International Journal of Science and Research (IJSR)
ISSN: 2319-7064
ResearchGate Impact Factor (2018): 0.28 | SJIF (2018): 7.426

Profile of Coronary Artery Disease in Patients of Hypothyroidism in a Tertiary Care Hospital of Central India: An Observational Study

Dr Pradeep Deshmukh[1], Dr Atul Singh Rajput[2*]

[1]DM DNB Cardiology, Associate Professor, Dept of Cardiology, GMC & SSH, Nagpur, Maharashtra, India, + 919823057346
[2]*Corresponding Author, DM cardiology, Senior Resident, Dept of Cardiology, GMC & SSH, Nagpur, Maharashtra, India, + 919168899991

Abstract: ***Hypothyroidism or Thyroid dysfunction to be more precise affects the cardiovascular system in varied forms. Acting through multiple octopus arms, hypothyroidism weakens the heart per se. The most dreaded mode of resilient injury is an accelerated atherosclerosis. [1] Other mechanisms being a dyslipidemic and procoagulant state, endothelial dysfunction and diastolic hypertension. [2][3][4] In this study, cardioascular profiling of patients with diagnosed hypothyroidism was undertaken and the pattern was analysed.Stable ischaemic heart disease was the most common presentation, with varying degrees of diastolic dysfunction being much frequent as compared to systolic dysfunction. Coronary pathology fell concordant with the clinical picture and a strong association was found between poorly controlled hypothyroidism (TSH > 20mIU/l) and the extent of coronary artery disease.***

Keywords: Hypothyroidism, accelerated atherosclerosis, diastolic dysfunction

1. Introduction

The prevalence of overt hypothyroidism is in the range of 1–2% and that of subclinical hypothyroidism is 4.0-20% of general population. [5] Commoner in females, the incidence increases with age. It has been implicated in cardiovascular morbidity as well as mortality in the form of accelerated atherosclerosis, direct negative inotropic action, rhythm disturbances and a thrombophilic state. Moreover, the occult adversaries have been also observed in patients with subclinical hypothyroidism. Some emerging risk factors for atherosclerosis like thyroid autoimmunity, increased C-reactive protein (CRP) level and hyperhomocysteinemia are also under intensive investigation to seek explanation of the relationship between hypothyroidism and heart disease. In this study, we evaluated the cardiovascular profile of 122 patients of diagnosed hypothyroidism admitted to the department of cardiology.

2. Materials and methods

Study was conducted in a tertiary care hospital of central India during September 2017 until November2018.After having obtained an ethical clearance from the Institute ethics committee and a written informed consent, all patients of diagnosed hypothyroidism. Cardiovascular evaluation was done in the form of history taking followed by proper clinical examination. This was followed by a baseline assessment in the form of a standard 12 lead electrocardiogram, echocardiogram (2D/3D).Diastolic dysfunction was further graded as per current guidelines (Fig 1) [6]. Systolic dysfunction was graded as in fig 2. [7]

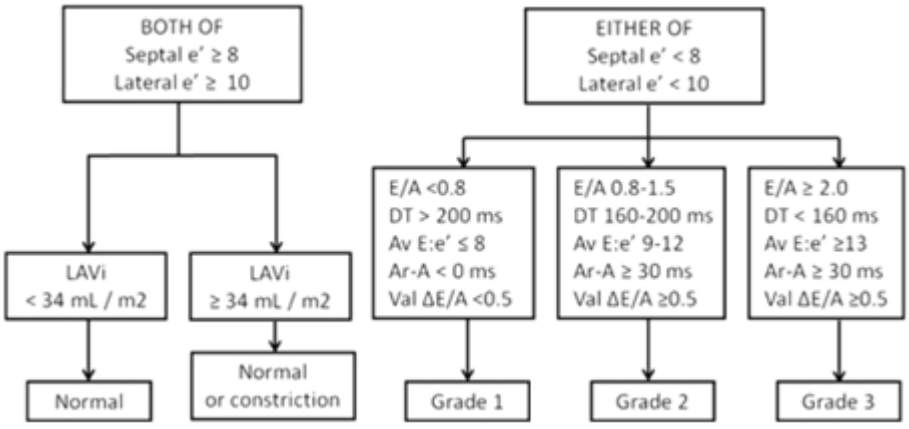

Figure 1: Echocardiographic classification of diastolic dysfunction

Grading of LV systolic dysfunction	Ejection fraction
Mild	41-50 %
Moderate	31-40 %
Severe	≤ 30 %

