www.jmscr.igmpublication.org
Index Copernicus Value: 79.54
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossrefDOI: https://dx.doi.org/10.18535/jmscr/v7i3.146

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

Original Research Article

A comparative study of changes in Carotid Intimal Thickness in presence TPO antibody in subclinical hypothyroidism and overt hypothyroidism replacement of levothyroxine

Authors
Diptiman Sahoo[1], Jaybhanu Kanwar[3], Chandan Das[1*], Adyakinkar Panda[2], Budankailu Abhisek subudhi[2], Srikant Kumar Dhar[1]
[1]Department of Medicine, IMS & SUM hospital, Siksha O Anusandhan University, K8, Kalinga Nagar, Bhubaneswar-751003, Odisha, India
[2]Department of Radiology, IMS & SUM hospital, Siksha O Anusandhan University, K8, Kalinga Nagar, Bhubaneswar-751003, Odisha, India
[3]Department of Endocrinology, IMS & SUM hospital, Siksha O Anusandhan University, K8, Kalinga Nagar, Bhubaneswar-751003, Odisha, India
*Corresponding Author
Dr Chandan Das
Department of Medicine, IMS & SUM hospital, Siksha O Anusandhan University, K8, Kalinga Nagar, Bhubaneswar-751003, Odisha, India

Abstract
Carotid Intimal Thickness (CIT) is an early prognostic assessment of carotid atherosclerotic vascular infections and their co-morbidities if there should arise an occurrence of subclinical hypothyroidism and clear hypothyroidism. Subclinical Hypothyroidism (SCH) characterized as biochemical affirmation of thyroid hormone inadequacy in patients who have few or no clear clinical highlights of hypothyroidism. The occurrence of hostile to TPO antibodies are most delicate test for identifying immune system thyroid malady like Hashimoto's sickness. The cardiovascular points of interest of levothyroxine substitution are not sketchy in obvious hypothyroidism but rather no assent has been accomplished up to this point about the unfriendly cardiovascular issue results of subclinical hypothyroidism and its treatment. So we compare the carotid intimal thickness (CIT) in subclinical and overt hypothyroidism and their relationship with associated co-morbidities and also we evaluate subclinical hypothyroidism (SCH) relation with carotid atherosclerotic diseases as well as lipid profile derangement in a tertiary care hospital of Institute of Medical Science and SUM Hospital. The result we obtained conclude that the decrease in Carotid Intimal Thickness (CIT) after taking Levothyroxin treatment in the patients with SCH. This data recommend early diagnosis of such patients and preventing them from further risks which can be done by early initiation of thyroid hormone replacement in such patients and their proper follow-up.
Keywords: *Carotid Intimal Thickness, SCH, Levothyroxin, TPO.*

Introduction

Carotid Intimal Thickness (CIT) is an early prognostic assessment of carotid atherosclerotic vascular illnesses and their co-morbidities in the event of subclinical hypothyroidism and plain hypothyroidism(1). At early finding may determine

the prerequisite for an increasingly relentless way to deal with deal with the compromising makes related heart ailments and cerebrovascular mishaps (CVA).

Subclinical Hypothyroidism (SCH) characterized as biochemical affirmation of thyroid hormone deficiency in patients who have few or no obvious clinical highlights of hypothyroidism[2]. There are no normally consented to any tributes for the treatment of SCH, however levothyroxine is proposed if the patient is a female who needs to get pregnant or is pregnant, or while Thyroid Stimulating Hormone (TSH) levels are more than 10 mlU/L. While Thyroid Stimulating Hormone levels are under 10 mlU/L, the board ought to be contemplated while tolerant has characteristic indications of hypothyroidism, nearness of against Thyroid peroxidase antibodies or any affirmation of cardiovascular sicknesses. Unmistakable hypothyroidism is characterized as uncontrolled T4 levels decline and expanded TSH level (for the most part > 10 mlU/L). Side effects are all the more eagerly apparent now. The frequency of against TPO antibodies are most touchy test for identifying immune system thyroid sickness like Hashimoto's ailment. Nearness of hostile to Thyroid peroxidase antibodies is essential for this investigation. BMI (Body mass file) is another marker to assess the co-morbidities in both the instances of subclinical hypothyroidism and plain hypothyroidism. The ordinary estimation of BMI is 19.5 to 25.

