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Risk Factors for Cardiovascular Disease Among Women with Subclinical Hypothyroidism in a Tertiary Care Hospital – A Retrospective Study

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Abstract

Background Subclinical hypothyroidism, defined as an elevated serum thyroid-stimulating hormones (TSH) level with normal levels of free thyroxine (FT4) affects up to 10% of the adult population. Subclinical hypothyroidism describes a situation in which thyroid function is only mildly low so that the blood level of thyroxine remains within the normal range but the blood level of TSH is elevated. Subclinical hypothyroidism is a common disorder that increases with age and affects up to 18% of the elderly, with a higher prevalence in women compared to men. The aim of this study was to determine associated risk factors for cardiovascular disease in untreated patients with subclinical hypothyroidism. **Material & Methods:** This was a retrospective study conducted in the Department of Biochemistry in cooperation with the Department of Endocrinology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh during the period from January,2013 to December,2013. In our study, we included 50 diagnosed subclinical hypothyroid individuals as cases and 50 euthyroid individuals as control. **Results:** The mean age was 45.69 ± 8.63 years. The mean of TSH was 9.84 ±6.14 mIU/L, TC & TG was 185.24± 48.15 & 272.43± 90.32 mg/dl respectively. The mean of HDL-C & LDL-C was found 41.83 ±12.56 & 136.4±42.7 mg/dl respectively in our patients. There was a significant increase in all variables of thyroid profile and lipid profile among SCH females except HDL, which was significantly decreased in SCH cases. The percent of patients having borderline elevated cholesterol (200-240 mg/dL), API (>0.21), AI (>3.46) & LCI (>28.10), hypercholesterolemia (>240 mg/dL) and hyperhomocysteinemia (>10.98 µmol/L) were detected in higher percentages in patients than controls. **Conclusion:** Women with subclinical hypothyroidism have significantly different lipid profiles from women with normal thyroid function. Females with subclinical hypothyroidism were more likely to suffer from cardiovascular disease than euthyroid women. Females with SCH experience a dyslipidemic condition, which is necessary for cardiovascular disease.

Keywords:- Subclinical hypothyroidism, Cardiovascular disease, Risk factors.

INTRODUCTION

Hypothyroidism is one of the most common endocrine disorders worldwide.[1] The prevalence of hypothyroidism is 3.80% in Bangladesh. [2] Hypothyroidism is caused by decreased levels of thyroid hormones and is among the most common endocrine disorders. Subnormal activity of the thyroid gland in hypothyroidism leads to mental and physical slowing because of a decrease in the basal metabolic rate.[3] The prevalence of spontaneous hypothyroidism is between 1% and 2% and is more common in older women and 10 times more common in women than in men.[4]

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Subclinical hypothyroidism (SH) is a very common disorder in the general population, especially among middle-aged and elderly patients. It represents a state with increased values of thyroid stimulating hormone (TSH) and normal values of thyroxine (T4) and triiodothyronine (T3).[5] In most cases, patients with SH have no symptoms that would indicate this disorder, so diagnosis is made based on laboratory findings.[6] As the values of thyroid hormone are normal, increased level of TSH represents a compensatory mechanism that stimulates the thyroid gland to produce sufficient amounts of thyroid hormones. The disorder can eventually progress to overt hypothyroidism (OH) which is characterized by increased values of TSH but reduced values of thyroid hormones.[7]

Subclinical hypothyroidism, defined as an elevated serum thyroid-stimulating hormones (TSH) level with normal levels of free thyroxine (FT4) affects up to 10% of the adult population.[8] Subclinical (without obvious symptoms) hypothyroidism (low thyroid function) describes a situation in which thyroid function is only mildly low, so that the blood level of thyroxine remains within the normal range but the blood level of TSH is elevated.[9] Subclinical hypothyroidism, which is defined as elevated thyroid-stimulating hormone (TSH) levels with free thyroxine concentrations within the reference range, is a common disorder that increases with age and affects up to 18% of the elderly, with a higher prevalence in women compared to men.[10]

SCH is asymptomatic; however, it can share the symptoms of hypothyroidism.[11] SCH patients have elevated lipid peroxidation, altered lipid profiles, and diminished arylesterase (ARE) activity compared to the control group.[12] Elevated lipid levels, increased arterial stiffness, disrupted coagulability, elevated homocysteine, carbohydrate reactive protein (CRP) levels, insulin resistance, and diastolic hypertension are possible risk factors for developing cardiovascular disease (CVD) in SCH.[13,14] In addition, CVDs like atrial fibrillation, heart failure, pericardial effusion, atrial tachyarrhythmia, and mitral valve dysfunction are associated with thyroid dysfunction.[15]

