ORIGINAL ARTICLE

Evaluation of an Association of Thyroid Disorder and Dyslipidemia in Patients with Cardiovascular Disease: A Cross-sectional Study

Pankaj K Chaudhary[1,*], Rajendra Kumar Verma[2], Puspendra K Singh[3]

[1]Department of Pharmacology, Government Medical College, Azamgarh, Uttar Pradesh, INDIA.
[2]Department of Medicine, GSVM Medical College, Kanpur, Uttar Pradesh, INDIA.
[3]Department of Radiology, Government Medical College, Azamgarh, Uttar Pradesh, INDIA.

ABSTRACT

Background: Subclinical Hypothyroidism (SCH) is defined as normal serum free thyroid hormone levels coexisting with elevated serum Thyroid-Stimulating Hormone (TSH) levels. SCH is a common condition observed in clinical practice with several unique features. The present study was conducted to find prevalence of subclinical hypothyroidism in patients with myocardial infarction and demographic differences between patients with and without SCH. **Materials and Methods:** A total of 100 patients with Myocardial Infarction of Adult (age > 18 years) males and females were selected from the patients attending Medicine OPD, IPD or Intensive Care Unit (ICU) in GMC, Azamgarh. Clinical examination, laboratory investigations for myocardial infarction, thyroid status and lipid profile was done in all patients in our study. All Patients with TSH values > 10mU/L or < 0.04mU/L or Known cases of Thyroid abnormalities were excluded from the study. Statistical analysis was done using excel and SPSS software. **Results:** Out of 100 patients 44 patients of MI had subclinical hypothyroid were as rest 56 patients were euthyroid. In both the groups no statistical difference was seen in the type of Myocardial infarction. There was significant difference in lipid profile ($p<0.05$) in SCH group as compared to euthyroid group. **Conclusion:** Patients with Subclinical hypothyroid and MI had more lipid abnormalities as compared to Euthyroid group although the type of myocardial infarction was similar in both the groups. Males had more myocardial infarction as compared to females in both the subclinical hypothyroid and euthyroid groups.

Keywords: Thyroid, Myocardial Infarction, Antibody, Lipid, CAD.

Article Information

Received: 23-12-2022
Revised : 03-01-2023
Accepted: 08-01-2023

Correspondence

Pankaj Kumar Chaudhary
Assistant Professor, Department of Pharmacology, Government Medical College, Azamgarh- 276128, Uttar Pradesh, INDIA.
Email id: chaudharypankaj847@gmail.com

INTRODUCTION

The definition of Subclinical Hypothyroidism (SCH) is biochemical in nature, namely elevated serum Thyroid-Stimulating Hormone (TSH) levels combined with normal levels of serum free thyroid hormones (i.e., within the population reference range).[1] Unlike overt hypothyroidism, patients with SCH may present without any clinical features of hypothyroidism and are often identified through routine health examinations. It is a challenge to determine the clinical meaning of this "subclinical" state.[2] Subclinical hypothyroidism or mild thyroid failure is a common problem, with a prevalence of 3% to 8% in the population without known thyroid disease. The prevalence increases with age and is higher in women.[3,4]

Antithyroid antibodies can be detected in 80% of patients with SCH, and 80% of patients with SCH have a serum TSH of less than 10mIU/L. There

Access this article online

Website: www.jcramonline.com

DOI: 10.5530/jcram.2.3.13

Quick Response code

is growing evidence that SCH is associated with increasing cardiovascular risk, particularly in older women.[5,6] Clinical hypothyroidism is associated with premature atherosclerosis and increased prevalence of coronary disease. Possible mechanisms behind the link between hypothyroidism and atherosclerosis, other than dyslipidemia, include the effects of thyroid hormones on coagulation, vasodilation, parasympathetic function, and homocysteine metabolism.[5,7]

Measurement of serum TSH is generally considered the best screening test for thyroid disease. Increased values indicate hypothyroidism. The relationship of thyroid hormonal abnormalities and cardiovascular disease goes well beyond the risk of atherosclerosis in association with hypothyroidism and the risk of a trial fibrillation in persons with hyperthyroidism.[2] A study, which examined the relation between cardiovascular disease and TSH levels in euthyroid patients, found significantly higher TSH in patients with coronary events compared to controls matched for age, gender, and body mass index.[8] The cross-sectional Rotterdam study showed an association of SCH with myocardial infarction and aortic calcification.[9] Several observational studies comparing the outcome of SCH individuals with euthyroid subjects have shown divergent results, and it has been debated for some time whether SCH is independently associated with Ischemic Heart Disease (IHD).[10,11]