Figure 2: Grading of systolic dysfunction

Biochemical assessment which was inclusive of a routine renal function test, a complete hemogram, viral markers, fasting and post prandial sugar levels, random lipid levels was accomplished. Cardiac biomarkers for a pre invasive work up classification into stable ischaemic heart disease (SIHD), Non ST elevated acute coronary syndrome (NSTE ACS) and ST elevated myocardial infarction (STEMI) were

measured. The last step was a quantitative coronary angiogram (irrespective of indications) performed either by femoral or a radial route. Thyroid function test (T3, T4 and serum TSH) was done in all patients. Statistical analysis was done by calculating the Pearson product moment correlation coefficient and further interpreting it as per the Cauchy–Schwarz inequality model. [8]

3. Results

1) Baseline characteristics

Table 1: Baseline characteristics

	Parameter	Observations
Demographics	Sex	Females (107), Males (17)
	Mean Age	58years
Biochemical parameters	Hypertension	n=74 (124)
	LDL (normal < 130mg/dl)	128mg/dl (49 - 268)
	HDL (normal > 40 mg/dl - males, > 50mg/dl - females)	41mg/dl (20 - 57)
	TG (normal < 150mg/dl)	147mg/dl (55 - 304)
	Fasting Blood sugar	95mg/dl (63 - 267)
	Post prandial Blood sugar	127mg/dl (78 - 351)
	eGFR in ml/min (Cockroft Gault)	101 (43 - 125)
	Haemoglobin	12.7g/dl (8.4 - 16.2)

Close to 85% were females with the mean age in to being 58years.Hypertension was observed in 59% of patients. Low density lipoprotein (LDL) was raised in 51 patients with the mean values of 128mg/dl (range 49 to 268mg/dl).High density lipoprotein was reduced in 80 patients with the mean values of 41mg/dl and the lowest being 20mg/dl. Triglycerides were found to be elevated in 59 patients, with a mean of 147mg/dl and the highest levels being 304mg/dl.

2) TSH levels in study subjects

Table 2: TSH levels in study subjects

Levels (mIU/ml)	Number of patients (%)	Current Levothyroxine dose in micrograms (mean with range)
0.5 - 5	8 (7%)	-
05-Oct	87 (70%)	53 (12.5 - 150)
Oct-15	14 (12%)	68 (12.5 - 125)
15 - 20	4 (3%)	72 (37.5 - 125)
> 20	9 (8%)	47 (25 - 200)

Majority of patients had their TSH levels between 5-10mIU/l, with only a few having a euthyroid state. Extreme elevations in TSH were observed in 9 patients with the highest levels observed as 100mIU/l.The current dose of levothyroxine supplementation is shown in the third column.

3) Clinico-echocardiographic characteristics of patients:

Table 3: Clinico-echocardiographic characteristics of patients

	Stable ischaemic heart disease (SIHD)	Unstable angina (UA)	Non ST elevated myocardial infarction (NSTEMI)	ST elevated myocardial infarction (STEMI)
Number of patients (%)	61 (49%)	31 (26%)	11 (8%)	21 (17%)
Left ventricular (LV) function				
Mild LV dysfunction (systolic)	0	2 (1%)	2 (1%)	4 (3%)
Moderate LV dysfunction (systolic)	0	0	1	13 (13%)
Severe LV dysfunction (systolic)	0	0	0	4 (3%)
Normal LV function (systolic)	61 (49%)	29 (24%)	8 (5%)	0
Diastolic dysfunction	43 (34%)	21 (19%)	4 (3%)	21 (17%)

Stable ischaemic heart disease was diagnosed in around 50% of patients with around 34% as having NSTE - ACS.ST elevated myocardial infarction was diagnosed in 21 patients, with majority being inferior wall infarction patients. All of the patients with stable ischaemic heart disease had a normal left ventricular ejection fraction. Amongst the patients of

unstable angina, only 2 patients had mild LV dysfunction in the form of mild anterior wall hypokinesia. Of the patients admitted as NSTEMI, 3 patients had LV systolic dysfunction and all the patients of ST elevated myocardial infarction had some degree of LV dysfunction. Severely depressed ejection fraction was present in 4 patients of acute anterior wall myocardial infarction. Diastolic dysfunction even more common was found in around 70%, 70%, 3% and 17% of patients of the above respective categories.
Seven patients had mild pericardial effusion (not mentioned in the table).