Whether subclinical hypothyroidism is related as a risk for premature cardiovascular disease is controversial.[16,17] Hak et al,[16] have shown that subclinical hypothyroidism was associated with atherosclerosis and myocardial infarction. Aortic atherosclerosis was diagnosed by radiographic detection of calcified deposits in the abdominal aorta. However, total cholesterol, high-density lipoprotein cholesterol (HDL-C), and blood pressure were similar in patients and in age-matched euthyroid women [18]. Our study was conducted to determine associated risk factors for cardiovascular disease in untreated patients with subclinical hypothyroidism.

MATERIAL AND METHODS

This was a retrospective study and was conducted in the Department of Biochemistry in cooperation with Department of Endocrinology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh during the period from January,2013 to December,2013. In our study, we included 50 diagnosed subclinical hypothyroid individuals as cases and 50 euthyroid individuals as control.

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These are the following criteria to be eligible for enrolment as our study participants: a) Patients aged between 20 to 70 years; b)Patients diagnosed with subclinical hypothyroidism; c) Patients with TSH value > 10mIU/L; d) Patients with FT4 value < 0.9ng/ml; e) Patients who were willing to participate were included in the study And a) Patients with uncontrolled DM, b) Patients diagnosed with thyroid disorder; c) Patients with thyroid hormone medication; d) Patients with hyperthyroidism; e) Patients with any history acute illness (e.g., renal failure, pancreatic diseases, etc.) were excluded from our study.

Operational Definition: Mild subclinical hypothyroidism having TSH values ≤ 10.0 mIU/L and severe subclinical hypothyroidism having TSH values > 10.0 mIU/L

Sample collection & preservation: With full aseptic precaution 5ml venous blood from each of the 120 study patients was collected after an overnight fast of at least 12 hours in a disposable syringe and was delivered immediately into a clean dry heparinized tube. Then plasma was separated after centrifuging at 3000 rpm for 5 minutes and stored in an ultra-freezer at -25°C until analytical measurements of plasma homocysteine, plasma triglyceride, HDL-C & LDL-C were done.

Statistical Analysis: All data were recorded systematically in preformed data collection form. Quantitative data was expressed as mean and standard deviation and qualitative data was expressed as frequency distribution and percentage. Statistical analysis was performed by using SPSS (Statistical Package for Social Sciences) for windows version 10. Probability value <0.05 was considered as level of significance. The study was approved by Ethical Review Committee of Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh.

RESULTS

[Table 1] shows the age distribution of SCH and euthyroid cases. Among the 50 euthyroid populations, the maximum population (28%) was under the age group 41-50 years, whereas, among the 50 subclinical hypothyroidism females, the majority patients (34%) were 51-60 years old and followed by 26% were under 41-50 years age group.

In [Table 2] we found the mean age was 45.69 ± 8.63 years. The mean BMI was 28.67±4.24 kg/m2. The mean SBP & DBP was 135.24 ± 20.78 & 83.94 ± 10.69 mmHg respectively. The mean of TSH was 9.84 ±6.14 mIU/L, TC & TG was 185.24± 48.15 & 272.43± 90.32 mg/dl respectively. The mean of HDL-C & LDL-C was found 41.83 ±12.56 & 136.4±42.7 mg/dl respectively in our patients.

Figure 1: Comparison of thyroid profile in SCH and euthyroid females

[Figure 1] compares the thyroid profile between case and control groups. There was a significant increase in all variables of thyroid profile

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among SCH females compared to euthyroid females.

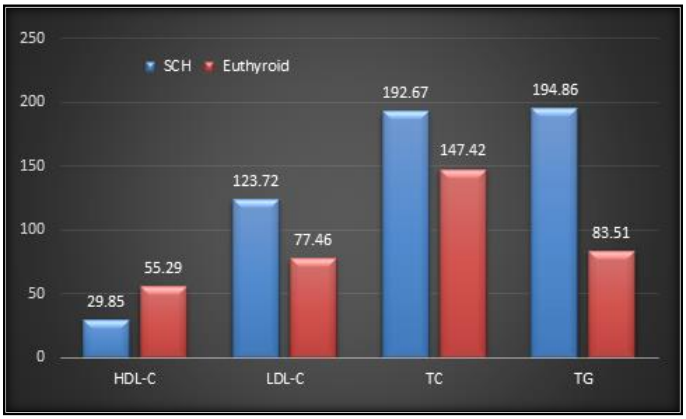

Figure 2: Comparison of lipid profile in SCH and euthyroid females

[Figure 2] compares the lipid profile between case and control groups. Among all variables of lipid profile, LDL-C, TC & TG increased in SCH females while HDL-C decreased in the case group compared to the control group.