Coronary Artery Disease (CAD), its acute form, and Acute Coronary Syndrome (ACS) are the major cause of death all over the world.[12] ACS is the umbrella term of clinical signs and symptoms of myocardial ischemia including Unstable Angina (UA), ST-Segment Elevation Myocardial Infarction (STEMI) and Non-STsegment elevation myocardial infarction (NSTEMI).[13] Several prospective, population-based cohort studies found that subclinical hypothyroidism was associated with increased risks of atherosclerotic coronary heart diseases and cardiovascular mortality, whereas other studies showed no correlation. Because of these conflicting reports and the large numbers of populations afflicted by this condition, there is an urgent need for settling the controversy. The objectives of our study were to find out the prevalence of sub clinical hypothyroidism in acute myocardial infarction and to correlate sub clinical hypothyroidism in STEMI and NSTEMI patients. As findings of several studies support the influence of fish on ischemic heart disease, the aim of the study waste investigate prevalence of SCH in Myocardial infarction patients.

MATERIALS AND METHODS

This present study was done at Department of Medicine, Government Medical College, Azamgarh, Uttar Pradesh, and India from the period of July 2020 to July 2021. This cross-sectional prospective study was done to find out an association of SCH in Myocardial infarction patients. Data collection and enrolment of the Patients was commenced following ethical clearance from college Institutional ethical committee, Government Medical College, Azamgarh Uttar Pradesh. 100 patients with Myocardial Infarction of Adult (age > 18 years) males and females were selected from the patients attending Medicine OPD or Intensive Care Unit (ICU) or admitted in GMC, Azamgarh as a case of STEMI or NSTEMI Myocardial infarction. Age and sex matched healthy volunteers were included in our study.

Inclusion Criteria

1. All Acute Myocardial Infarction Patients presenting to the OPD, IPD, EMERGENCY, ICU.
2. All MI patients with normal T3, T4, TSH levels.
3. MI Patients with Normal T3, T4 and TSH levels between 4.5 – 10 mU/L and no clinical feature suggestive of hypothyroid condition.

Exclusion Criteria

1. All subjects with TSH values > 10mU/L or < 0.04mU/L.
2. Known cases of Thyroid diseases.
3. Patients who had undergone surgery of the thyroid gland.
4. Very sick or critically injured patients.
5. Stable angina, Unstable angina, CKD, CLD patients.

Methodology

1. Clinical examination and laboratory investigations of all patients were collected at the time of admission to the hospital. Standard reference values for thyroid function tests were followed for categorizing patients.
2. Free T3, free T4, and TSH levels of 100 patients (age >18years) was done in all patients who were admitted at Medicine department, GMC, Azamgarh with the diagnosis of ST Elevation (STEMI) or Non-ST Elevation Myocardial Infarction (NSTEMI).
3. Patients were classified into 2 groups based on their thyroid function tests.
   a. Group I (Sub clinical hypothyroid)-TSH Level >4.5 to 9.9mU/L.

b. Group II (Euthyroid)-TSH Level- 0.04-4.4mU/L.

4. After 12 hr overnight fasting, blood samples were collected from all participants for measuring biochemical parameters. The samples were immediately centrifuged at 3000 rpm for 5 min and serum was separated. The sera were stored at -20°C until assayed. Serum T3, T4 and TSH levels were measured by the Enzyme-Linked Immunosorbent Assay (ELISA) method using commercial kits.
5. Serum levels of LDL, HDL, Cholesterol and TG were measured using a spectrophotometric assay with commercial Serum levels of C and TG were determined by enzymatic colorimetric assay.

Statistical Analysis

The data was compiled and descriptive statistical analysis was carried out in the present study. Results on categorical measurements were presented in number (%). Chi-square test was used to find the significance of study parameters on categorical scale between two or more groups. *P* value <0.05 were considered statistically significant.

RESULTS

Following results were obtained from the study.

