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Research Article

A CROSS SECTIONAL STUDY OF THYROID STATUS IN PATIENTS OF DILATED CARDIOMYOPATHY

Anil kumar Yadav, Parinita Ranjit, Kaushik Das, Sujoy Sarkar*, Saumik Datta and Partha Pratim Mukherje

Calcutta National Medical College & Hospital

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A B S T R A C T

Dilated cardiomyopathy (DCM) is one of the common form of cardiomyopathy and major cause of morbidity and mortality worldwide. Thyroid hormone plays a major role in cardiac function. **Material & method:** The cross sectional study was conducted at the department of General medicine, Calcutta National Medical College & Hospital in collaboration with department of cardiology. 100 patients of dilated cardiomyopathy were studied after matching inclusion and exclusion criteria from outdoor and inpatients over period of 18 months from January 2019 to June 2020.

Result: In our study 44% patients were male and 56% female. 15% patients were diabetic. 53% were in NYHA grade IV heart failure. TSH ranges from 0.1 uIU/ml to 16 uIU/ml. Mean TSH was 3.281 ± 2.681 uIU/ml. The mean LVEF in subclinical hypothyroid, hypothyroid, euthyroid and subclinical hyperthyroid were 31.50 %, 28.00%, 32.18% & 29.50 % respectively. In our study, on comparing left ventricular ejection fraction (%) with TSH (uIU/ml) in all patients as well as euthyroid, the scatter plot showed negative correlation implying that with increasing values of TSH, the left ventricular ejection fraction showed a decreasing trend. Similarly, on comparing left ventricular ejection fraction (%) with fT4 (ng/dl) in all studied patients as well as euthyroid, the scatter plot showed positive correlation, that a higher fT4 (ng/dl) was associated with higher ejection fraction, similarly lower fT4 (ng/dl) was associated with lower ejection fraction. **Conclusion:** An increase in thyroid dysfunction was found in patients who had a longer duration of dilated cardiomyopathy. Patients with diabetes as a comorbidity were found to present with more severe heart failure (NYHA class IV). A statistically significant positive correlation between left ventricular ejection fraction (LVEF) and fT4 (ng/dl) was observed even in the euthyroid population.

INTRODUCTION

Dilated cardiomyopathy (DCM) is characterized by a dilated left ventricle with systolic dysfunction that is not caused by ischemic, valvular, congenital heart diseases, or severe hypertension [1]. DCM is the most common form of cardiomyopathy and is responsible for approximately 10,000 deaths and 46,000 hospitalizations each year. Cardiomyopathy accounts for 5-10 % of heart failure. The lifetime incidence of DCM is about 30 cases per 100,000 persons. [2]

Dilation of the cardiac chambers and varying degrees of hypertrophy is the anatomical hallmark which happens secondary to progression of any of the process involving etiologies which affect the myocardium; the ensuing dilation is directly related to neurohormonal activation. [3] Thyroid hormones can cause both physiological and pathological myocardial hypertrophy. In its initial phases, cardiac hypertrophy presents a physiological process which includes increased expression of adenosine triphosphatase (ATP) and sarcoplasmic reticulum Ca^{2+} ($SERCa^{2+}$) and decreased expression of MHCβ. T_3-activated TR (thyroid receptor) also regulates cation transport. Intracellular Ca^{2+} ($[Ca^{2+}]_i$) is important for both normal systolic and diastolic function. While T_3 promotes increases in $SERCa^{2+}$ ATPase and the ryanodine channel, it is also found to decrease phosphorylation/activation of phospholamban (which inhibits the $SERCa^{2+}$ pump). In cardiomyocytes, most of the $[Ca^{2+}]_i$ lowering is brought about by pumping $[Ca^{2+}]_i$ into the sarcoplasmic reticulum by the $SERCa^{2+}$ pump. The speed of diastolic relaxation in the heart is significantly influenced by lowering of the $[Ca^{2+}]_i$ levels. Animal models of hypothyroidism show that the level and activity of the $SERCa^{2+}$ pump is markedly decreased while that of inhibitory phospholamban increased, which is probably responsible for decrease in the rate of diastolic relaxation. Further, the ryanodine receptor is also decreased in hypothyroid hearts. Finally, TRα receptors and the β_1 adrenergic receptors are negatively and positively regulated by T_3 respectively; this promotes optimal modulation of T_3-activated TR inotropic and chronotropic effects.[4,5]