Angiographic characteristics of study subjects

Table 4: Angiographic characteristics of study subjects

Vessel involvement	Stable ischaemic heart disease (SIHD) n=59	Unstable angina (UA) n=31	Non ST elevated myocardial infarction (NSTEMI) n=11	ST elevated myocardial infarction (STEMI) n=21
Left main coronary artery (LMCA)	4	2	0	2
Left anterior descending artery (LAD)	4	4	3	10
Left circumflex artery ((LCx)	6	4	1	7
Right coronary artery (RCA)	5	4	1	9
Significant double vessel disease	0	1	0	7
Significant triple vessel disease	3	0	0	3
Insignificant	44	19	6	2

Of the 59 patients of stable ischaemic heart disease, 4 patients each had an LMCA lesion, significant LAD disease. Six and 5 patients had LCx and RCA lesions respectively. Triple vessel disease was there in 3 patients and an insignificant coronary artery disease (CAD) was detected in around 44 patients. Amongst the patients of unstable angina, 2 patients had LMCA involvement, 4 patients each had LAD, LCx and RCA lesions. Significant double vessel disease was detected in 1 patient and 19 patients had insignificant CAD.In patients with NSTEMI, 3 patients had LAD disease and 6 patients had insignificant CAD. Two patients who presented with STEMI had significant LMCA disease and rest majority had multiple lesions in other vessels. Two post fibrinolysis patients had recanalised infarct related arteries.

4. Discussion

Hypothyroidism is characterized by a decrease in oxygen and substrate utilization by all the major organ systems of the body. As a result, the demands for cardiac output decrease; in addition, hypothyroidism directly alters cardiac function through changes in myocyte-specific gene expression. [9]

Pathophysiology — The major cardiovascular changes that occur in hypothyroidism include a decrease in cardiac output and cardiac contractility, a reduction in heart rate, and an increase in peripheral vascular resistance. [10]

There are also significant changes in modifiable atherosclerotic risk factors, including hypercholesterolemia, diastolic hypertension, carotid intimal media thickness, and endothelial derived relaxation factor (nitric oxide), which accompany overt hypothyroidism. [11] [12] [13]

Hypothyroidism and coronary artery disease
The most common cause of hypothyroidism in autoimmune. The development of anti thyroid peroxidase antibodies results in a systemic inflammatory state which leads on the coronary endothelial damage, thus accelerating atherosclerosis. [14] The predisposition of females to develop and autoimmune state owing the imbalance between cellular and innate immunity can be explained by this very concept of anti thyroid peroxidase antibodies. [15] In this study, the higher incidence of hypothyroidism in females lies concordant with this theory.

The occurrence of diastolic hypertension in hypothyroid subjects has been observed in around 30-40% of patients. The pathophysiologic basis stands the increased vascular stiffness and depressed cardiomyocyte function leading to a secondary rise in peripheral vascular resistance. [16] [17] [18] The peculiarity of hypertension observed in hypothyroidism lies in the reversibility following levothyroxine supplementation and achievement of a euthyroid state. In our study, hypertension was detected in more than half of the patients. The possible reason behind this could be a coexisting essential hypertension.

Thyroid hormone deficiency is accompanied by a reduced number of low density lipoprotein (LDL) receptors in the liver and a decreased LDL receptor activity, which leads to impaired LDL clearance. As a result, overt hypothyroidism is characterized by hypercholesterolemia and a marked increase in LDL-C.LDL-C is also increased in subclinical hypothyroidism. The lipid profile changes are reversible with thyroid hormone replacement. The dyslipidemia and the diastolic hypertension predispose the hypothyroidism patients to accelerated atherosclerosis and CAD. [19] [20] [21] [22] In our study, close to 40% of patients had hypercholesterolemia and in this subgroup, was the incidence of significant coronary artery disease, higher. In contrast to what was observed in the other studies regarding the elevation of HDL levels in hypothyroidism owing to decreased catabolism [23], our study didn't witness any elevation per se in HDL levels. Whether this was secondary to a dyslipidemic state because of some other confounding factor is not clear. High TG levels resulting from an inhibition of lipoprotein lipase activity might also contribute to increasing the cardiovascular risk in hypothyroid patients. [24] This was co-related well in our study too where we documented the highest TG levels of over 300mg/dl.