Baseline clinical characteristics

- The present study included 100 patients with myocardial infarction in the period from July 2020 to July 2021. Out of 100 patients, 62% were males and 38% were females.

DISCUSSION

Thyroid hormones are responsible for regulating different functions regarding metabolism and performance in multiple organs. When the thyroid hormones axis is altered, it can leadto either hypo-or hyperthyroidism.

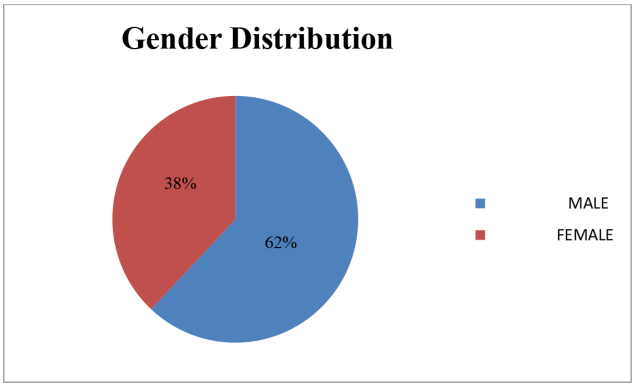

Figure 1: Gender Distribution of Patients.
- Out of 100 Patients, 44(44%) were of SCH and 56(56%) were Euthyroid Patients.

Table 1: Prevalence of Subclinical Hypothyroidism (SCH) and Euthyroid in patients of Myocardial infarction.

Thyroid Status	No. of cases (*n*=100)	Percentage (%)
SCH	44	44.0
Euthyroid	56	56.0
Total	100	100.0

x^2 =2.45 p= 0.365

In the present study out of 100 patients, majority of patients in both gender were in the age group of 51-60 years of age. In our study Myocardial infarction was found more among males as compared to females and the difference was statistically significant.

Table 2: Association of age and gender with MI (*n*=100).

Age group(years)	Patients with MI		Percentage (%)
	Male (%) (*n*=62)	Female (%) (*n*=38)	
30-40	04 (6.45)	03 (7.89)	7
41-50	14 (22.58)	08 (21.05)	22
51-60	23 (37.09)	16 (42.10)	39
61-70	18 (29.03)	09 (23.68)	27
>70	03 (4.83)	02 (5.26)	05
Total	62 (100)	40 (100)	100
Grand Total (%)	**62**	**38**	**100**

x^2= 2.11 p= 0.02821* (Mean ± SD: 24.08±15.12)

The study results showed that Subclinical Hypothyroidism Patient presenting with STEMI was 29(65.90%) while Patient Presenting with NSTEMI was 15(34.09%). Similarly Euthyroid patients presenting with STEMI was 38(67.85%) while Patient Presenting with NSTEMI was 18(32.14%). More cases of STEMI were observed in both Subclinical Hypothyroidism and euthyroid patients. But the difference was not statistically significant among both the group.

Table 3: Subclinical Hypothyroidism and Euthyroid patients with STEMI and NSTEMI.

Thyroid Status	Myocardial Infarction	No of Cases (*n*=100)	Percentage (%)
Subclinical Hypothyroidism	STEMI	29	65.90
	NSTEMI	15	34.09
	Total	**44**	**100.0**
Euthyroid	STEMI	38	67.85
	NSTEMI	18	32.14
	Total	**56**	**100.0**
	Grand Total	100	100

x^2= 5.11 p= 0.6102

Out of 100 patients, Male patient with STEMI were 44(44%) and female Patient with STEMI were 23(23%) while Male patient with NSTEMI were 18(18%) and female Patient with NSTEMI were 15(15%). There were 67% patients who had STEMI while 37% had NSTEMI. Significant association was observed between gender with SCH and Euthyroid patient with MI (STEMI and NSTEMI).

Table 4: Association between gender of Subclinical Hypothyroidism and Euthyroid Patients with STEMI and NSTEMI.

