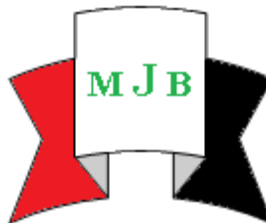


Cardiovascular Manifestations of Primary Hypothyroidism

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Abstract

Hypothyroid patients are liable for cardiovascular complications, especially arrhythmias hypertension, ventricular dysfunction ischemic heart disease, and pericardial effusion.

To detect the above-mentioned cardiovascular manifestations in hypothyroid patients before and after treatment.

92 cases of hypothyroidism, (Collected within 25 years) diagnosed by hormonal assay were studied for their cardiovascular manifestations, clinically, by ECG, chest X-ray, echocardiography and sometimes exercise ECG at time of diagnosis (from 1988-2002) and followed for the first 10 years from the starting point of the treatment.

Among 92 hypothyroid patients studied, cardiovascular manifestations were not high before treatment, while after treatment and during the first 10 years of follow-up, no relevant cardiovascular disease could be detected.

Although hypothyroid patients are liable for cardiovascular complications, in this study cardiovascular manifestations are not common in hypothyroid patients neither before nor after the treatment.

Key words: Cardiovascular manifestations, hypothyroidism

العلامات القلبية – الوعائية في مرضى هبوط الغدة الدرقية الأولى

الخلاصة

المرضى المصابين بهبوط فعالية الغدة الدرقية قد يكونون معرضين أكثر من غيرهم لأمراض القلب و جهاز الدوران مثل ارتفاع ضغط الدم و عدم انتظام ضربات القلب و عدم كفاءة الشرايين التاجية و عجز القلب (أو قصور وظيفة البطين) و انصباب التامور. و عليه تم دراسة تلك الأمراض على المرضى المصابين بهبوط الغدة عند تشخيص المرض و خلال العشر سنوات الأولى من العلاج . أجريت الدراسة على ٩٢ مريضاً تم تشخيصهم سريرياً و مختبرياً (بالفحص الهرموني) و بعد التحري عن تلك الأمراض سريرياً بواسطة الأعراض و العلامات و اجراء تخطيط القلب الكهربائي و اشعة الصدر و فحص صدى القلب (الايكو) وتخطيط بعد الجهد احياناً , تبين من هذه الدراسة انه بالرغم من كون مرضى هبوط الغدة معرضين لتلك الأمراض الا ان نسبة الاصابة قليلة او غير شائعة لا عند تشخيص المرض و لا في فترة العشر سنوات الأولى من العلاج و هي اشارة مطمئنة نوعاً ما .

Introduction

The thyroid gland and heart share a close relationship in embryology both migrate together [1]. In contrast to the dramatic clinical signs and symptoms of hyperthyroidism, the cardiovascular findings of hypo-

thyroidism are more subtle [2]. Hypothyroidism is a clinical syndrome caused by deficiency of thyroid hormones. It is usually primary (thyroid failure), but may be secondary (hypothalamic or pituitary deficiency) or

the result of resistance at the thyroid hormone receptor [3].

Overt hypothyroidism is defined as an elevated serum TSH concentration and reduced free thyroxin concentration (fT₄) [4], while subclinical hypothyroidism is defined as an elevated serum TSH level with a normal serum (fT₄) concentration [5].

Primary hypothyroidism is the etiology in approximately 99% of the cases of hypothyroidism, with less than 1% being due to TSH deficiency or other causes.

The prevalence of primary hypothyroidism is 1:100 but increases to 5:100 if patients with subclinical hypothyroidism are included.

The female to male ratio is approximately 6:1 [5].

Estimates of the incidence of hypothyroidism vary depending on the population studied. [6-8] In the United States, 0.3% have overt hypothyroidism, and 4.3% have subclinical or mild hypothyroidism [8].

Clinically, hypothyroidism can affect all organ systems, [4] Skin and its appendages, cardiovascular system, respiratory system, alimentary system, central and peripheral nervous system, musculoskeletal, renal, hematopoietic system, pituitary and adrenocortical, reproductive function and energy metabolism.

The major cardiovascular changes that occur in hypothyroidism include a decrease in cardiac contractility and mass, a reduction in heart rate, and an increase in peripheral vascular resistance. Regarding cardiac contractility, all measures of left ventricular performance are impaired, leading to a reduction in cardiac output. [9-12].

Regarding vascular resistance, thyroid hormone relaxes vascular smooth muscle cells, thereby reducing

peripheral vascular resistance. Conversely, hypothyroidism causes contraction of these cells [14] and increasing peripheral vascular resistance. This change results in reductions in cardiac output [15].

The mean arterial pressure rises with up to 20 percent of the patients having significant diastolic hypertension. [13].

Pericardial effusion can occur. Occasionally, the pericardial effusions are quite large, causing the appearance of cardiomegaly on chest radiograph. Echocardiography demonstrates small to moderate effusions in up to 30 percent of overtly hypothyroid patients, which resolve over a period of weeks to months after initiation of thyroid hormone replacement [2].

