

Hypothyroidism Associated with Echocardiographic Abnormalities

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Abstract

Objective: To evaluate the relationship between hypothyroidism and pericardial effusion, dilate cardiomyopathy and the LV ejection fraction (EF) through an echocardiographic scan.

Design: Retrospective study.

Settings: Single tertiary center, King Abdulaziz University Hospital, from January 2015 to January 2017.

Patients: 314 patients followed up for hypothyroidism.

Intervention: None.

Main outcome measures: Echocardiographic abnormalities.

Results: The average age of the subjected group was 57 which is significantly older than control group (P value=0.0001). In addition, the subjected group were treated with higher doses of amiodorone than the control group which was quite a drastic difference (p value=0.037).

Similarly, such a drastic difference between both groups due to the low p value at <0.0001 - was also identified by how the ejection fraction (EF) of the subjected group was statically much lower than in the control group. The p values calculated in both cases were determined using the simple regression model.

It was also found that there was a negative to weak relationship as explained by the B coefficient (Regression Coefficient) amongst the cases/controls and the laboratory parameters. However, there was a significant correlation between EF and the FT3 level (r=0.818; p value=0.045).

Conclusion: The study showed the clear association of hypothyroidism with echocardiographic abnormalities; like cardiomyopathy and pericardial effusion. It was also deduced that patients suffering from severe hypothyroidism as well as cardiomyopathy had quite low levels of EF.

Keywords: Cardiomyopathy; Echocardiography; Pericardial effusion; Hypothyroidism

Introduction

One of the functions of the thyroid hormones is to regulate the cardiovascular system and the heart [1,2]. Such a link has been established for almost a century now. In 1918, Zondek introduced the term 'myxoedema heart', referring to pericardial effusion, ventricular dilatation and hypertrophy, as well as interstitial oedema alongside the swelling of myocardial fibres [3].

Patients suffering from overt hypothyroidism also suffer from bradycardia, decreased ventricular filling and decreased cardiac contractility; which eventually leads to dilated cardiomyopathy and a decrease in the cardiac output [4,5]. As for patients with subclinical hypothyroidism, they have also been associated with systolic and diastolic cardiac dysfunction [6,7].

Such disorders caused by overt hypothyroidism have been associated with various different heart pericardial effusion. The incidence of hypothyroidism causing such diseases is 3% to 6% [8,9]. Pericardial effusion and cardiomyopathy are caused by the hypothyroid disorder due to its association with high cholesterol levels [10], well-known risk factors for coronary artery atherosclerosis, independent of either age or sex. Simply by treating the hypothyroidism and restoring its normal value can reverse any abnormal cardiovascular hemodynamic [11,12].

The aim of this study was to evaluate the association between hypothyroidism and cardiac diseases using echocardiography. The diseases found ranged from either pericardial effusion, dilate cardiomyopathy to even left ventricle (LV) ejection fraction (EF%). Echocardiography was used since it is a more recent technique that provides an approach to LV myocardial mechanics, giving information about the three spatial dimensions of cardiac deformation [13].

Subjects and Methods

The first step in our case-controlled study was to gather the data records of patients at King Abdulaziz University Hospital from the electronic medical database. The time frame selected was from January 2015 to January 2017. Three hundred and eighteen patients, all of whom suffer from hypothyroidism, were chosen and we further investigated to obtain their age, sex, nationality, lipid profile total cholesterol (TCL), triglycerides (TG), low-density lipoprotein (LDL) cholesterol and high density lipoprotein (HDL) cholesterol as well as data concerning their thyroid stimulating hormone (TSH), free triiodothyronine (FT3), and free thyroxine (FT4).

We then conducted the echocardiographic procedure on them all. The results obtained from the scan provided us with a clear difference between the patients; 157 (50%) of them had severe echocardiographic abnormalities such as cardiomyopathy or pericardial effusion. The control group, which also consisted of 157 patients, suffered from only mild cardiomyopathy or pericardial effusion.