Thyroid Status		No of Cases (*n*=100)		Total (%)	Myocardial Patients
		Male (%) (*n*=62)	Female (%) (*n*=38)		
Subclinical Hypothyroidism	STEMI	19(43.18)	10(22.72)	29(65.90)	STEMI=67% NSTEMI=33%
	NSTEMI	09(20.45)	06(13.63)	15(34.09)	
	Total	28(63.63)	16(36.35)	44(100.0)	
Euthyroid	STEMI	25(44.64)	13(23.21)	38(67.85)	
	NSTEMI	09(16.07)	09(16.07)	18(32.14)	
	Total	34(60.71)	22(39.28)	56(100.0)	
	Grand Total	62(62)	38(38)	100(100.0)	

x^2= 1.03 p= 0.04580

Amongst 100 screened Patients, 44 SCH and 56 Euthyroid Patients presenting with Myocardial infarction were found whose mean LDL was found to be 142.253 and 128.254 respectively. Similarly HDL in SCH and Euthyroid group was found to be 32.954 and 48.114 while Triglycerides in SCH and Euthyroid group were found to be 54.2148 and 45.6984. Cholesterol in SCH and Euthyroid group was found to be 61.2478 and 46.5964. There was significant difference of lipid profile (p<0.05) found in SCH and euthyroid group. Lipid profile was found higher in SCH group as compared to euthyroid which showed that SCH group was associated dyslipidemia which could be precipitating factor for causation of myocardial infarction.

Table 5: Lipid profile level of SCH and Euthyroid group.

Lipid Profile (mg/dL)	Thyroid Status	N	Mean	Std. Deviation	t-test(p)
LDL	SCH	44	142.253	44.2554	0.0354*
	Euthyroid	56	128.254	32.1145	
HDL	SCH	44	32.954	17.5428	0.0354*
	Euthyroid	56	48.114	11.2135	
Triglycerides	SCH	44	184.568	54.2148	0.0125*
	Euthyroid	56	152.114	45.6984	
Cholesterol	SCH	44	242.123	61.2478	0.0452*
	Euthyroid	56	199.659	46.5964	

Hypothyroidism is classified according to the clinical presentation as overt and subclinical. Subclinical hypothyroidism is defined as an increase in the levels of thyroid-stimulating hormone (TSH) with a normal level of T3 and T4 in the absence of symptoms. Overt hypothyroidism has been studied more than subclinical hypothyroidism and is well known to be associated with cardiovascular disease such as accelerated atherosclerosis and coronary artery disease.

Subclinical hypothyroidism is a common clinical problem, diagnosed mainly by laboratory methods. Screening is needed to detect SCH in most cases since most patients with this disorder are asymptomatic. It is recognized by abnormally high serum TSH value with normal FT4 and FT3 concentrations. Although it was recently reported that SCH is associated with elevated risks of cardiovascular events, cardiac dysfunction, lipid metabolism abnormalities and neuropsychiatric disorders, it is still debated whether long-term subclinical hypothyroidism is associated with systemic complications.

Our study results reported that male males were more susceptible to myocardial infarction than female which was in accordance with the results of Sudeb Mukherjee *et al*.[14] stating male predominance in their study. However, it was contradictory to the findings of Kosuke Inoue *et al*.[15] Who reported male and female preponderance was almost equal in their study. The male prevalence is much more in this study although subclinical hypothyroidism is said to be more common in females. The study report revealed that patients belonging to age group 51-60 (39%) were 39% which was different from the findings of Wilson *et al*.[16] Who reported that majority of patients in their study were in the age group of 65 and above. However almost similar findings were observed by Ng M *et al*.[17] The present study finding suggest that since males are more liable to get exposed to stress and because of their lifestyle changes like smoking, drinking they are more prone to MI.

Regarding prevalence of SCH, the study result showed that the prevalence of SCH was 44% among the whole MI patients (STEMI, and NSTEMI) while 56(56%) were Euthyroid Patients. These results are disconcordant to the findings of Cooper *et al*. study which showed that the prevalence of SCH in adults has been reported to range from 4% to 20%. This wide range can be explained by differences in age, gender, race, body mass index, and dietary iodine intake in the studied populations as well as differences in serum TSH evaluation methods.[18] Our results are also concordant with the results of the Colorado study in which the prevalence of SCH ranged from 4 to 21% in women and 3 to 16% in men.[19] However, our results were according to the results of Wickham Survey[20] and NHANES III[3] which showed higher prevalence of SCH in their study.

