Research Paper Medical Science

A Study of Pericardial Effusion in Patients of Hypothyroidism At Government Medical College Amritsar

Dr Gian Chand	Associate Professor, Department of Medicine, Government Medical College, Amritsar
Dr Ajay Chhabra	Assistant Professor, Department of Medicine, Government Medical College, Amritsar
Dr Shanker Deep Sondhi	Post-graduate Student, Department of Medicine, Government Medical College, Amritsar
Dr Santokh Singh	Professor, Department of Medicine, Government Medical College, Amritsar

ABSTRACT

Problem statement: Hypothyroidism is one of the common hypoendocrine disorders. Besides overt disease because of lack of routine screening and patient awareness many patients of subclinical disease remain undiagnosed and hence untreated. Hypothyroidism affects a number of organs and has deleterious effects on cardiovascular system. Pericardial involvement in the form of pericardial effusion is an important observation. This study plans to ascertain the prevalence of pericardial effusion in patients of hypothyroidism.

Aims and objectives: To study the prevalence of pericardial effusion in hypothyroid patients and to correlate it with TSH levels.

Materials and methods: This study was conducted on 50 patients of hypothyroidism at Government Medical College, Amritsar. Every patient was subjected to trans-thoracic echocardiography and TSH levels were done. Data thus derived was statistically analyzed.

Results: A total of 7 patients (14%) were having pericardial effusion, 6 of these were females and 1 was male. Serum T3 and T4 levels were lower and serum TSH levels were higher in hypothyroid patients with pericardial effusion as compared to those patients who were not having pericardial effusion. The data obtained from our study indicated that association between TSH or T4 levels and pericardial effusion was stronger than the one that existed between T3 levels and pericardial effusion.

KEYWORDS : pericardial effusion, hypothyroidism, thyroid stimulating hormone(TSH)

Introduction

Hypothyroidism is a clinical syndrome resulting from decreased production of thyroid hormones. Manifestations of hypothyroidism are variable and proportionate to both the degree and duration of thyroid hormone deficiency as well as of onset. Function of thyroid gland is directed to the secretion of T3 & T4 hormones that influence a diversity of metabolic processes. Thyroid hormones influence the growth & maturation of tissues, cell respiration, total energy expenditure and the turnover of essentially all substrates, vitamins and hormones including the thyroid hormones. Diseases of the thyroid are manifested by qualitative or quantitative alterations in hormone secretions or enlargement of the thyroid or both. Insufficient hormone secretions results in hypothyroidism or myxedema, in which decreased caloric expenditure i.e. hypo metabolism is a principle feature.[1]

The prevalence of hypothyroidism in the developed world is about 4-5%. The prevalence of subclinical hypothyroidism in the developed world is about 4-15%.[2,3,4] The prevalence of hypothyroidism is high, affecting approximately one in every 10 Indians.[5] There is often a delay in diagnosis which is attributable to lack of awareness and ineffective screening programs. Among adult people in India, the prevalence of hypothyroidism has been recently studied. In a population-based study done in Cochin on 971 adult subjects, the prevalence of hypothyroidism was 3.9%. The prevalence of subclinical hypothyroidism was also high in this study, the value being 9.4%. In women, prevalence was higher at 11.4%, when compared with men, in whom the prevalence was 6.2%. The prevalence of subclinical hypothyroidism increased with age. About 53% of subjects with subclinical hypothyroidism were positive for anti-TPO antibodies.[6]

Cardiovascular system is an important target of thyroid hormone action and is sensitive to slight variation in circulating thyroid hormone levels. The thyroid hormones, especially T3 regulates cardiac inotropy and chronotropy though a variety of direct and indirect mechanisms.[7]