There are obvious actualities that clear hypothyroidism is identified with a few useful cardiovascular variations from the norm and expanded danger of atherosclerotic maladies. The cardiovascular preferences of levothyroxine substitution are not faulty in unmistakable hypothyroidism but rather no assent has been accomplished as of not long ago about the unfavorable cardiovascular issue results of subclinical hypothyroidism and its treatment. In any case, numerous literary works have discovered that subclinical hypothyroidism is likewise identified with upgraded danger of atherosclerosis as these subjects additionally share a similar potential atherogenic factors, for example, high low thickness lipoprotein cholesterol, expanded high touchy C-Reactive Protein, hyper homocysteinemia, modified coagulation profile, expanded blood vessel firmness and endothelial brokenness[3] Here in this experiment we think about the progressions in Carotid Intimal Thickness (CIT) in presence of anti TPO antibody in subclinical hypothyroidism and overt hypothyroidism substitution of levothyroxine.

Materials and Methods

Source of data

The study was carried out with the help of observational study in tertiary care hospital of Institute of Medical Sciences and SUM Hospital in Post Graduate Department of Medicine. The Duration was 2 years from September 2016 to August 2018**.**

Inclusion criteria

Age gathering of patients who were over 18 years old analyzed as essential plain and subclinical hypothyroidism which was taken a crack at five subgroups basing on their biochemical research facility parameters i.e.T4, TSH and serum hostile to thyroid peroxidase (TPO) antibodies and a control amass having age or sex coordinated. The subgroups will be separated in to two gatherings like subclinical hypothyroidism and Overt Hypothyroidism. Subclinical hypothyroidism again ordered in to classification TPO+ and TPO-, comparatively Overt Hypothyroidism likewise characterized in to TPO+ and TPO-. Based on TSH, subclinical hypothyroidism was characterized as TSH level < 10 miniaturized scale Iu/L and > 4.2 small scale Iu/L yet T4 inside typical point of confinement (5.13-14.06 smaller scale g/dl) and the plain hypothyroidism likewise characterized as TSH level > equivalent to 10 smaller scale I u/L with low T4. Every patient was enlisted with age, sex, and BMI[4].

Exclusion criteria

Tolerant related with diabetes mellitus, h/o smoking and liquor, pituitary issue, pregnancy, fundamentally poorly, related medications like oral prophylactic pills and statins and patients taking levothyroxine was prohibited from the examination. Patients having highlights of accompanying constant incendiary illness, coronary course ailment, cerebral vascular mishaps were prohibited from the investigation.

Methods and tools

The strategy of the examination was conceded by institutional moral board of trustees of IMS and SUM emergency clinic preceding the beginning of the investigation. The informed consent was taken from every one of the patients enlisted in the examination. Every one of the patients distinguished with essential hypothyroidism having clinical and research facility proof was enlisted in the investigation as indicated by the expansion and oversight standard. Every patient got experience careful clinical evaluation and examinations including total blood check (CBC), liver capacity test (LFT), kidney work test (KFT) , thyroid profile, serum against TPO antibodies and fasting lipid profile. T4 and TSH will be estimated by electrochemiluminescence, Cobas e411 strategy. Carotid Intimal thickness will be estimated by B-mode Ultrasonography utilizing direct test at recurrence of 9-11MHz. The basic carotid supply route will be checked at the dimension of bifurcation on either side of carotid. The higher esteem will be considered for examination[5]. Observational cohort study was performed at Institute of Medical science and SUM Hospital. A total of 88 patients were taken for all subgroup including a control as well and statistical analysis were done by SPSS software.

Results

A sum of 88 participants was approached to be taken in the study. Out of these, three were excluded from the study due to exclusion criteria while five did not consent for participating in the study. Thus a sum of 80 members were finally taken in the study (n=80). Mean age of the members in the study was 43.3 years with 9.9 as standard deviation. Lower limit and upper limit of age among the members was 19 and 64 years respectively. Majority of the study participants belonged to female (51 participants, 63.8%). Females were more in all age groups except beyond 50 years of age.

The mean body mass index at baseline for the study participants was 25.6 kg/m^2 with a SD of 3.6 kg/m^2. There were 41 overweight cases (51.3%) having BMI ≥25 kg/m^2 and eight were obese among these (10%). There was no considerable changes in the mean values among male and female participants (p>0.05) at baseline.

1. **Thyroid Profile**

Mean levels of T3 at baseline was 110 ng/dl with a standard deviation of 22.7, while that for T4 was found to be 4.84 mcg/dl with a SD of 2.9. TSH was found to have a mean of 8.72 mIu/ml with a SD of 7. There was no considerable changes in the mean values among male and female participants (p>0.05) at baseline for any of the thyroid parameters.