Lastly, as a result of increases in risk factors including hypercholesterolemia, hypertension, and elevated levels of homocysteine, patients with hypothyroidism may have increased risk for atherosclerosis and coronary and systemic vascular disease [16,17].

Patients and Methods

Through the years 1988-2002, 92 cases of primary hypothyroidism were diagnosed clinically and by hormone levels, having high TSH and low or normal T₄ levels. These cases were studied regarding the cardiovascular manifestations by two stages, the first was for detection of cardiovascular manifestations for cases gathered from 1988-2002 before treatment being started, and the second stage prospective during the initial 10 years of treatment till 2012 (January). Cardiovascular assessment included:

1- Clinical assessment of symptoms of dyspnoea, chest pain, palpitation and syncope and of signs like pulse rate, blood pressure, jugular venous pressure, cardiac apex and heart sounds.

2- Resting ECG was done and analysed.

Exercise ECG was done for some patients with non- specific T- wave flattening or inversion and questionable chest pain to exclude or confirm ischemic heart disease.

3- Chest X- Ray was done for all the patients for cardiac size.

4- Echocardiographic examination was done looking for pericardial effusion and special emphasis paid for chamber size and function and septal motion

Exclusion criteria were patients with

- Normal or low TSH.
- Overt heart failure and acute myocardial infarction
- Known case of hypertension before the start of symptoms
- Known case of ischemic heart disease before the symptoms
- Known case of brady or tachyarrhythmia before the symptoms
- early (thyroid) post-operative patients.

Although the total number participated were 92, only 60 of them could be followed for 10 years, the other 32 cases did not complete the study. So, the post-treatment or post-thyroxin group comprised only 60 cases.

Results

Although cardiovascular manifestations of hypothyroidism was studied, but it is worth to mention here that in none of them the presentation was cardiovascular and it is interesting to mention their presentations as groups.

The Patients presented to us were mainly under four groups as shown in table No.1 The greatest number of the patients presented as puffy eyes and "swellings" of hands and feet, where they consulted mainly physicians to exclude what they think "renal"

disease, the second group consulted for weakness and anaemia the third group was for musculoskeletal pains or "rheumatologic" disorders and the fourth groups were miscellaneous such as postthyroidectomy-patients, menstrual irregularities (referred from gynaecologists), casual laboratory findings etc.

Regarding Age distribution, it was between 25-60 years.

Regarding Gender distribution, female outnumber males by 70 to 22

Study of Cardiovascular manifestations was made through 2 stages before and after treatment and included analysis of both clinical manifestations and investigation results (Stage one- at time of diagnosis and before treatment)

Analysis of cardiovascular manifestations at presentation (Table 2). Among the 92 cases diagnosed as primary hypothyroidism, none had a cardiovascular symptom or sign as a presenting feature except for

1- Dyspnoea, which was due tiredness and anemia rather than heart failure

2- Bradycardia - discovered, as part of physical examination not as presenting feature or patient's complaint
Analysis of findings made by investigation, were shown in tables 3, 4 & 5.

Chest X-Ray

Cardiac silhouette enlarged = 4 cases

Pericardial effusion in 4 cases by chest x-ray, again as part of general assessment and not as a presenting feature but in 12 cases by echocardiography.

ECG was abnormal (flattening and/or T-inversion) in 35 cases

Stage 2-after treatment

(Cardiovascular manifestations during follow-up period for 10 years-among the remaining 60 cases).

No patient had a significant cardiovascular illness, especially regarding the development of hypertension, ischemic heart disease, heart failure or arrhythmias. Clinically, non developed symptoms of heart disease

Five, (8.33%) patients had hypertension. Chest x-ray (2 yearly) remained normal. Echocardiography (yearly) did not reveal any abnormality like ventricular dysfunction or dilatation or pericardial effusion. ECG was normal regarding arrhythmias but abnormal (flattening and T inversion) in 22, (36.66%) the other cases (out of the remaining 60 cases).

Fourteen, (23.33%) patients with abnormal ECG had symptoms suspicious of ischemic heart disease, so exercise ECG was done for them and all were negative.

No patient developed ischemic heart disease.

Discussion

Compared to hyperthyroidism, in general, cardiovascular manifestations are not so common in hypothyroid patients; the overall cardiovascular manifestations were not high. A strange finding in a good number of patients was misinterpretation of hypothyroid clinical manifestations as nephritic syndrome! (body swelling, weakness, high cholesterol).

As a presenting feature, no patient had a cardiovascular feature of arrhythmia, hypertension, pericardial effusion, ischemic heart disease and heart failure.

Regarding arrhythmia_other than sinus bradycardia which was found in 12, (20%) patients before the treatment, any type of Brady or tachyarrhythmia could not be found before treatment and none thereafter.

Most literatures agree with the finding in the study that only bradycardia is considered as a common finding, like Nikoo who mentions that sinus bradycardia is considered as a usual and the others as rare [18]. there were few reported cases in the net of ventricular ectopics and one report of Torsades de pointes.