The percentages of patients and controls of risk factors like elevated blood pressure, abnormal lipid profiles, and homocysteine levels are given in [Table 3]. The percent of patients having borderline elevated cholesterol (200-240 mg/dL), total cholesterol/ HDL-C (>5.51), triglycerides (>200 mg/dL), API (>0.21), AI (>3.46) & LCI (>28.10) was significantly higher in case group than the control group with a significant p <0.05 value. Hypercholesterolemia (>240 mg/dL) and hyperhomocysteinemia (>10.98 µmol/L) were detected in higher percentages in patients than controls.

Table 1: Distribution of SCH and euthyroid cases in different age groups.

Age	**SCH**		**Euthyroid**	
	N=50	**P (%)**	**N=50**	**P (%)**
20-30 years	6	12	7	14
31-40 years	10	20	13	26
41-50 years	13	26	14	28
51-60 years	17	34	11	22
>60 years	4	8	5	10

Table 2: Clinical and biochemical characteristics of our study patients.

Clinical characteristics	**N**	**P (%)**	**P-value**
Mean age (years)	45.69 ± 8.63		>0.05
Height (cm)	154.97±15.107		
Weight (kg)	61.05±14.24		
BMI (kg/m2)	28.67±6.24		>0.05
Heart Rate (per minute)	86 ± 17		
Systolic blood pressure (mm Hg)	135.24 ± 20.78		
Diastolic blood pressure (mm Hg)	83.94 ± 10.69		
Biochemical characteristics			<0.05
FT3 (pg/ml)	2.93 ± 0.44		<0.05
FT4 (ng/ml)	1.18 ±0.61		<0.05

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TSH (mIU/L)	9.84 ±6.14	<0.05
TC (mg/dl)	185.24± 48.15	<0.05
TG (mg/dl)	272.43± 90.32	<0.05
HDL-C (mg/dl)	41.83 ±12.56	<0.05
LDL-C (mg/dl)	136.4±42.7	<0.05

TSH: thyroid stimulating hormone; TC: total cholesterol; TG: triglyceride; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol

Table 3: Distribution of SCH and euthyroid cases by the risk factors for cardiovascular disease.

Risk factors	**SCH**		**Euthyroid**		**P-value**
	N=50	**P(%)**	**N=50**	**P(%)**	
Total homocysteinea ≥10.98 µmol/L	19	38	11	22	<0.05
Hypertension ≥140/90 mm Hg	33	66	8	16	<0.05
Total cholesterol ≥240 mg/dL	42	84	6	12	<0.05
LDL-C ≥130 mg/dL	19	38	7	14	<0.05
Triglycerides ≥200 mg/dL	18	36	5	10	<0.05
TC/HDL-C >5.51	21	42	2	4	<0.05
API > 0.21	20	40	3	6	<0.05
AI >3.46	22	44	2	4	<0.05
LCI >28.10	21	42	3	6	<0.05

DISCUSSION

Primary hypothyroidism is characterized by a decrease in fT3 and fT4 and a rise in serum TSH as a result of a feedback process via the hypothalamus-pituitary-thyroid axis.[19] Contrary to primary hypothyroidism, the patient does not exhibit symptoms, hence the diagnosis of subclinical hypothyroidism is based on laboratory findings. Every year, 2% to 5% more people develop overt hypothyroidism from subclinical hypothyroidism.[20] Insulin resistance, inflammation, hypertension, oxidative stress, and irregular coagulation all demonstrate the multifactorial basis of atherosclerosis, even if dyslipidemia plays a significant role in the development of atherosclerosis.[21,22]

In subclinical hypothyroidism, our study found a mean age of 45.69 years, which is similar to studies in Chennai, India,[23] Southern India,[24] Greece,[25] and but higher in studies in Turkey,[26] and Italy.[27]