Drugs used in cardiac diseases also interact with thyroid hormones. Amiodarone is a potent anti-arrhythmic drug that is used to treat ventricular and supraventricular tachyarrhythmias. Each 200-mg tablet is estimated to contain about 75 mg of organic iodide, 8-17% of which is released as free iodide, which may lead to either amiodarone induced thyrotoxicosis or Amiodaron induced hypothyroidism. Diuretics used in management of heart failure, particularly thiazide, may decrease serum protein-bound iodine levels .[6,7]

AIMS AND OBJECTIVES

To find out the prevalence of hypothyroidism, subclinical hypothyroidism, hyperthyroidism and subclinical hyperthyroidism in DCM patients.

To correlate thyroid status among patients with DCM with higher ejectionfraction versus lower ejection fraction.
To correlate thyroid status among DCM patients across different NYHAclasses.

MATERIALS & METHODS

The cross sectional study was conducted at the department of General medicine, Calcutta national medical college & hospital in collaboration with department of cardiology. 100 patients of dilated cardiomyopathy were recruited from outdoor and inpatients over period of 18 months from January 2019 to June 2020.

Categorical variables were expressed as number of patients and percentage of patients and these were compared across the groups using Pearson's Chi Square test for Independence of Attributes or using Fisher's Exact Test, as appropriate. Continuous variables were expressed as mean, median and standard deviation and compared across the groups using Kruskal Wallis Test. The statistical software SPSS version 20 was used for the analysis. An alpha level of 5% was taken, i.e. if any p value was less than 0.05 it was considered as significant

Inclusion Criteria

All Patients diagnosed to have Dilated Cardiomyopathy.

Exclusion Criteria

Patients who were hemodynamically unstable.
Patients who had chronic liver diseases
Patients with end stage renal diseases
History of alcohol intake
Drug history of levothyroxine, methimazole, carbimazole, propylthiouracil, phenytoin, isoniazid, amiodarone, chemotherapy, radiotherapy, glucocorticoids, Drug addicts
Patients with hypothyroid, Graves' disease, multinodular goiter, thyroiditis
Patients with history of radioiodine treatment and thyroid surgery.
Multiple pituitary hormone diseases

RESULT AND ANALYSIS

In our study population, out of 100 patients, 44 (44%) were male and 56 (56%) were female; 25% of the study population belonged to the age group of 40-50 years, 47% belonged to age group of 51-60 years and 28% to the age group of 61-70 years. Mean age at presentation was 56.33 + 7.176 years In the study, out of 100 patients, 15 (15%) had a history of diabetes mellitus and 85% were non-diabetic. 11% of the study population presented with NYHA class II heart failure (HF), 36 (36%) presented with NYHA class III and the rest (53%) presented with class IV.

Among the 100 patients studied, 2 patients were found to be hypothyroid, 12 patients were found to have subclinical hypothyroidism, 78 were euthyroid and 8 patients were found to have subclinical hyperthyroidism.

In our study, the mean age of presentation of DCM patients having hypothyroid, subclinical hypothyroid, euthyroid and subclinical hyperthyroid were 55 years, 57.58 years, 55.97 years & 58.25 years respectively. 8 (66.67%) out 12 subclinical hypothyroid, 2 (100%) of 2 hypothyroid and 5 out of 8 (62.5%) subclinical hyperthyroid patients were female. Among 12 Subclinical Hypothyroid patients, 5 (41.67%) presented with NYHA class III & 7 (58.33%)with NYHA class IV; both the patients with hypothyroidism (2 patients) presented with NYHA grade IV; out of 78 euthyroid patients, 10 (12.82 %) presented with NYHA class II HF, 29 (37.18%) presented with NYHA class III & 39 (50%) presented with class IV. Among 8 patients with subclinicalhyperthyroidism, 1 (12.5 %) presented with NYHA class II, 2 (25%) presented with NYHA class III and 5 (62.50%) presented with NYHA class IV.