Regarding blood pressure only 5, (8.33%) patients had hypertension (after diagnosis), though it was not sure whether it is a natural development or due hypothyroid itself, but even though the figure is not that high. This is rather a low figure as compared with what has been mentioned by Klein and Streeten that approximately 20 to 40 percent of hypothyroid patients have hypertension, even though the cardiac output is reduced [19, 20]. Moreover, it has been mentioned that among large groups of patients with hypertension, however, hypothyroidism is a contributory factor in only a few percent [20].

Regarding angina or Ischemic heart disease in spite of the high incidence of "non-specific" T-inversion, angina was not found in any patient. In the literature, we found different opinions regarding this point; Keating *et al*, mentioned that angina pectoris may first appear or worsen during the treatment of the hypothyroid state with thyroid hormone, although most patients with hypothyroidism and coronary artery disease had no change, or improvement, in angina symptoms with thyroxin treatment [21].

While Ojamaa mentioned that patients with angina pectoris probably have symptoms less often if they become hypothyroid, because they are less active and peripheral oxygen demands decrease. The occurrence of anginal-like pain in some hypothyroid patients and the frequent occurrence of hypercholesterolemia have led to

suggestions that hypothyroidism is associated with accelerated coronary artery disease [22]. However, there is little direct evidence to support this hypothesis [19].

Hypothyroidism has been shown to be a risk factor for atherosclerosis and cardiovascular disease by several studies, although others have not shown this association. In Rotterdam study, a population-based survey designed to examine the determinants of chronic disease in postmenopausal women, subclinical hypothyroidism was associated with a significant risk of both aortic atherosclerosis and a history of myocardial infarction [23]. Yet, the risk during a subsequent 4-6 year follow-up period was not significantly increased. [24].

A prospective study from Japan showed an increase risk of ischemic heart disease in men, but not women, with subclinical hypothyroidism [25].

Whickham study showed no increase in cardiovascular mortality in patients with subclinical hypothyroidism followed up for more than 20 years. [26]. Another prospective study in the United States, following up men and women age 65 or elder for more than 10 years, showed no influence of hypothyroidism (overt or subclinical), on cardiovascular outcome or mortality [27].

Regarding ventricular function and heart failure no patient was found to have neither systolic nor diastolic dysfunction and no case of dilated cardiomyopathy was found. This goes with what has been mentioned by J. Larry Jameson *et al.* that though alterations in myosin heavy chain isoform expression have been documented, cardiomyopathy is unusual, [28] but it has been mentioned that the myocardium may be dilated [4].

Although it has been mentioned by Biondi that Echocardiographic studies have revealed resting left ventricular diastolic dysfunction is overt, and in some studies, subclinical hypothyroidism as well [29]. These findings normalize..... when the hypothyroidism is treated.

Regarding pericardial effusion, this was found only in 4, (6.66%) patients by Chest-ray and 12, (20%) patients by echocardiography (before treatment). This figure looks low as compared to what has been mentioned by J. Larry Jamson *et al.* that pericardial effusions occur in up to 18, (30%) of the patients but rarely compromise cardiac function. [28].

Radiologically, we found patients to have cardiomegaly, this has been mentioned by Hardisty *et al.* that In severe primary hypothyroidism, the cardiac silhouette is enlarged, and the heart sounds are diminished in intensity [30].

Conclusion

Cardiovascular manifestations were not common in hypothyroid patients. Possibly, early detection and treatment of clinical and subclinical hypothyroidism patients will have less cardiovascular manifestations.

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Table 1: Presenting features

	presentation	No. of cases (%)
Group 1	Puffy eyes& swellings	35(38%)
Group 2	Weaknes and anemia	30(30.2%)
Group 3	musculoskeletal pains or “rheumatologic”	20 (21.7%).
Group 4	miscellaneous	12 (13%).

Table 2: Clinical features

SYMPTOMS	No. of patients (%)
Chest pain	0
Dypnea	10, (10.87)
Palpitation	0
Syncope	0

SIGNS	No. of patients (%)
Pulse-looking for bradycardia	12, (13%)
BP- looking for hypertension	0
JVP-raises	0
Pericardium- looking for Poorly localized apex-----→	0
Displaced apex -----→	0
Pericardium- looking for muffled heart sounds	0

Table 3: radiological findings

CHEST X-RAY	No. of patients (%)
Features of pericardial effusion	4, (4.3%)
Features of heart failure	0

Table 4 : ECG findings

ECG Findings	No. of patients (%)
Sinus bradycardia	12, (13.33%)
Ventricular ectopic	0
Atrioventricular block-	0
Bundle branch block	0
Prolonged QT-interval	0
Low voltage P,QRS & T	3
ST-segment alteration	0
T-flattening or inversion	35, (38.88%)

Table 5: Echocardiographic findings

Echocardiographic findings	No. of patients (%)
Pericardial effusion	12, (13.33%)
Left ventricular dilatation	0
Right ventricular dilatation	0
Increased or increased IV septal thickness	0
Abnormal IV septal motion	0
Decreased ejection fraction	0