This mean discrepancy could be the result of various study populations. The fT3 and fT4 were significantly different in subclinical hypothyroidism than in euthyroid, which is in contradiction with Karthick et al.'s study,[23] but similar to James et al.'s study.[24] This discrepancy may be related to the greater population size, ethnicity, age, and iodine intake.[24] TSH was considerably greater in the SCH group than in the euthyroid group and our findings were consistent with several studies.[23,24]

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A significant alteration of lipid profiles in subclinical hypothyroid females makes them more prone to CVD risk. Our study outlined a significant increase in LDL-C and TC, which was supported by Lioudaki et al,[28] Canaris et al,[29] and Hussain et al.[30] The study illustrated decreased LDL-C in subclinical hypothyroid females than in euthyroid populations.[24] The most common lipid changes in SCH are hypercholesterolemia because LDL-C levels are high, LDL-C receptor activity reduces LDL catabolism, intermediate-density lipoprotein is impacted, and these changes ultimately lead to an increase in TC and LDL-C in the bloodstream.[24]

The HDL-C was significantly higher in the euthyroid group than in the subclinical hypothyroidism group, which is in agreement with Karthick et al,[23] James et al,[24] Caron et al,[31] and Erdem et al,[32] but contradicts Regmi et al., who found increased HDL-C in the subclinical hypothyroid population compared to normal euthyroid females.[33] Some research, however, failed to detect a difference in HDL-C between euthyroid and subclinical hypothyroid females.[24] As thyroid hormones have an impact on the expression of HDL binding sites in liver cells, a crucial location for HDL metabolism, some studies have indicated that the plasma clearance rate of HDL-C is lowered. As a result, HDL-C levels in subclinical hypothyroid females may be lower than in those with normal thyroid function. Similar to prior research,[24] our investigation found that AIP was considerably greater in the subclinical hypothyroidism group of females than in the euthyroid group. Increased TG and decreased HDL-C relative to normal euthyroid control are the causes of the higher AIP in subclinical hypothyroidism. According to the mean AIP of subclinical hypothyroid females, SCH women had a greater risk of cardiovascular disease than euthyroid women.[19]

Our study found that subclinical hypothyroid females had a significant increase in AI compared to euthyroid females. Elevated LDL-C and decreased HDL-C are the causes of increased AI. This claim is supported by the research done by Althaus and Staub, et al.[34,35] Another study found that for every additional unit of AI, the risk of myocardial infarction rises by 75%.[36] In addition, our study shows a significant rise in LCI in subclinical hypothyroid females when compared to normal euthyroid females, which is comparable to the work of Cai et al,[37] which showed an increase in LCI in coronary artery disease (CAD) when compared to healthy controls. The higher TG, TC, and LDL-C readings, in contrast to the declining HDL-C, are the cause of the increased LCI. In our study, SCH had considerably higher TSH readings than euthyroid subjects. According to studies by Kumar et al., in patients with mild and severe SCH, TSH and fT3 levels significantly increased while fT4 levels remained stable. [38]

Limitations of the study

Our study was a single-centre study. We could study a few risk factors due to our short study period. There are more risk factors of CVD in subclinical hypothyroid women that needs to be evaluated. After evaluating those patients, we did not follow up with them for a long term and have not known other possible interference that may happen in the long term with these patients.

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CONCLUSIONS

In our study, we found women with subclinical hypothyroidism have significantly different lipid profiles from women with normal thyroid function. Females with subclinical hypothyroidism were more likely to suffer from cardiovascular disease than euthyroid women. Females with SCH experience a dyslipidemic condition, which is necessary for cardiovascular disease. AIP was substantially linked with TSH among the lipid indices. As a result, AIP was deemed to be a superior marker for determining CVD risk, followed by AI and LCI.

So further study with a prospective and longitudinal study design including a larger sample size needs to be done to validate and identify more risk factors of CVD in subclinical hypothyroidism women.