The changes seen in hypothyroidism in cardiovascular hemodynamics include increased vascular resistance, decreased cardiac output, diastolic hypertension, bradycardia, decreased cardiac contractility and decreased blood volume. Pericardial effusion is a common abnormality in cases of hypothyroidism. Pericardial effusion is a constant, an early and major factor in the syndrome of myxedema heart. However, pericardial effusion in myxedema does not embarrass the cardiac function and had lack of tamponade effect.[8,9,10] The low incidence of cardiac tamponade due to myxedema pericardial effusion may be due to slow fluid accumulation and pericardial distensibility.[11] However in case of large accumulation of pericardial effusion, features of cardiac tamponade may be seen.[11,12] Cardiomegaly on chest X-ray and low voltage ECG are not reliable indicators of pericardial effusion. Transthoracic echocardiography is a sensitive method for the detection of pericardial effusion and can detect as little as 20ml of pericardial fluid.[13] Therefore echocardiography is employed as method of choice for diagnosing pericardial effusion. In the light of the above facts, it is very obvious that, hypothyroidism which is a very common disease, has important cardiovascular implications.

CARDIOVASCULAR EFFECTS

Hypothyroidism has a profound effect on cardiovascular system. This may be due to altered lipid metabolism or due to direct effect of thyroid hormones on heart or due to indirect effect on cardiovascular system due to change in hemodynamic parameters.

Myxedema heart as an entity was first recognised by Zondek in 1918 when he reported four unusual cases of myxedema in which he demonstrated cardiac enlargement along with bradycardia and alteration in the electrocardiogram. A remarkable decrease in transverse diameter of the heart and return of the ECG to its normal contour occurred after the administration of thyroid extract.[15] It was seen that in myxedema patients in congestive heart failure, the patient showed rapid clearance of signs and symptoms of congestive heart failure with thyroid medication. In one of the cases, decrease in transverse

diameter of heart from 19cm to 12.7cm occurred. After the withdrawal of therapy, heart again dilated and signs of myxedema reappeared.[16]

Meens et al in a later study concluded that 'Myxedema heart' is not a disease of heart but a manifestation of a thyroid disease termed myxedema.[17] Myxedema heart was described, as a great increase in the size of cardiac dullness on percussion, faintness of the heart sounds, diminished cardiac output, reduced voltage on electrocardiogram especially of T waves, these may be flattened or inverted and complete reversibility of these changes to normal on treatment with thyroid hormones.[18] Myxedema heart may be due to increase in direct effect of thyroid hormones on the cardiac cells, or due to indirect effect though decrease in peripheral oxygen consumption, changes in hemodynamic parameters and vascular resistance. Myocardium shows accumulation of mucopolysaccharides disrupting myocardial continuity and integrity. Histopathological evidence of pericardial damage is seen.[18] Douglas et al described necropsies of ten hypothyroid patients. Myocardial cells containing bluish and PAS positive substances were seen. Basophilic degeneration of the myocardium was present in extreme degree of hypothyroid disease.[19]

ECG IN HYPOTHYROIDISM

ECG changes in hypothyroidism consists of sinus bradycardia, low voltage QRS complexes and the T wave changes. Meens et al reported the occurrence of ECG evidence of hypothyroid heart in 70% to 80% cases of established hypothyroidism.[17] ECG changes in heart are largely, if not completely, be caused by the fluid in pericardial sac and myocardial edema is responsible for some of the changes. ECG changes observed in hypothyroidism other than sinus bradycardia include prolonged QT interval.[20] Hardisty et al found ECG changes only in the minority of the hypothyroid patients, some of these changes occurred in cases without pericardial effusion indicating that free pericardial fluid is not essential component in their pathogenesis.

