- This finding justifies the use of effective hormone replacement therapy in SCH patients to at least slow down the atherosclerosis process and to prevent further cardiac adverse effects.
- This study also suggests that CIMT is positively correlated with metabolic parameters like LDL, triglycerides, total cholesterol, VLDL, hypertension, BMI and waist circumference.
- This study also tells that there is no correlation between CIMT and HDL.

REFERENCES

1) Harrison's endocrinology 4rth edition , page number 86.
2) Canaris GJ, Manowitz NR, Mayor G, Ridgway EC. The Colorado thyroid disease prevalence study.
3) Pucci E, Chiovato L, Pinchera A. Thyroid and lipid metabolism. Int J Odes Relat Metab

Disord. 2000; 24(suppl 2):S109-12. [PubMed:10997623]
4) Anne R.Cappola, Paul W.Ladenson – The Journal of clinical endocrinology & metabolism, pages 2438-2444.
5) Efstathiadou Z, Bitsis S, Milionis HJ, Kukuvitis A, Bairaktari ET, Elisaf MS, et al. Lipid profile in subclinical hypothyroidism: Is L- thyroxine substitution beneficial? Eur J Endocrinol. 2001; 145:705-10 [PubMed: 11720894).
6) O'Leary DH and Bots ML, Imaging of atherosclerosis: carotid intima media thickness. European Heart Journal 2010; 31: 1682-1689.
7) Knapp M, Lisowska A, Sobkowicz B, Tycinska A, Sawicki R and Musial WJ. Myocardial perfusion and intima media thickness in patients with subclinical hypothyroidism. Adv Med Sci 2013; 58(1): 44-49.
8) Farhana Rahman, Fatema Sultana Haque, Shankar Kumar Biswas, Rubina Begum et al, Evaluation of carotid intima media thickness in subclinical hypothyroid patients 2016.
9) Valentina et al Pieter Muntendam,Carol McCall,Javier Sanz,Erling Falk, Fuster,High risk Plaque Initiative. Am Heart J.2010 Jul;160(1):49-57
10) Muhammed Aziz, Yugandhar Kandimalla and Khurram Nasir. Effect of Thyroxin treatment on carotid intima media thickness (CIMT) reduction in patients with subclinical hypothyroidism: a metaanalysis of clinical trials-J Atheroscler Thromb.2017 Jul 1;24(7):643- 659.
11) Akkoca AN, Ozdemir ZT, Ozler GS and Karabulut L. The evaluation of carotid intima media thickness in clinical and subclinical hypothyroidism and effects of thyroid hormone treatment. American Journal of Clinical and Experimental Medicine 2014; 2(4):59-63.
12) Marwaha RK, Tandon N, Garg MK, Kanwar R, Sastry A, Narang A, et al. Dyslipidemia in subclinical hypothyroidism in an Indian population. Clin Biochem.2011; Vol.44 (14-15):1214-1217.
13) Monzani F, Caraccio N, Kozakowa M et al. Effect of levothyroxine replacement on lipid profile and intima media thickness in subclinical hypothyroidism: a double blind, placebo-controlled study. J Clin Endocrinol Metab 2004; 89: 2099-106.
14) Gao et al ,Chong-Bo Yang and Jia-Jun Zhao Ming lu, Ling; Mechanism of subclinical hypothyroidism accelerating endothelial dysfunction-,2015 Jan;9(1):3-10.PMID:25452768.
15) David Karasek, Helena Vaverkova, Milan Halenka, Dagmar Jackuliakova, Zdenek Frysak, Jiri Orsag, Dalibor Novotny. Prehypertension in dyslipidemic individuals; relationship to metabolic parameters and intima-media thickness, 2013 Mar; 157(1):41-49.
16) T.A.Lakka, H.M.Lakka, R.Salonen, G.A.Kaplan, and J.T.Salonen, "Abdominal obesity is associated with accelerated progression of carotid atherosclerosis in men", Atherosclerosis, vol.154, no.2, pp.497-504, 2001.
17) M. de.Michele, S.Panico,A.Iannuzzi et al., "Association of obesity and central fat distribution with carotid artery wall thickening in middle aged women",Stroke,vol.33,no 12,pp.2923-2928,2002.
18) Hala Abd El-Hafez, Mohammed M, Elrakhawy, Azza A.El-baiomy, and Mervat M.El-Eshmawy, CIMT is independently associated with male gender, middle age and IGF-1 in Metabolically Healthy Obese Individuals.