REFERENCES

1. Unnikrishnan AG, Menon UV. Thyroid disorders in India: An epidemiological perspective. Indian J Endocrinol Metab. 2011;15(Suppl 2):S78-81. doi: 10.4103/2230-8210.83329.
2. Das KC, Sarker BC, Sarker PK, Sana NK, Islam MS, Sayeed M. Thyroid dysfunction in a cross section of population in Dhaka city. Bangladesh J Med Sci. 2010;16:19-23.
3. Ashmaik AS, Gabra HM, Elzein AOM, Shrif NEMA, Hassan EE. Assessment of serum levels of calcium and phosphorous in Sudanese patients with hypothyroidism. Asian J Biomed Pharma Sci. 2013;2:21-6.
4. Vanderpump MP, Tunbridge WM. Epidemiology and prevention of clinical and subclinical hypothyroidism. Thyroid. 2002;12:839-47.
5. Surks MI, Ortiz E, Daniels GH, Sawin CT, Col NF, Cobin RH et al. Subclinical thyroid disease scientific review and guidelines for diagnosis and management. JAMA. 2004; 291(2): 228-38.
6. Gillett M. Subclinical Hypothyroidism: Subclinical Thyroid Disease: Scientific Review and Guidelines for Diagnosis and Management. Clin Biochem Rev. 2004;25(3):191–4.
7. McDermott MT, Ridgway EC. Subclinical hypothyroidism is mild thyroid failure and should be treated. J Clin Endocrinol Metab. 2001;86(10):4585-90. doi: 10.1210/jcem.86.10.7959.
8. Biondi B, Cappola AR, Cooper DS. Subclinical Hypothyroidism: A Review. JAMA. 2019;322(2):153-160. doi: 10.1001/jama.2019.9052.
9. Pluta RM, Burke AE, Glass RM. JAMA patient page. Subclinical hypothyroidism. JAMA. 2010;304(12):1402. doi: 10.1001/jama.304.12.1402.
10. Baumgartner C, Blum MR, Rodondi N. Subclinical hypothyroidism: summary of evidence in 2014. Swiss Med Wkly. 2014;144:w14058. doi: 10.4414/smw.2014.14058.
11. Peeters RP. Subclinical Hypothyroidism. N Engl J Med. 2017;376(26):2556-2565. doi: 10.1056/NEJMcp1611144.
12. Villanueva I, Alva-Sánchez C, Pacheco-Rosado J. The role of thyroid hormones as inductors of oxidative stress and neurodegeneration. Oxid Med Cell Longev. 2013;2013:218145. doi: 10.1155/2013/218145.
13. Delitala AP, Fanciulli G, Maioli M, Delitala G. Subclinical hypothyroidism, lipid metabolism and cardiovascular disease. Eur J Intern Med. 2017;38:17-24. doi: 10.1016/j.ejim.2016.12.015.
14. Duntas LH, Chiovato L. Cardiovascular Risk in Patients with Subclinical Hypothyroidism. Eur Endocrinol. 2014;10(2):157-160. doi: 10.17925/EE.2014.10.02.157.
15. Grais IM, Sowers JR. Thyroid and the heart. Am J Med. 2014;127(8):691-8. doi: 10.1016/j.amjmed.2014.03.009.
16. Kung AW, Pang RW, Janus ED. Elevated serum lipoprotein(a) in subclinical hypothyroidism. Clin Endocrinol (Oxf). 1995;43(4):445-9. doi: 10.1111/j.1365-2265.1995.tb02616.x.
17. Danese MD, Ladenson PW, Meinert CL, Powe NR. Clinical review 115: effect of thyroxine therapy on serum lipoproteins in patients with mild thyroid failure: a quantitative review of the literature. J Clin Endocrinol Metab. 2000;85(9):2993-3001. doi: 10.1210/jcem.85.9.6841.
18. Hak AE, Pols HA, Visser TJ, Drexhage HA, Hofman A, Witteman JC. Subclinical hypothyroidism is an independent risk factor for atherosclerosis and myocardial infarction in elderly women: the Rotterdam Study. Ann Intern Med. 2000;132(4):270-8. doi: 10.7326/0003-4819-132-4-200002150-00004.
19. N S M, Shankar M, Narasimhappa S. Subclinical Hypothyroidism (SH) and Atherogenic Index of Plasma (AIP) in Women: A Case-Control Study From a Tertiary Care Hospital in South India. Cureus. 2020;12(9):e10636. doi: 10.7759/cureus.10636.