Table 1: Thyroid profile of the study participants (n=80)

	Female		Male		Total	
	Mean	Standard Deviation	Mean	Standard Deviation	Mean	Standard Deviation
T3 at visit 1 (ng/dl)	113	22.6	104	22.3	110	22.7
T4 at visit 1 (mcg/dl)	4.92	2.9	4.70	2.8	4.84	2.9
TSH at visit 1 (mIu/ml)	8.70	5.7	8.76	9.0	8.72	7.0

Anti-thyroid antibodies were found to be positive in 21 participants (26.3%), with no gender difference (p>0.05, using chi-square test).

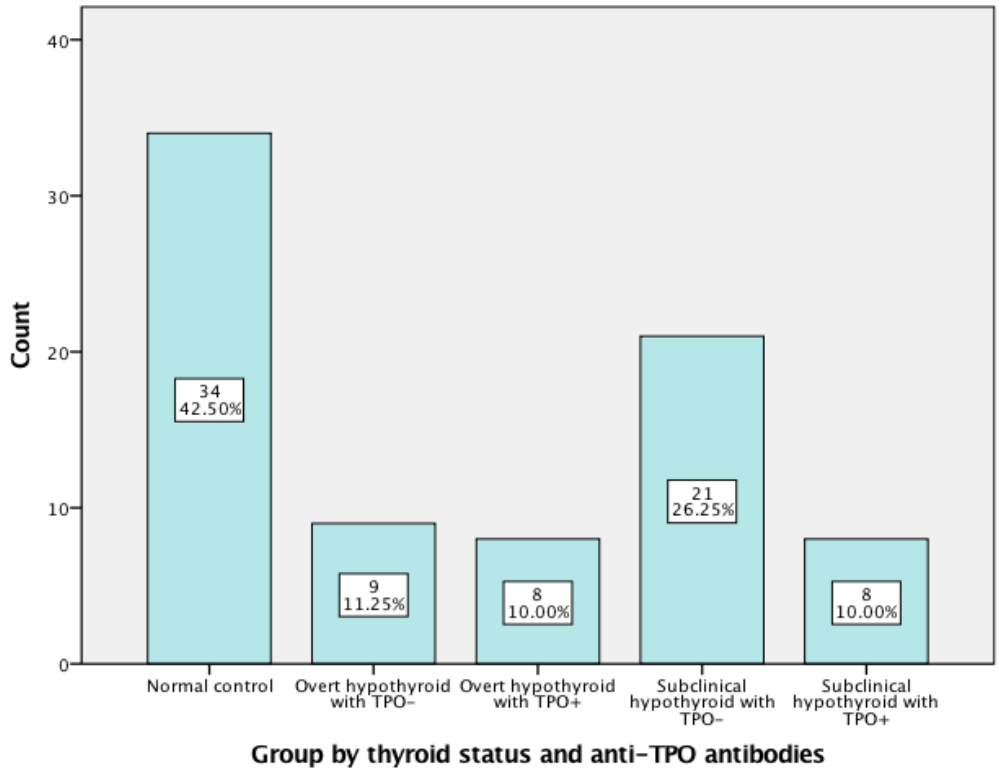
Table 2: Anti-thyroid antibodies among the study participants by gender (n=80)

Anti-TPO	Female		Male		Total	
	Nos.	%	Nos.	%	Nos.	%
Negative	37	72.5%	22	75.9%	59	73.8%
Positive	14	27.5%	7	24.1%	21	26.3%
Total	**51**	**100.0%**	**29**	**100.0%**	**80**	**100.0%**

Table 3: Group of thyroid cases among the study participants (n=80)

	Female		Male		Total	
	Nos.	%	Nos.	%	Nos.	%
Overt hypothyroidism	11	21.6%	6	20.7%	17	21.3%
Sub-clinical hypothyroidism	20	39.2%	9	31.0%	29	36.3%
Normal control	20	39.2%	14	48.3%	34	42.5%
Total	**51**	**100.0%**	**29**	**100.0%**	**80**	**100.0%**

Fig 1: Group of thyroid cases as per anti-TPO anti-bodies among the study participants (n=80)



2. Lipid profile

The mean lipid profile of the male participants was found to be visibly better as compared to those of the female participants, as can be seen from the table below. But this change was not found to be statistically important (p>0.05 using free sample t test).

a. Carotid Intimal Thickness

It was seen that the mean carotid intimal thickness (CIT) of the participants in the study participants was 0.45 mm with a Standard Deviation of 0.07 mm on right side and 0.44 with a SD of 0.07 on the left side. There was no gender difference observed on statistical analysis (p>0.05 by free sample t test).