The echocardiograph performed was standard and two-dimensional and was done according to the requirements published by the American society of Echocardiography. The echocardiograph performed determined whether or not the patients suffered from a cardiac disease and the intensity of the disease which they had. The LV ejection fraction (EF%) was calculated according to the Simpson method.

Statistical Methodology

A case-control study was carried out among 314 subjects all whom had hypothyroidism, with an equal number of cases suffering from cardiomyopathy (N=157) and matching controls suffering from only mild cardiomyopathy. The categorical data was summarized using frequency and percentages, while the continuous data was summarized using mean and Standard deviation.

As for the independent t test was performed to find out the difference in mean of continuous variable in two groups whereas the Z-test for proportion in two populations was done for the categorical data.

The association between categorical data was found out using the chi-square test. Odds ratio with 95% CI was calculated to have an idea about the likelihood of risk among the two groups. The bar graph was even drawn out to highlight the difference in frequency between the two groups. All the statistical analysis was carried out using Statistical Packages for Social Sciences (SPSS) version 20.1.

Laboratory analysis

The thyroid hormone parameters were assessed using the immunochemiluminescence assay method. The normal reference levels of the thyroid panel, according to the standards of the biochemistry of our laboratory, were 0.27 mIU/ml to 4.30 mIU/ml for TSH, 1.80 pmol/l/ml to 4.60 pmol/l/ml for FT3, and 0.93 pmol/l to 1.70 pmol/l for FT4.

When symptoms of hypothyroidism were present and patients exhibited TSH levels between 9 mIU/ml to 14.9 mIU/ml, or TSH levels higher than 15 mIU/ml alongside low levels of FT4 and FT3, were diagnosed with severe hypothyroidism. As for patients with TSH levels less than 10 mIU/ml and normal levels of FT4, and FT3 in the absence of the symptoms of hypothyroidism were diagnosed with subclinical hypothyroidism [14].

Certain patients were excluded from the study such as those whom were prescribed to medication that could affect the serum thyroid hormone levels. In addition, patients with angina pectoris, a history or suspicion of coronary artery disease, a bundle branch block on electrocardiography, or a history of chronic obstructive pulmonary disease were also excluded from the study.

Results

By looking at Table 1, we were able to derive most of the clinical and biomedical characteristics of both the subjected and control groups. In both groups, most of the patients were female and non-Saudi; however, the median age of the subjected group was 57 whilst the control group's average age was 34 years. Such a difference is quite significant due to the P value between the two groups was 0.0001.

Similarly, the subjected group used significantly more doses of amiodarone than the control group; the P value between both groups is 0.037. As for parameters such as FT4, FT3, TSH, cholesterol, triglyceride, LDL cholesterol, thyroxine dose and Vitamin D levels the two groups did not exhibit significant difference

Variables	Hypothyroidism		P-value
	Cases	Controls	
^a Sex			
Male	57 (36.3)	39 (24.8)	0.028*
Female	100 (63.7)	118 (75.2)	0.028*
Nationality			
Saudi	64 (40.8)	70 (44.6)	0.50
Non-Saudi	93 (59.2)	87 (55.4)	0.49
RAI	34 (21.7)	34 (21.7)	1.00
^b Age			
FTa	5.55 (4.1)	7.43 (14.2)	0.112
FT3	1.85 (1.24)	2.21 (1.34)	0.014*
TSH	73.27 (25.81)	70.39 (27.93)	0.344
VITD3	14.91 (17.23)	18.63(19.2)	0.072
Cholesterol	3.33 (2.05)	3.51 (2.24)	0.462
TG	4.42 (41.5)	1.03 (1.04)	0.307
Thyroxine (dose)	89.8 (39.5)	88.53 (40.08)	0.51
Amiodarone	21.3 (110.39)	2.54 (22.5)	0.037*
a: Frequency (percentage); b: Mean (SD); *statistically significant with p-value <0.05			

Table 1: Demographic characteristics.