ECHO IN HYPOTHYROIDISM

Echocardiography is a non-invasive mean of assessment of cardiac parameters. It is a sensitive method for the detection of pericardial effusion.[22] Kerber et al in examined 30 hypothyroid patients by using echocardiography and found evidence of pericardial effusion in 10 i.e 33% patients. In their study no significant difference was seen in serum levels of thyroxine and TSH in patients with or without effusions.[23] Santos et al described reversible cardiomyopathy resembling hypertrophic obstructive cardiomyopathy in hypothyroid patients. They examined 19 untreated patients of hypothyroidism by echocardiography and found end diastolic interventricular septal thickness (IVSD) to be increased, with mean interventricular septal thickness (end diastolic) of 15.4mm. End diastolic left ventricular posterior wall thickness (LVPW) remained within normal limits for all patients. Mean left ventricular posterior wall thickness (end diastolic) was 10 mm. Asymmetrical septal hypertrophy (ASH) defined as ratio of IVS(ED) to LVPW equal to or greater than 1.3 was found in 17 out of 19 patients. It was seen that IVS thickness decreased after giving L- thyroxine.[24] Pericardial effusion has been reported in 0-80% of patients of hypothyroidism.[21,22,25] LVPW(ED) was found to be greater hypothyroid patients as compared to normal persons but it was within the normal range. Mean LVPW(ED) in hypothyroid group was 9mm. IVS(ED) thickness was found to be within normal range in 12 hypothyroid patients while it was increased in remaining 3 patients. Left ventricular internal dimension end diastolic [LVID(ED)] and left ventricular internal dimension end systolic [LVID(ES)] were found to be normal with mean end diastolic left ventricular internal dimension [LVID(ED)] of 42mm and mean end systolic left ventricular internal dimension[LVID(ES)] of 27mm in hypothyroid patients.[25] Ratio between IVS(ED) and LVPW (ED) was found to be increased.[24,25] Other echocardiographic findings detected by them were thickened wall of right ventricle, decreased wall motion of interventricular septum, decreased wall motion of right ventricular and decreased global function of right ventricle. These findings were reversed by L-thyroxine therapy. IVS thickness was significantly increased in severe overt hypothyroidism. Left ventricular posterior wall thickness was increased in overt hypothyroid group only. Pericardial effusion and diastolic dysfunction was detected only in overt hypothyroid patients.[26] Cardiac failure in uncomplicated hypothyroidism is uncommon, however on the other hand in the presence of coincidental cardiac diseases e.g coronary artery disease and hypertension, myxedema heart undoubtedly precipitate heart failure too. It may result from prolonged diastolic relaxation, slowed contraction velocity during systole and decreased force development. The hemodynamic response to exercise is normal in hypothyroid patients. Pericardial effusion is a common abnormality in hypothyroidism.[27] Pericardial effusion is a constant, an early and major factor in the syndrome of myxedema heart wall motion of interventricular septum, decreased wall motion of right ventricular and decreased global function of right ventricle. These findings were reversed by L-thyroxine therapy.[28] Parving et al concluded that increased capillary pemeability, impaired lymphatic drainage and enhanced avidity for salt and water may be responsible for pericardial effusion in hypothyroidism.[29] Antonis reported cases of hypothyroid patient presenting with features of cardiac tamponade.[30]

MATERIAL AND METHODS

A total of fifty cases of either sex, above the age of 14 years, suspected to be having hypothyroidism, either attending the outdoor patient department or admitted in Government Medical College, Amritsar were selected for the study. Informed consent was taken from these patients. A thorough history was taken and clinical examination was done. Diagnosis of hypothyroidism was confirmed by T3, T4 and TSH. Patients with other comorbidities, congenital heart disease, rheumatic heart disease and pulmonary disease were excluded from the study. Every patient of study was subjected to transthoracic echocardiography and examined for the evidence of pericardial effusion. Results were be analysed statistically to see association between levels of thyroid function and pericardial effusion.

OBSERVATIONS

Out of 50 total patients 45 were females (90%) and 5 were males (10%). Majority of the patients in this study comprised of females. The total number of patients in l4-30 years age group were 5, those in 3l-40 years age group were l4, in the 41-50 years age group were 18, in the 51-60 years age group were 8 and only 5 patients in the age group of more than 60 years. The mean age of patients in the study was 54.6 years for males and 44.31 years in females, clearly pointing to the earlier onset of hypothyroidism in females and higher risk in females.