Table 4: Carotid intimal thickness among the participants of the study at baseline (n=80)

Carotid Intimal Thickness	Female		Male		Total	
	Mean	Standard Deviation	Mean	Standard Deviation	Mean	Standard Deviation
Right side (mm)	.45	.07	.45	.08	.45	.07
Left side (mm)	.45	.07	.44	.07	.44	.07

On comparing the carotid intimal thickness at baseline among the various of groups of thyroid cases, it was seen that there was a important variation ($p<0.05$, using one way ANOVA test) between overt, subclinical and normal cases. Pair wise comparison using post-hoc study (Tukey's HSD test) found that changes among the groups was due to the difference between subclinical and normal, and overt and normal cases ($p<0.05$).

Table 5: Carotid intimal thickness in different groups of thyroid patients (n=80)

		Group of thyroid		
		Overt hypothyroidism (n=17)	Sub-clinical hypothyroidism (n=29)	Normal control (n=34)
Carotid Intimal Thickness Right (mm)	Mean	0.47	0.47	0.42
	SD	0.06	0.06	0.08
Carotid Intimal Thickness Left (mm)	Mean	0.47	0.45	0.42
	SD	0.05	0.06	0.07

3. Findings at follow up (after one year)

a. Thyroid profile

There was a mean decrease in TSH levels of 5.5 mIu/ml after one year of follow up with a SD of 6.5. Decrease in TSH was of the order of Overt hypothyroidism > Sub-clinical hypothyroidism > Normal control. The decrease in TSH was considerably unlike among the groups ($p=0.000$, using one-way ANOVA test). Post-hoc analysis showed that the observed variation between the groups was due to the difference between overt hypothyroidism with other groups ($p=0.000$ using Tukey's HSD test).

Table 6: Change in TSH levels at follow up among various group of thyroid patients (n=80)

		TSH at visit 1 (mIu/ml)	TSH at visit 2 (mIu/ml)	Change in TSH
Overt hypothyroidism	Mean	19.0	4.0	15.0
	SD	8.7	1.7	8.4
Sub-clinical hypothyroidism	Mean	7.6	3.4	4.2
	SD	1.3	1.1	1.3
Normal control	Mean	4.5	2.6	1.9
	SD	2.3	1.1	2.0
Total	**Mean**	**8.7**	**3.2**	**5.5**
	SD	**7.0**	**1.3**	**6.5**

It was seen that there was a mean change in T3 at follow up among all the groups of thyroid groups, with highest change seen in sub-clinical cases. The change was of the following order Sub-clinical hypothyroidism > Overt hypothyroidism > Normal control. However, the change was not found to be significant ($p=0.162$ using one-way ANOVA test).

Table 7: Change in T3 levels at follow up among various group of thyroid patients (n=80)

		T3 at visit 1 (ng/dl)	T3 at visit 2 (ng/dl)	Change in T3
Overt hypothyroidism	Mean	100.2	90.5	9.7
	SD	19.3	10.5	12.9
Sub-clinical hypothyroidism	Mean	122.0	103.4	18.5
	SD	20.7	12.7	21.5
Normal control	Mean	103.7	95.1	8.6
	SD	21.8	13.0	24.1
Total	**Mean**	**109.6**	**97.1**	**12.5**
	SD	**22.7**	**13.3**	**21.5**

Mean levels of T4 were found have a change by -1.1 mcg/dl with a SD of 3.2 (mean increase of 1.1 mcg/dl as compared to the baseline). The change was most seen in overt hypothyroidism cases, and the order that followed was Sub-clinical hypothyroidism > Normal control > Overt hypothyroidism. There was a considerable variation in the changes observed among each of the groups. Thus, the order of difference mentioned was a significant difference to be noted.