Furthermore, the data from Table 2 asserted that in both groups the majority of the patients suffered from severe Hypothyroidism -151(96.2%) in the subjected group and 144(91.7%) in the control group. The remaining patients in both groups suffered from subclinical hypothyroidism -6(3.8%) in the subjected group and 8(8.3%) in the control group.

Type of Hypothyroidism	Hypothyroidism		P-values	Odds Ratio
	Cases (N=157)	Controls (N=157)		
Subclinical	6 (3.8)	13 (8.3)	0.098	1.62 (0.83-3.17)
Severe	151 (96.2)	144 (91.7)		

Table 2: Association of hypothyroidism with cardiomyopathy.

Table 3, which analyzed the laboratory parameters using the B coefficient (Regression Coefficient), found that there was a weak relationship amongst the cases/controls and the majority of the laboratory parameters. However, a significant correlation between EF and the low FT3 level was found due to the r value being at 0.818 and the p value being at 0.045.

Variable	Echo Finding		Controls	P-value
	Pericardial (N=59)	Dilated (N=128)		
Ejection fraction	51.56 (18.14)	49.75 (17.38)	23.02 (31.52)	<0.0001**

**statistically significant with p-value <0.05

Table 3: Comparison of mean ejection fraction with echo finding among cases and controls.

In Table 4, the echocardiographic findings were evaluated for the patients in both groups. It was found that in the subjected group 128 (81.5%) patients suffered from either cardiomyopathy or pericardial effusion. As for the control group, only 59 (37.7%) patients were reported with one of the two disorders. The mean ejection fraction was significantly lower in subjected group in comparison to the control group with a p value of <0.0001 (Figure 1) found using the simple regression model.

Furthermore, in Figure 2 the graph limns that from the patients suffering from severe hypothyroidism, 70% had dilated cardiomyopathy and 30% were afflicted with pericardial effusion. As for patients suffering from subclinical hypothyroidism 40% were afflicted with cardiomyopathy and 60% had pericardial effusion.

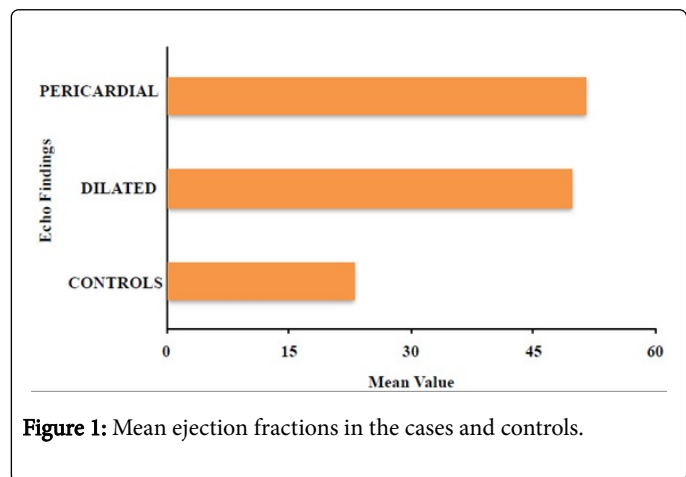


Figure 1: Mean ejection fractions in the cases and controls.