PERICARDIAL EFFUSION

The incidence of pericardial effusion in hypothyroid patients in the study was 16%, showing that hypothyroid state is a risk for having pericardial effusion. Of the total 5 male patients only 1 (20%) had pericardial effusion whereas out of the 45 female patients only 6 (13.3%) had pericardial effusion. Further as seen from the sex wise distribution, pericardial effusion was more common in females than males (85.7% vs 14.3%), though males had higher rates of suffering from pericardial effusion (20% vs 13.3 %).

Pericardial Effusion	Mean T_3 [ng/dl]	Mean T_4 [µg/dl]	Mean TSH [µIU/L]
Present	66.42 + 20.96	2.67 + 2.11	67.22 + 26.84
Absent	84.95 + 17.45	6.74 +1.06	13.72 + 4.69
Variables	't'	'p'	Inference
T_3 and pericardial effusion	2.667	0.010	Significant
T_4 and pericardial effusion	5.295	<0.001	Highly significant
TSH and pericardial effusion	3.265	<0.001	Highly significant

Hypothyroid patients with pericardial effusion in this study group had a higher mean TSH values as compared to those without pericardial effusion and lower the values of T3 and T4 more were the chances that patient could have of pericardial effusion i.e value of TSH was directly proportional whereas values of T3 and T4 had an inverse relation with pericardial effusion. The p-value for the T3 and pericardial effusion was less than 0.05, thus this relationship was significant. The p-value for T4 and pericardial effusion was less than 0.001 showing a highly significant relationship. Similarly the p - value for TSH and pericardial effusion was less than 0.001 hence indicating a highly significant relationship. **[Table 1]**

DISCUSSION

The mean age of patients who were studied was 45.34 years. The mean age of female patients was 44.3 years and the mean age of male patients was 54.6 years so it can be inferred that hypothyroidism

is mostly a disease of middle age groups. The mean age of female patients was lower than that of male patients indicating the early onset of disease in females. The mean age of patients in group with pericardial effusion was 45.75 years and in second group of patients without pericardial effusion was 45.26 years.

A total of 50 patients were studied among whom 7 patients (14%) were found to have pericardial effusion as detected by trans thoracic echocardiography. Out of these 7 patients , 6 were female and 1 was male. Thus majority of total patients i.e. 85.7% were females who had pericardial effusion. Males accounted for 14.3% of total cases only.

The patients without pericardial effusion had TSH levels 13.72±4.69 IU/L and those with pericardial effusion had TSH levels 67.22 ±26.84 IU/L, supporting the evidence that higher the TSH levels are, severer the hypothysoidism and more is the risk of pericardial effusion. The p value for TSH and pericardial effusion was <0.001, indicating that it was highly significant. The patients without pericardial effusion had T3 levels 84.95±17.45 and those with pericardial effusion had T3 levels 66.42 ±20.96, supporting the evidence that the patients who had pericardial effusion were having lower levels of T3 hormone. The p value for T3 and pericardial effusion was <0.05. indicating that it was significant. Patients in whom pericardial effusion was not detected had T4 levels 6.74±2.11 and those with pericardial effusion had T4 levels 2.67 ±1.06, supporting the evidence that the patients who had pericardial effusion were having lower levels of T4 hormone. The p value for T4 and pericardial effusion was <0.001, indicating that it was highly significant. It was clear from the above discussion that there was a direct relation between occurrence of pericardial effusion and levels of TSH and an inverse relation between occurrence of pericardial effusion and levels of T3 and T4. The p-value we obtained from our data suggested that TSH and T4 levels had a stronger relationship with occurrence of pericardial effusion as compared to association between T3 levels and pericardial effusion. Several other studies conducted in past were showing consistent findings. Crowley et al, reported 9 out of 15 hypothyroid patients studied by him had pericardial effusion.[31] Hardisty et al examined 39 patients with untreated hypothyroidism using echocardiography and found out that pericardial effusion was present in 12 patients who had severer hypothyroidism.[21] Khaleeli et al detected pericardial effusion in 5 out of 6 consecutive untreated patients with severe hypothyroidism.[22] Kerber et al examined 33 hypothyroid patients and found echocardiographic evidence of pericardial effusion in 10 patients i.e 33% of total patients.[23] Verma et al conducted a study on 44 patients of hypothyroidism, dividing them into two groups of 22 patients each with overt hypothyroidism and subclinical hypothyroidism respectively. Pericardial effusion was found in patients with overt hypothyroidism only, thus with severer hypothyroidism.[26] Rawat and Satyal conducted a study on 20 hypothyroid patients (12 female and 8 male) and found out a striking correlation between severity of disease i.e. hypothyroidism and pericardial effusion. Our study is consistent with the above mentioned studies further validating that the higher the TSH levels, the higher is the incidence of pericardial effusion.[32]