Table 8: Change in T4 levels at follow up among various group of thyroid patients (n=80)

		T4 at visit 1 (mcg/dl)	T4 at visit 2 (mcg/dl)	Change in T4(mcg/dl)
Overt hypothyroidism	Mean	0.6	6.6	-6.0
	SD	0.8	2.0	2.2
Sub-clinical hypothyroidism	Mean	7.4	6.1	1.3
	SD	1.3	1.3	1.8
Normal control	Mean	4.8	5.6	-0.8
	SD	1.6	1.0	1.6
Total	**Mean**	**4.8**	**6.0**	**-1.1**
	SD	**2.9**	**1.4**	**3.2**

b. Carotid intimal thickness

The mean change in carotid intimal thickness was 0.05 mm with Standard Deviation of 0.04 mm for right and 0.04 mm with SD of 0.03 for left side. There was no considerable vary at follow up among the groups on left side (p=0.075, using one-way ANOVA test). But the change observed at follow up was statistically significant on the right side (p=0.040, using one-way ANOVA test). Post-hoc analysis was done and it was seen that the observed difference on the right side was due to the difference between sub-clinical hypothyroidism with normal control group (p=0.037, using Tukey's HSD).

Table 9: Change in right carotid intimal thickness (CIT) in follow up patients (n=80)

Groups of participants		CIT Right side at visit 1 (mm)	CIT Right side at visit 2 (mm)	Change in CIT Right side
Overt hypothyroidism	Mean	.47	.43	.04
	SD	.06	.06	.03
Sub-clinical hypothyroidism	Mean	.47	.41	.06
	SD	.06	.05	.04
Normal control	Mean	.42	.38	.04
	SD	.08	.05	.04
Total	**Mean**	**.45**	**.40**	**.05**
	SD	**.07**	**.06**	**.04**

Table 10: Change in left carotid intimal thickness (CIT) in follow up patients (n=80)

Groups of participants		CIT Left side at visit 1 (mm)	CIT Left side at visit 2 (mm)	Change in CIT Left side (mm)
Overt hypothyroidism	Mean	.47	.43	.04
	SD	.05	.06	.03
Sub-clinical hypothyroidism	Mean	.45	.40	.05
	SD	.06	.06	.03
Normal control	Mean	.42	.38	.04
	SD	.07	.05	.04
Total	**Mean**	**.44**	**.40**	**.04**
	SD	**.07**	**.06**	**.03**

Table 11: Right Carotid intimal thickness (CIT) with respect to subgroups of thyroid (n=80)

Groups of participants	CIT Right side at visit 1 (mm)		CIT Right side at visit 2 (mm)		Change in CIT Right side (mm)	
	Mean	SD	Mean	SD	Mean	SD
Normal control	.42	.08	.38	.05	.04	.04
Overt hypothyroid with TPO-	.45	.05	.40	.05	.05	.03
Overt hypothyroid with TPO+	.50	.06	.47	.05	.03	.01
Subclinical hypothyroid with TPO-	.47	.06	.40	.04	.07	.04
Subclinical hypothyroid with TPO+	.49	.06	.45	.06	.04	.02

Table 12: Left Carotid intimal thickness (CIT) with respect to subgroups of thyroid (n=80)

Groups of participants	CIT Left side at visit 1 (mm)		CIT Left side at visit 2 (mm)		Change in CIT Left side(mm)	
	Mean	SD	Mean	SD	Mean	SD
Normal control	.42	.07	.38	.05	.04	.04
Overt hypothyroid with TPO-	.45	.05	.40	.06	.05	.03
Overt hypothyroid with TPO+	.49	.04	.47	.05	.02	.01
Subclinical hypothyroid with TPO-	.45	.06	.39	.05	.06	.03
Subclinical hypothyroid with TPO+	.46	.07	.43	.07	.03	.02

It was seen that the carotid internal thickness on the right side was different in between the groups, and this was statistically important (p=0.015, by one-way ANOVA). The observations were similar also for the left side (p=0.003, using one-way ANOVA). The difference was attributed to the difference seen in between sub-clinical hypothyroidism without TPO antibodies and normal control in both cases (using Tukey's HSD test for post-hoc analysis).