Majority of patients with hypothyroidism in our study had a clinical profile matching a stable ischaemic heart disease. Acute coronary syndrome in the form of unstable angina was the next common presentation followed by ST elevated myocardial infarction. Till date, there have not been many studies detailing the clinical cardiovascular profile of inpatients having pre existing hypothyroidism.

Echocardiography played novel role in assessment of patients in our study with a much higher incidence of diastolic dysfunction in hypothyroid subjects. Almost 2/3rd of patients in our study had evidence of diastolic dysfunction as detected by tissue doppler imaging and speckle tracking. The link between hypothyroidism and impaired myocardial relaxation falls in the grey zone. Triidothyronine leads to an increase in the speed of diastolic relaxation, which is caused by the more efficient pumping of the calcium ATPase of the sarcoplasmic reticulum. [25]

Amongst patients with thyroid dysfunction, the entity of sick euthyroid syndrome has been well studied.It is characterized by low T3 levels, normal T4 and TSH levels and increased reverse T3 levels; hence the name. These subgroups of patients have been found to have the most consistent prevalence of significant coronary artery disease as compared to other sub groups of patients with thyroid dysfunction. [26] The diagnosis of sick euthyroid syndrome couldnt be entertained in our study owing to the financial constraints. The pattern of coronary artery involvement in our study correlated with the clinical presentation of the patient. However, strikingly, of the 9 patients with higher TSH levels (>20mIU/l), 5 patients had significant coronary artery disease.

This proportional association of poorly controlled hypothyroidism and significant coronary artery disease warrants a large population analysis.

Though the study glances on some lesser studied coronary correlations in hypothyroidism its limited in the following ways. Multivariate analysis inclusive of other risk factors for coronary artery disease wasn't done. Along with this, a comparison was not done between the specific coronary anatomy in patients with significant lesions (LMCA > 50%, other vessels > 70%) and other patients without hypothyroidism visiting the cardiology department who have underwent a coronary angiogram. To conclude, a histopathological implication of hypothyroidism in causing coronary atherosclerosis could have been affirmed by a routine optical coherence tomography which was however the scope of the study centre.