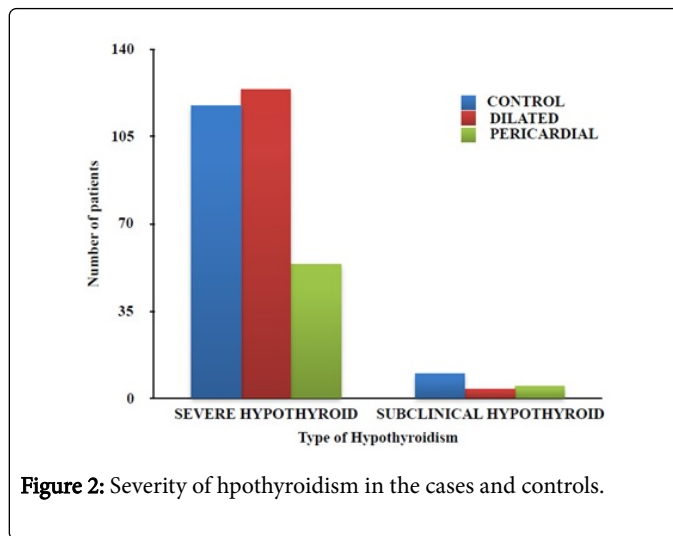


Figure 2: Severity of hypothyroidism in the cases and controls.

Variables	B	S.E.	p-value	Exp (B)
FT4	-0.016	0.022	0.455	0.984
FT3	-0.201	0.1	0.045	0.818
TSH	0	0.005	0.925	1.000
VITD3	-0.009	0.006	0.153	0.991
Cholesterol	-0.116	0.069	0.093	0.891
TG	0.212	0.144	0.142	1.236

Table 4: Relationship of echo findings with laboratory parameters.

Discussion

FT3, or triiodothyronine, is essential for maintaining cardiovascular homeostasis; furthermore, FT3 has an impact on the left ventricle (LV) systolic function via cardiac contractility, systemic vascular resistance, and total blood volume, which eventually results in cardiomyopathy [15]. Low FT3 level leads to increased phos-pholamban and decreased SERCA activity, as a result of that the systolic and diastolic functions of the heart decrease- hence causing cardiomyopathy [16].

After intense and thorough research, we have deduced that such a correlation between FT3, EF and cardiomyopathy clearly does exist; however, the other laboratory parameters such as FT4, TSH, cholesterol, triglyceride and vitamin D3 levels exhibited weak or no relationship with factors resulting in cardiomyopathy. Such a result was inferred from the significant p value (<0.0001) of the relation between the low EF and FT3 levels in the subjected group and the control group [14]. It was also clear that patients whom suffered from cardiomyopathy were also afflicted with arrathymeia establishing a strong correlation between the two disorders and was treated using amaidiorone

As shown in previous studies, untreated subclinical hypothyroidism (SH) was commonly associated with pericardial effusion and such an association was also present in our study with the echocardiographic findings presenting how 60% of patients with subclinical hypothyroidism also had cardiomyopathy and pericardial effusion whilst 70% of patients with severe hypothyroidism had

cardiomyopathy and pericardial effusion [17,18]. This could be explained by the fact that patients with severe hypothyroidism are much older and the duration of their disease was much longer than those with subclinical hypothyroidism with a significant p value <0.0001 . Both these factors working conjointly with each other result in impairment in the LV longitudinal myocardial function.

It is well known how simply by treating hypothyroidism using thyroxin any disease incurred by the disorder such as cardiomyopathy or pericardial effusion would no longer be of much concern [19,20].

Limitation of the study

The study acknowledges several limitations, firstly and most importantly the cross-sectional nature of the study as well as the small number of patients which we had contributed to limiting the study in many respects such as the ability to generalize the correlation. Furthermore, patients with hypothyroidism had other diseases such as hypertension or even diabetes and some patients were smokers which can contribute to causing cardiac diseases especially cardiomyopathy.

Conclusions and Recommendation

Overall, on the completion of this study we have reached a solid conclusion and a clear association of hypothyroidism with cardiac diseases especially those of cardiomyopathy and pericardial effusion. Furthermore, it was also established that those patients suffering from the two disorders caused by severe hypothyroidism also suffered from a significantly low ejection fraction. The findings also stress the importance of early detection and effective treatment of cardiac abnormalities in patients affected by thyroid disorders. In order to do so close cooperation between endocrinologists and cardiologists is essential to improve the prognosis of severe cardiac involvement in patients with severe, mild and subclinical thyroid dysfunction and to optimize the treatment of such patients.

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Competing interests

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