Table 13: Carotid intimal thickness by Anti-TPO Ab status at baseline (n=80)

	Anti-TPO status	N	Mean	Std. Deviation
Carotid Intimal Thickness Left side at visit 1 (mm)	Negative	59	0.4320	0.06648
	Positive	21	0.4738*	0.05679
Carotid Intimal Thickness Right side at visit 1 (mm)	Negative	59	0.4366	0.07124
	Positive	21	0.4862*	0.05518

*CIT was established to be considerably greater than the other group at p=0.05 levels using independent sample t test

Discussion

As indicated by Bozkus F, Dikmen N, et al[6] The effect of obstructive rest apnea issue and hypothyroidism to intimal thickness of carotid course a positive relationship was found among thyroid enabling hormone levels and intimal thickness (r = 0.426, p = .002), while free T3 levels and intimal thickness were unfavorably related (r = - 0.463, p = .001). Intimal thickness and apnea-hypopnea record were furthermore strongly associated (r = 0.403, p = .003). In our examination Mean dimensions of T3 at gauge was 110 ng/dl with a standard deviation of 22.7, while that for T4 was observed to be 4.84 mcg/dl with a

SD of 2.9. TSH was found to have a mean of 8.72 mIu/ml with a SD of 7. There was no essential variety of the mean qualities among male and female members ($p>0.05$) at gauge for any of the thyroid parameters, which was proved beforehand (7). Our meta-investigation gave a solid proof of expanded subclinical cardiovascular dangers as expanded CIT, more elevated amount atherogenic lipids, and expanded SBP and DBP in subjects with subclinical hypothyroidism. An expansion in CIT was essentially corresponded with an increment in the dimension of atherogenic lipids. The adjusted lipid levels could be the significant system causing early atherosclerotic vascular changes in subjects with subclinical hypothyroidism. In all subgroup analyses, the association between increased CIT in subjects with subclinical hypothyroidism remained significant except in subjects with subclinical hypothyroidism with a mean TSH $\leq$ 10.0 mIU/l, where SCH was no longer associated with an increased CIT.

Conclusion

The end says that the diminishing in Carotid Intimal Thickness (CIT) subsequent to taking Levothyroxin treatment in the patients with SCH. Early time of atherosclerotic changes is likewise run over in the hypothyroidism. Subclinical hypothyroidism and clear hypothyroidism may effectively affect endothelial capacity independently of other perceived atherosclerosis danger highlights. Levothyroxine substitution may diminish or anticipate atherosclerotic changes in the SCH too. In this manner, patients with SCH ought to be overseen same as hypothyroidism. CIT is a critical pointer for atherosclerotic illnesses; yet long haul and fake treatment controlled studies. That would survey advantage of levothyroxine substitution on CVDs and demise in Subclinical hypothyroidism is required. In this way, we closed from our examination that SCH is increasingly regular in females, there is high pervasiveness of TPO counter acting agent in SCH patients that implies immune system etiology, dyslipdemia is critical if TPO inspiration is there and females with SCH are progressively inclined to create dyslipidemia, particularly with TPO energy when contrasted with male. Thus, we prescribe early determination of such patients and keeping them from further dangers which should be possible by early inception of thyroid hormone substitution in such patients and their appropriate development.

References

1. Vijayan A, Jayasingh K, Jayaraman G, Green SR, Deyagarasan E. Assessment of carotid intima-media thickness in hypothyroidism and the effect of thyroid replacement therapy**.** International journal of Advance in Medicine. 2018; 5:2.
2. Kim SK, Kim SH, Park KS, Park SW, and Cho YW. Regression of the increased common carotid artery-intima media thickness in subclinical hypothyroidism after thyroid hormone replacement. *Endocrine Journal 2009; 56: 753-758.*
3. Valetina VN, Marijan Bosevski, Chedo Dimitrovski, Branka Krstevska. Subclinical hypothyroidism and risk of carotid atherosclerosis. *Arq Bras Endocrinol Metlab, 2011; 55/7.*
4. GaoNing, Zhang Wei, Zhang Yu-zhen, Yang Qing, Chen Shao-hua. Carotid intima-thickeness in patients with subclinical hypothyroidism: A Meta analysis. *Pubmed, Embase Cochrane Library 2011.*
5. Tunbridge WM, Evered DC, Hall R, Appleton D, Clark F, et al. Lipid profile and cardiovascular disease in the Whickham area with particular reference to thyroid failure. *ClinEndocrinol (Oxf). 1977; 7:495-508.*
6. Bozkus F1, Dikmen N2, et al The impact of obstructive rest apnea disorder and hypothyroidism to intima-media thickness of carotid course.Sleep Breath. 2015 Mar;

19(1):239-46. doi: 10.1007/s11325-014-1002-0. Epub 2014 May 22.

7. Nagasaki T1, Inaba M, et al Decrease in carotid intima-media thickness in hypothyroid patients after standardization of thyroid capacity. Clin Endocrinol (Oxf). 2003 Nov; 59(5):607-12.