Among 15 diabetic patients, 14 (93.33%) presented with NYHA class IV and among the rest 85 patients, 39 (45.88%) patients presented with NYHA class IV,35 (41.18%) presented with NYHA class III and 11 (12.94%) presented with NYHA class II HF.

In our study, value of TSH ranges from 0.1 uIU/ml to 16 uIU/ml. Mean TSH was 3.281 ± 2.681 uIU/ml. Among various thyroid disorder patients, the mean TSH were 7.96 uIU/ml, 14.00 uIU/ml, 2.06 uIU/ml & 0.19 uIU/ml in subclinical hypothyroid, hypothyroid, euthyroid and subclinical hyperthyroidism respectively. The value of fT_4 ranges from 0.3 ng/dl to 1.7 ng/dl. Mean fT_4 was 1.111± 0.238 ng/dl. Among various thyroid disorder patients, the mean fT_4 (ng/dl) values were 1.28 ng/dl, 0.36 ng/dl, 1.07 ng/dl & 1.48 ng/dl in subclinicalhypothyroid, hypothyroid, euthyroid and subclinical hyperthyroidism respectively.

In our study, the values of left ventricular ejection fraction ranges from 22% to 45%. The mean ejection fraction was 31.8 ± 5.685. The mean LVEF in subclinicalhypothyroid, hypothyroid, euthyroid and subclinical hyperthyroid were 31.50 %,28.00%, 32.18% & 29.50 % respectively. Left ventricular diastolic diameter ranges from 59 mm to 79mm and mean diameter was 69.32 ± 3.76. The mean left ventricular diastolic diameter in Subclinical hypothyroid, hypothyroid, euthyroidand subclinical hyperthyroid were 70.75 mm, 72.00 mm, 69.18mm, 67.88 mm respectively. Left atrial diameter ranges from 38 mm to 48 mm and mean diameter was 42.93 ± 1.876 and the mean left atrial diameter in Subclinical hypothyroid, hypothyroid, euthyroid and subclinical hyperthyroid patients was 44.58 mm, 43 mm, 42.79 mm, 41.75 mm respectively.

	THYROID STATUS													
	Subclinical Hypothyroid			Hypothyroid			Euthyroid			Subclinical Hyperthyroid				
	Mean	Median	SD	Mean	Median	SD	Mean	Median	SD	Mean	Median	SD	p Value	Significance
AGE (YEARS)	57.58	58.00	6.22	55.00	55.00	7.07	55.97	57.50	7.23	58.25	62.50	8.80	0.683	Not Significant
Diseases duration (months)	18.00	18.00	6.28	27.00	27.00	4.24	10.92	9.50	6.32	16.13	15.00	7.85	0.001	Significant
FT4(ng/dl)	1.28	1.29	0.11	0.36	0.36	0.08	1.07	1.03	0.18	1.48	1.47	0.13	<0.001	Significant
TSH(uIU/ml)	7.96	8.10	0.96	14.00	14.00	2.83	2.60	2.45	1.08	0.19	0.19	0.07	<0.001	Significant
LVEF(%)	31.50	31.50	1.68	28.00	28.00	2.83	32.18	30.00	6.21	29.50	28.00	3.96	0.360	Not Significant
LVIDd(mm)	70.75	70.50	3.89	72.00	72.00	2.83	69.18	70.00	3.88	67.88	68.00	1.25	0.108	Not Significant
LVIDs(mm)	59.50	60.00	4.89	62.00	62.00	1.41	57.92	59.00	5.47	58.50	57.50	4.04	0.260	Not Significant
LA(mm)	44.58	44.00	1.44	43.00	43.00	1.41	42.79	42.00	1.86	41.75	41.50	1.28	0.002	Significant

			LVEF(%)
Spearman'srho	FT4(ng/dl)	CorrelationCoefficient	0.299
		p Value	0.002
	TSH (uIU/ml)	CorrelationCoefficient	-0.046
		p Value	0.647

In our study, on comparing left ventricular ejection fraction (%) with TSH (uIU/ml) in all patients as well as euthyroid, the scatter plot showed negative correlation implying that with increasing values of TSH, the left ventricular ejection fraction showed a decreasing trend.