The study results showed that Subclinical Hypothyroidism Patient presenting with STEMI was 29 (65.90%) while Patient Presenting with NSTEMI was 15 (34.09%). Similarly Euthyroid patients presenting with STEMI was 38 (67.85%) while Patient Presenting with NSTEMI was 18 (32.14%). No significant association was observed between gender with SCH and Euthyroid patient with MI (STEMI and NSTEMI). So amongst all MI patients, there were 67% patients who had STEMI while 37% had NSTEMI which was contradictory to the findings of Sudeb Mukherjee *et al*.[14] stating 44% of patients had STEMI. However no studies were found in literature which was comparable to our study findings.

Hypothyroidism also increases total and Low-Density Lipoprotein (LDL) cholesterol, TG and TC in proportion to the rise in serum TSH levels.[21] Regarding association between lipid profile and thyroid status, our study results revealed that 44 SCH Patients and 56 Euthyroid Patients presenting with Myocardial infarction were found to have LDL level 142.253 and 128.254 respectively. Similarly Triglycerides in SCH and Euthyroid group were found to be 54.2148 and 45.6984. Cholesterol in SCH and Euthyroid group was found to be 61.2478 and 46.5964. HDL in SCH and Euthyroid group was found to be 32.954 and 48.114 which suggest that a Euthyroid patient has slightly better HDL level.

Our study findings was consistent with the results of Colorado study in which patients with SCH had higher serum total cholesterol concentrations than euthyroid individuals.[19] However, our results were disconcordant with NHANES III cohort study which showed higher total cholesterol and triglycerides concentrations in subclinical hypothyroid patients than in euthyroid subjects, but these changes were no longer observed after adjustment of different variables such as age, sex, race, and management with lipid lowering drugs.[3] The inconsistency between these studies may bedew to the differences of the populations studied, including selection criteria based on sex, age, race, smoking history, and insulin resistances well as variations in serum TSH concentrations used to define SCH. Lipid profile was found to be deranged in this study in both the groups. There was significant difference of lipid profile ($p<0.05$) found in SCH and euthyroid group. Lipid profile was found higher in SCH group as compared to euthyroid which showed that SCH group was associated dyslipidemia which could be precipitating factor for causation of myocardial infarction.

CONCLUSION

SCH is associated with adverse outcomes in terms of cardiovascular risk, metabolic conditions, and quality of life. Prevalence of SCH was 44% among patients with Myocardial infarction. Higher prevalence of STEMI (67%) was seen in SCH as compared to Euthyroid patients but that was not statistically significant.

There was significant difference of lipid profile ($p<0.05$) found in SCH and euthyroid group. Lipid profile was found higher in SCH group as compared to euthyroid which showed that SCH group was associated dyslipidemia which could be precipitating factor for causation of myocardial infarction.

Suggestion

This study in Northern India shows high prevalence of subclinical hypothyroidism in cardiovascular patients. Therefore treatment algorithm should be initiated in those groups of patients. The causal association between abnormal thyroid hormone levels and cardiovascular disease is not fully understood. Different studies support a biologically plausible role for hypothyroidism increasing the risk of atherosclerotic cardiovascular diseases.

Limitation of study

Longitudinal prospective study of larger groups of subclinical hypothyroid patients, after exclusion of other baseline confounding factors is needed. Large-scale studies are needed to clarify the effects of SCH on myocardial infarction both on etiologic and prognostic grounds.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