It was seen that mean heart rate in hypothyroid patients without pericardial effusion was 77 ± 4.35 and in cases with pericardial effusion was 64.5 ± 2.07.Thus in patients with pericardial effusion the heart rate was lower than in patients without pericardial effusion. The p value was found out to be less than 0.001, suggesting it to be highly significant. Klen and Ojama conducted a study on hypothyroid patients and found out that the heart rate was between 60 to 80. Bradycardia and decreased stroke volume both account for decreased cardiac output in patients of hypothyroidism.[33] Kral et al studied 19 patients of hypothyroidism and documented decreased cardiac index in these patients which was reversible with thyroid homone replacement.[34] In the study done by Rawat and Satyal, mean heart rate was 58 beats per minute in untreated patients as compared to 69 beats per minute in treated patients. These findings were in accordance with the above study hence it could be concluded that heat rate decreases with increase in TSH levels.

REFERENCES:

1. Surks MI, Ocampo E. Subclinical thyroid disease. *Am J Med* 1996; 100: 217-223.
2. 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;87:489–99.
3. Hoogendoorn EH, Hermus AR, de Vegt F, Ross HA, Verbeek AL, Kiemency LA, et al. Thyroid function and prevalence of anti-thyroperoxidase antibodies in a population with borderline sufficient iodine intake: Influences of age and sex. Clin Chem. 2006;52:104–11.
4. Bemben DA, Hamm RM, Morgan L, Winn P, Davis A, Barton E. Thyroid disease in the elderly. Part 2. Predictability of subclinical hypothyroidism. J Fam Pract. 1994;38:583–8.
5. Unnikrishnan AG, Kalra S, Sahay RK, Bantwal G, John M, Tewari N. Prevalence of hypothyroidism in adults: An epidemiological study in eight cities of India. *Indian Journal of Endocrinology and Metabolism*. 2013;17(4):647-652. doi:10.4103/2230-8210.113755.
6. Usha Menon V, Sundaram KR, Unnikrishnan AG et al. High prevalence of undetected thyroid disorders in an iodine sufficient adult south Indian population. J Indian Med Assoc 2009; 107: 72-7.
7. Levy GS, Klein I. Catecholamine thyroid hormone interactions and the cardiovascular manifestations of hyperthyroidism. Am J Med 1990; 88 : 642-6.
8. Wartofsky L, Burman KD. Alterations in thyroid function in patients with systemic illness: the "euthyroid sick syndrome". Endocr Rev. 1982 Spring;3(2):164–217.
9. Ridgway EC, Ladenson PW, Cooper DS, Daniels GH, Francis GS, Maloof F. Cardiac function in mild and severe primary hypothyroidism. Life Sci. 1982 Feb 15;30(7-8):651–658.
10. Buccino RA, Spann JF, Jr, Pool PE, Sonnenblick EH, Braunwald E. Influence of the thyroid state on the intrinsic contractile properties and energy stores of the myocardium. J Clin Invest. 1967 Oct;46(10):1669–1682.
11. Smolar EN, Rubin J et al: Cardiac tamponade in primary myxedema and review of literature. American Journal Med. Science 1976; 272: 345.
12. Bermett JM, Steyn AF: The heart and hypothyroidism. South Afr. Medical Jouma11983; 63: 564.