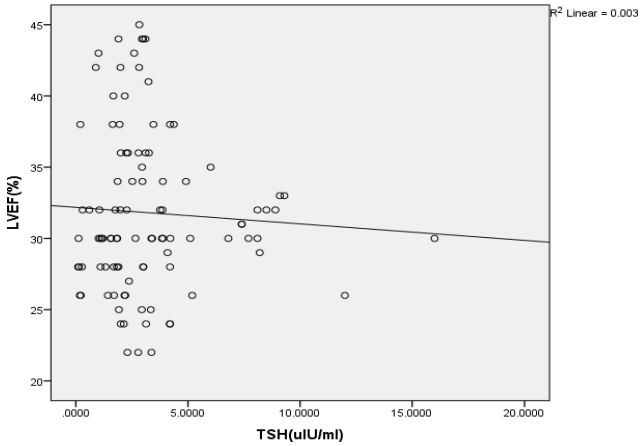
Table 1 Comparison between different parameters among patientswith different thyroid status.

	THYROID STATUS													
	Subclinical Hypothyroid			Hypothyroid			Euthyroid			Subclinical Hyperthyroid				
	Mean	Median	SD	Mean	Median	SD	Mean	Median	SD	Mean	Median	SD	p Value	Significance
AGE (YEARS)	57.58	58.00	6.22	55.00	55.00	7.07	55.97	57.50	7.23	58.25	62.50	8.80	0.683	Not Significant
Diseasesduration (months)	18.00	18.00	6.28	27.00	27.00	4.24	10.92	9.50	6.32	16.13	15.00	7.85	0.001	Significant
FT4(ng/dl)	1.28	1.29	0.11	0.36	0.36	0.08	1.07	1.03	0.18	1.48	1.47	0.13	<0.001	Significant
TSH(uIU/ml)	7.96	8.10	0.96	14.00	14.00	2.83	2.60	2.45	1.08	0.19	0.19	0.07	<0.001	Significant
LVEF(%)	31.50	31.50	1.68	28.00	28.00	2.83	32.18	30.00	6.21	29.50	28.00	3.96	0.360	Not Significant
LVIDd(mm)	70.75	70.50	3.89	72.00	72.00	2.83	69.18	70.00	3.88	67.88	68.00	1.25	0.108	Not Significant
LVIDs(mm)	59.50	60.00	4.89	62.00	62.00	1.41	57.92	59.00	5.47	58.50	57.50	4.04	0.260	Not Significant
LA(mm)	44.58	44.00	1.44	43.00	43.00	1.41	42.79	42.00	1.86	41.75	41.50	1.28	0.002	Significant

Scatter plot 1: Comparison between TSH and LVEF

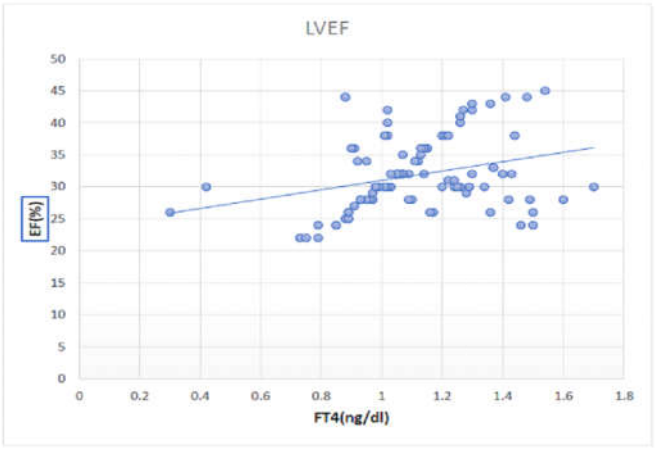
			LVEF(%)
Spearman'srho	FT4(ng/dl)	CorrelationCoefficient	0.299
		p Value	0.002
	TSH (uIU/ml)	CorrelationCoefficient	-0.046
		p Value	0.647

Fig 1



Comments:
Among 100 patients studied, on comparing value of Left ventricular ejection fraction with TSH on a scattered plot, a negative correlation was found.