1. Braverman LE, Cooper DS, Kopp PA. Chapter 50. Subclinical hypothyroidism. In: Werner and Ingbar's the thyroid. 11th ed. Philadelphia: Wolters Kluwer. 2021:635-40.
2. Cooper DS. Clinical practice. Subclinical hypothyroidism. N Engl J Med. 2001;345(4):260-5. doi: 10.1056/NEJM200107263450406, PMID 11474665.
3. Hollowell JG, Staehling NW, Flanders WD, Hannon WH, Gunter EW, Spencer CA, *et al*. Serum TSH, T(4), and thyroid antibodies in the United States population (1988 to 1994): National Health and Nutrition Examination Survey (NHANES III). J Clin Endocrinol Metab. 2002;87(2):489-99. doi: 10.1210/jcem.87.2.8182. PMID 11836274.
4. Karmisholt J, Andersen S, Laurberg P. Variation in thyroid function tests in patients with stable untreated subclinical hypothyroidism. Thyroid. 2008;18(3):303-8. doi: 10.1089/thy.2007.0241, PMID 18303960.
5. Kahaly GJ. Cardiovascular and atherogenic aspects of subclinical hypothyroidism. Thyroid. 2000;10(8):665-79. doi: 10.1089/10507250050137743, PMID 11014311.
6. 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, PMID 11720894.
7. Johnson JL, Duick DS. Diabetes and thyroid disease: A likely combination. Diabetes Spec. 2002;15(3):140-2. doi: 10.2337/diaspect.15.3.140.
8. Miura S, Iitaka M, Suzuki S, Fukasawa N, Kitahama S, Kawakami Y, *et al*. Decrease in serum levels of thyroid hormone in patients with coronary heart disease. Endocr J. 1996;43(6):657-63. doi: 10.1507/endocrj.43.657, PMID 9075605.
9. Hak AE, Pols HAP, Visser TJ, Drexhage HA, Hofman A, Witteman JCM. 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, PMID 10681281.
10. Chu JW, Crapo LM. The treatment of subclinical hypothyroidism is seldom necessary. J Clin Endocrinol Metab. 2001;86(10):4591-9. doi: 10.1210/jcem.86.10.7961, PMID 11600508.
11. 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, PMID 11600507.
12. Kumar A, Sivakanesam R, Gumasekera S. Ischemia modified albumin: A potential marker in acute myocardial infarction in normolipidemia. Pak J Med Sci. 2006;24:364-7.
13. Overbaugh KJ. Acute coronary syndrome. Am J Nurs. 2009;109(5):42-52; quiz 53. doi: 10.1097/01.NAJ.0000351508.39509.e2, PMID 19411905.
14. Mukherjee S, Datta S, Mandal SC. Prevalence of Subclinical Hypothyroidism in Acute Coronary Syndrome in Nondiabetics: Detailed Analysis from Consecutive 1100 Patients from Eastern India. J Thyroid Res. 2018;2018:9030185. doi: 10.1155/2018/9030185. PMID 30254730.
15. Inoue K, Ritz B, Brent GA, Ebrahimi R, Rhee CM, Leung AM. Association of subclinical hypothyroidism and cardiovascular disease with mortality. JAMA Netw Open. 2020;3(2):e1920745. doi: 10.1001/jamanetworkopen.2019.20745, PMID 32031647.
16. Wilson S, Parle JV, Roberts LM, Roalfe AK, Hobbs FD, Clark P, *et al*. Prevalence of subclinical thyroid dysfunction and its relation to socioeconomic deprivation in the elderly: A community-based cross-sectional survey. J Clin Endocrinol Metab. December 2006;91(12):4809-16. doi: 10.1210/jc.2006-1557, PMID 17003083.
17. Ng M, Fleming T, Robinson M, Thomson B, Graetz N, Margono C, *et al*. Global, regional, and national prevalence of overweight and obesity in children and adults during 1980-2013: A systematic analysis for the Global Burden of Disease Study 2013. Lancet. 2014;384(9945):766-81. doi: 10.1016/S0140-6736(14)60460-8, PMID 24880830.
18. Cooper DS, Biondi B. Subclinical thyroid disease. Lancet. 2012;379(9821):1142-54. doi: 10.1016/S0140-6736(11)60276-6, PMID 22273398.
19. 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, PMID 10695693.
20. Tunbridge WM, Evered DC, Hall R, Appleton D, Brewis M, Clark F, *et al*. The spectrum of thyroid disease in a community: The Whickham survey. Clin Endocrinol (Oxf). 1977;7(6):481-93. doi: 10.1111/j.1365-2265.1977.tb01340.x, PMID 598014.
21. Duntas LH, Brenta G. The effect of thyroid disorders on lipid levels and metabolism. Med Clin North Am. 2012;96(2):269-81. doi: 10.1016/j.mcna.2012.01.012, PMID 22443975.

Cite this Article : Chaudhary PK, Verma RK, Singh PK. Evaluation of an Association of Thyroid Disorder and Dyslipidemia in Patients with Cardiovascular Disease: A Cross-sectional Study. J. Clin. Res. Applied Med. 2022;2(3):54-9.