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Page no- 53-60 | Section- Research Article (Biochemistry)

20. Vanderpump MP, Tunbridge WM, French JM, Appleton D, Bates D, Clark F, et al. The incidence of thyroid disorders in the community: a twenty-year follow-up of the Whickham Survey. Clin Endocrinol (Oxf). 1995;43(1):55-68. doi: 10.1111/j.1365-2265.1995.tb01894.x.
21. Peppa M, Betsi G, Dimitriadis G. Lipid abnormalities and cardiometabolic risk in patients with overt and subclinical thyroid disease. J Lipids. 2011;2011:575840. doi: 10.1155/2011/575840.
22. Gomberg-Maitland M, Frishman WH. Thyroid hormone and cardiovascular disease. Am Heart J. 1998;135(2 Pt 1):187-96. doi: 10.1016/s0002-8703(98)70081-x.
23. Karthick N, Dillara K, Poornima KN, Subhasini AS. Dyslipidaemic changes in women with subclinical hypothyroidism. J Clin Diagn Res. 2013;7(10):2122-5. doi: 10.7860/JCDR/2013/5777.3448.
24. James SR, Ray L, Ravichandran K, Nanda SK. High atherogenic index of plasma in subclinical hypothyroidism: Implications in assessment of cardiovascular disease risk. Indian J Endocrinol Metab. 2016;20(5):656-661. doi: 10.4103/2230-8210.190550.
25. 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(6):705-10. doi: 10.1530/eje.0.1450705.
26. Erem C. Blood coagulation, fibrinolytic activity and lipid profile in subclinical thyroid disease: subclinical hyperthyroidism increases plasma factor X activity. Clin Endocrinol (Oxf). 2006;64(3):323-9. doi: 10.1111/j.1365-2265.2006.02464.x.
27. Caraccio N, Ferrannini E, Monzani F. Lipoprotein profile in subclinical hypothyroidism: response to levothyroxine replacement, a randomized placebo-controlled study. J Clin Endocrinol Metab. 2002;87(4):1533-8. doi: 10.1210/jcem.87.4.8378.
28. Lioudaki E, Mavroeidi NG, Mikhailidis DP, Ganotakis ES. Subclinical hypothyroidism and vascular risk: an update. Hormones (Athens). 2013;12(4):495-506. doi: 10.14310/horm.2002.1437.
29. Canaris GJ, Manowitz NR, Mayor G, Ridgway EC. The Colorado thyroid disease prevalence study. Arch Intern Med. 2000;160(4):526-34. doi: 10.1001/archinte.160.4.526.
30. Hussain A, Elmahdawi AM, Elzeraidi NE, Nouh F, Algathafi K. The Effects of Dyslipidemia in Subclinical Hypothyroidism. Cureus. 2019;11(11):e6173. doi: 10.7759/cureus.6173.
31. Caron P, Calazel C, Parra HJ, Hoff M, Louvet JP. Decreased HDL cholesterol in subclinical hypothyroidism: the effect of L-thyroxine therapy. Clin Endocrinol (Oxf). 1990;33(4):519-23. doi: 10.1111/j.1365-2265.1990.tb03889.x.
32. Erdem TY, Ercan M, Ugurlu S, Balci H, Acbay O, Gundogdu S. Plasma viscosity, an early cardiovascular risk factor in women with subclinical hypothyroidism. Clin Hemorheol Microcirc. 2008;38(4):219-25.
33. Regmi A, Shah B, Rai BR, Pandeya A. Serum lipid profile in patients with thyroid disorders in central Nepal. Nepal Med Coll J. 2010;12(4):253-6.
34. Duntas LH, Chiovato L. Cardiovascular Risk in Patients with Subclinical Hypothyroidism. Eur Endocrinol. 2014;10(2):157-160. doi: 10.17925/EE.2014.10.02.157.
35. Mahto M, Chakraborthy B, Gowda SH, Kaur H, Vishnoi G, Lali P. Are hsCRP Levels and LDL/HDL Ratio Better and Early Markers to Unmask Onset of Dyslipidemia and Inflammation in Asymptomatic Subclinical Hypothyroidism? Indian J Clin Biochem. 2012;27(3):284-9. doi: 10.1007/s12291-012-0206-y.
36. Gaziano JM, Hennekens CH, O'Donnell CJ, Breslow JL, Buring JE. Fasting triglycerides, high-density lipoprotein, and risk of myocardial infarction. Circulation. 1997;96(8):2520-5. doi: 10.1161/01.cir.96.8.2520.
37. Cai G, Shi G, Xue S, Lu W. The atherogenic index of plasma is a strong and independent predictor for coronary artery disease in the Chinese Han population. Medicine (Baltimore). 2017;96(37):e8058. doi: 10.1097/MD.0000000000008058.
38. Suh S, Kim DK. Subclinical Hypothyroidism and Cardiovascular Disease. Endocrinol Metab (Seoul). 2015;30(3):246-51. doi: 10.3803/EnM.2015.30.3.246.

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