Scatter plot 2: Showing comparison between FT4 and LVEF



Comments:
Among 100 patients studied, on comparing value of Left ventricular ejection fraction with fT4 on a scattered plot, a positive correlation was found.

Similarly, on comparing left ventricular ejection fraction (%) with fT_4 (ng/dl) in all studied patients as well as euthyroid, the scatter plot showed positive correlation, that a higher fT_4 (ng/dl) was associated with higher ejection fraction, similarly lower fT_4 (ng/dl) was associated with lower ejection fraction.

DISCUSSION

Hyperthyroidism and hypothyroidism do not commonly cause clinical heart failure in an otherwise normal heart, but often exacerbate heart failure. Tests of thyroid function are part of routine evaluation of cardiomyopathy, as clinical signs of thyroid diseases may be masked.

To date, several studies have been performed which claim a clear association between thyroid dysfunction and increased risk of mortality in patients with DCM and HF; their results further strengthen the premise that monitoring of thyroid function in HF patients is a necessity, thus encouraging the need for further studies to evaluate this group of patients.

In our study, after proper selection of patients as per all inclusion and exclusion criteria, we investigated 100 patients of dilated cardiomyopathy using a detailed history, thorough clinical examination, routine biochemical and haematological tests and by echocardiography.

Mean age at presentation was 56.33 + 7.176 years. The mean ejection fraction was 31.8 ± 5.685. The mean LVEF in subclinical hypothyroid, hypothyroid, euthyroid and subclinical hyperthyroid were 31.50 %, 28.00%, 32.18% & 29.50 % respectively. The mean left ventricular diastolic diameter in Subclinical hypothyroid, hypothyroid, euthyroid and subclinical hyperthyroid were 70.75 mm, 72.00 mm, 69.18mm, 67.88 mm respectively. Left atrial diameter ranges from 38 mm to 48 mm and mean diameter was 42.93 ± 1.876 and the mean left atrial diameter in Subclinical hypothyroid, hypothyroid, euthyroid and subclinical hyperthyroid patients was 44.58 mm, 43 mm, 42.79 mm, 41.75 mm respectively. Similar finding were seen in the study conducted by Xiaoping Li *et al*.[8]

In our study, on comparing left ventricular ejection fraction (%) with TSH (uIU/ml) in all patients as well as euthyroid, the scatter plot showed negative correlation implying that with increasing values of TSH, the left ventricular ejection fraction showed a decreasing trend. The study findings obtained were substantiated by a study by Ravishankar *et al*.[9]

Similarly, on comparing left ventricular ejection fraction (%) with fT4 (ng/dl) in all studied patients as well as euthyroid, the scatter plot showed positive correlation, that a higher fT4 (ng/dl) was associated with higher ejection fraction, similarly lower fT4 (ng/dl) was associated with lower ejection fraction similar finding were seen in the study conducted by Arif *et al*.[10]

CONCLUSION

Our study incorporated various thyroid disorders and their relation with dilated cardiomyopathy. It was found that patients with DCM presented with different forms of thyroid status, encompassing a wide spectrum which included euthyroid (78%), hypothyroidism, subclinical hypothyroidism and subclinical hyperthyroidism.

An increase in thyroid dysfunction was found in patients who had a longer duration of dilated cardiomyopathy. Patients with diabetes as a comorbidity were found to present with more severe heart failure (NYHA grade IV). A statistically significant positive correlation between left ventricularejection fraction (LVEF%) and fT_4 (ng/dl) was observed even in the euthyroid population.

Our study helps to establish the increasing relevance of thyroid function testing in patients presenting with cardiovascular compromised states like DCM. Earlier and more rigorous identification of thyroid hormone imbalance in such patients will be beneficial in terms of increased survival when treatment is initiated, as substantiated by multiple other studies. Further, earlier identification of patients with diabetes among those with thyroid disorders also appears to have its own importance in prognosis of such patients; judicious treatment may go a long way in improving overall survival, and may decrease the frequency of acuteevents and hospital admissions.

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