13. Kerber RE, Sherman B et al: Echocardiographic evaluation of pericardial effusion in myxedema. Circulation 1975; 52: 823.
14. Horowitz MS, Schultz CS, Harrison D et a1: Sensitivity and specificity of echocardiographic diagnosis of pericardial effusion. Circulation 1974; 50: 239.
15. Zondek H. Das myxodemherz (Article in German). Munch Med Wschr 1918;65:1180–3
16. Forfar JC, Wathen CG et al. Left ventricular perfomance in subclinical hypothyroidism. Quarterly Journal Medicine 1985; 57: 857.
17. Meens JH, Lerman J, Clark RJ et al. Heart in myxedema: ECG and roentgen- ray measurement before and after therapy. Armal Internal Medicine 1933; 6: 1251.
18. Fahr G. Myxedema heart. J Am Med Assoc 1925;84:345–9
19. Douglass RC, Jacobson SD. Pathologic changes in adult myxedema: survey of 10 necropsies. J Clin Endocrinol Metab. 1957 Nov;17(11):1354–1364.
20. Surawicz B, Mangiardi ML et al. Electrocardiographic changes in endocrine and metabolic disorders. Clinical Electrocardiographic Correlations. Philadelphia FA Davis Co (Publishers) 1977; 243.
21. Hardisty CA, Naik DR, Munro DS. Pericardial effusion in hypothyroidism. Clin Endocrinol (Oxf) 1980;13:349–54
22. Khaleeli AA, Memon N et al. Factors affecting resolution of pericardial effusion in prinary hypothyroidism. Post Graduate Medical Journal I982; 58: 1073.
23. Kerber RE, Sherman B et al. Echocardiographic evaluation of pericardial effusion in myxedema. Circulation 1975; 52: 823.
24. Santos AD, Miller P, Mathew K, et al. Echocardiographic characterisation of reversible cardiomyopathy of hypothyroidism. American Joumal Medicine I980; 68: 675.
25. Vora J, O'Mally B, Peterson S et al. Reversible abnormality of myocardial function in hypothyroidism. Journal Clinical Endocrinology Metabolism 1985: 61:269.
26. Verma R, Jain AK, Ghose T. Heart in hypothyroidism - an echocardiographic study. JAPI. 1996;44:390–392.
27. Kabadi UM, Kumar SP. Pericardial effusion in primary hypothyroidism. Am Heart J 1990;120(6 pt 1):1393–5
28. Shenoy MM, Goldman JM. Hypothyroid cardiomyopathy: echocardiographic documentation of reversibility. Am J Med Sci. 1987 Jul;294(1):1-9.
29. Parving HH, Hansen JM, Nielsen SL, Rossing N, Munck O and Lassen A. Mechanism of edema formation in myxedema-increased protein extravasation and relatively slow lymphatic drainage. New England Journal Medicine. 1979; 301(9):460-5.
30. Antonis S, Phillip V, Roman in et al. Hypothyroid cardiac tamponade. Archives Internal Medicine 1987; 147: 1167.
31. Crowley WF, Ridgway EC et al. Non-invasive evaluation of cardiac function in hypothyroidism. New England Journal Medicine 1977; 298: 1.
32. Rawat B, Satyal A. An echocardiographic study of cardiac changes in hypothyroidism and the response to treatment. Kathmandu Univ Med J (KUMJ). 2004 Jul-Sep;2(3):182-7.
33. Klen I and Ojaama K. Thyroid Hormone and Cardiovascular system. NEJM 2001; 344: 501-9.
34. Kral J, Hradec JL. Heart in thyroid disease. Corvasa 1992;34(2):108