References

[1] M. Coceani, G. Iervasi, A. Pingitore, C. Carpeggiani, A. L'Abbate.Thyroid hormone and coronary artery disease: from clinical correlations to prognostic implications, Clin Cardiol, 32 (2009), pp. 380-385
[2] A.R. Cappola, P.W. Ladenson .Hypothyroidism and atherosclerosis, J Clin Endocrinol Metab, 88 (2003), pp. 2438-2444
[3] O. Mayer Jr., J. Simon, J. Filipovsky, M. Plaskova, R. Pikner, Hypothyroidism in coronary heart disease and its relation to selected risk factors Vasc Health Risk Manage, 2 (2006), pp. 499-506
[4] I. Klein Endocrine disorders and cardiovascular disease D.P. Zipes, P. Libby, R. Bonow, E. Braunwald (Eds.), Braunwald's heart disease: a textbook of cardiovascular medicine (7th ed.), W.B. Saunders, Philadelphia (2005), pp. 2051-2065
[5] Becker C. Hypothyroidism and atherosclerotic heart disease: pathogenesis, medical management, and the role of coronary artery bypass surgery. Endocr Rev. 1985;6:432–40.
[6] Recommendations for the evaluation of left ventricular diastolic function by echocardiography. Nagueh SF, Appleton CP, Gillebert TC, Marino PN, Oh JK, Smiseth OA, Waggoner AD, Flachskampf FA, Pellikka PA, Evangelista A.J Am Soc Echocardiogr. 2009 Feb; 22 (2):107-33.
[7] Hypertension Journal, July september 2016;2 (3) 113-117
[8] SPSS tutorials;Pearson product magnitude correlation coefficient, https://libguides.library.kent.edu/SPSS/PearsonCorr
[9] Thyroid disease and the heart. AU Klein I, Danzi S Circulation. 2007;116 (15):1725.
[10] Impaired endothelium-dependent vasodilatation in subclinical hypothyroidism: beneficial effect of levothyroxine therapy.Taddei S, Caraccio N, Virdis A, Dardano A, Versari D, Ghiadoni L, Salvetti A, Ferrannini E, Monzani F J Clin Endocrinol Metab. 2003;88 (8):3731.
[11] Thyroid hormone and the cardiovascular system.AU Klein I, Ojamaa K SO N Engl J Med. 2001;344 (7):501.
[12] A correlation of clinical and hemodynamic studies in patients with hypothyroidism. Graettinger JS J Clin Invest. 1958;37 (4):502.
[13] Impaired endothelium-dependent vasodilatation in subclinical hypothyroidism: beneficial effect of levothyroxine therapy.Taddei S, Caraccio N, Virdis A, Dardano A, Versari D, Ghiadoni L, Salvetti A, Ferrannini E, Monzani F J Clin Endocrinol Metab. 2003;88 (8):3731.
[14] Asymptomatic autoimmune thyroiditis and coronary heart-disease. Cross-sectional and prospective studies.Bastenie PA, Vanhaelst L, Golstein J, Smets P.Lancet. 1977 Jul 23;2 (8030):155-8.
[15] Lancet. 1972 Apr 8;1 (7754):785-6. Symptomless autoimmune thyroiditis in coronary heart-disease. Heinonen OP, Gordin A, Aho K, Punsar S, Pyörälä K, Puro K. Lancet. 1972 Apr 8;1 (7754):785-6.
[16] Effects of thyroid function on blood pressure. Recognition of hypothyroid hypertension.D H Streeten, G H AndersonJr, T Howland, R Chiang, and H Smulyan Originally published1 Jan 1988Hypertension. 1988;11:78–83
[17] A. R. Cappola and P. W. Ladenson, "Hypothyroidism and atherosclerosis, " The Journal of Clinical Endocrinology & Metabolism, vol. 88, no. 6, pp. 2438–2444, 2003
[18] C.-H. Jung, E.-J. Rhee, H.-S. Shin et al., "Higher serum free thyroxine levels are associated with coronary artery disease, " Endocrine Journal, vol. 55, no. 5, pp. 819–826, 2008
[19] K. H. Yun, M. H. Jeong, S. K. Oh et al., "Relationship of thyroid stimulating hormone with coronary atherosclerosis in angina patients, " International Journal of Cardiology, vol. 122, no. 1, pp. 56–60, 2007.
[20] B. O. Åsvold, T. Bjøro, C. Platou, and L. J. Vatten, "Thyroid function and the risk of coronary heart disease: 12-year follow-up of the HUNT Study in Nor-

way, ” Clinical Endocrinology, vol. 77, no. 6, pp. 911–917, 2012

[21] G. G. Gensini, “A more meaningful scoring system for determining the severity of coronary heart disease, ” The American Journal of Cardiology, vol. 51, no. 3, p. 606, 1983.

[22] W. T. Friedewald, R. I. Levy, and D. S. Fredrickson, “Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge, ” Clinical Chemistry, vol. 18, no. 6, pp. 499–502, 1972.

[23] Thyroid function and lipid subparticle sizes in patients with short-term hypothyroidism and a population-based cohort.Pearce EN, Wilson PW, Yang Q, Vasan RS, Braverman LE J Clin Endocrinol Metab. 2008 Mar; 93 (3):888-94.

[24] Plasma triglyceride metabolism in thyroid disease. Nikkilä EA, Kekki M J Clin Invest. 1972 Aug; 51 (8):2103-14.

[25] Endocr Rev. 2005 Aug;26 (5):704-28. Epub 2005 Jan 4.Thyroid hormone action in the heart. Kahaly GJ1, Dillmann WH.

[26] Effects of thyroid dysfunction on the severity of coronary artery lesions and its prognosis Min-fuBai MDaChuan-Journal of Cardiology Volume 64, Issue 6, December 2014, Pages 496-500