



THE ASSOCIATION OF THYROID DYSFUNCTION WITH THE ACUTE ISCHEMIC HEART DISEASE

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ABSTRACT

Thyroid dysfunction has a great impact on lipid as well as cardiovascular risk factors. The objective of this study was to assess the prevalence of thyroid dysfunction and its correlation with acute ischemic heart disease. Fifty patients with acute ischemic heart disease were admitted to Ibin-Al-Nafes (cardiac disease hospital), (between May 2011 to September 2011). (19 females with age range from 40 -60 years) and (31 males with age range from 35- 70 years). Acute ischemic heart disease severity was recorded for each patient on admission. Serum thyroid stimulating hormone (TSH), thyroxin (T4) and triiodothyronin (T3) levels were measured for all patients by gama counter method, and lipid profile by enzymatic method. The prevalence of thyroid dysfunction was found in males and females as follows: 14 patients out of 50 show (T3) concentration (28%) $P < 0.05$ and 8 patients out of 50 with high (TSH) concentration (16%), ($P < 0.05$) and 5 patients out of 50 with high (T4) concentration (10%) ($P < 0.05$) tables, fig 2, 3 and 4 respectively. While their lipid profile show dyslipidemia for all patients (table, fig 5). The result showed that hypothyroidism is associated with and increased risk for ischemic heart disease.

KEY WORDS: hypothyroidism, dyslipidemia, acute ischemic heart disease.

INTRODUCTION

Thyroid function regulates a wide array of metabolic parameters. Thyroid function significantly affects lipoprotein metabolism as well as some cardiovascular disease (CVD) risk factors, thus influencing overall (CDV) risk⁽¹⁻³⁾. Indeed, even within the normal range of thyroid stimulating hormone (TSH) values, a linear increase in total cholesterol (TC) low density lipoprotein cholesterol (LDL-C) and triglycerides (TGs) and linear decrease in high density lipoprotein cholesterol (HDL-C) levels has been observed with increasing TSH⁽⁴⁾. Thyroid hormones induce the 3-hydroxyl-3-methylglutaryl-coenzyme A (HMG-Co A) reductase, which is the first step in cholesterol biosynthesis. Moreover, triiodothyronine (T3) up regulates LDL receptors by controlling the LDL receptors gene activation. This T3-mediated gene activation is done by the direct binding of T3 to specific thyroid hormone responsive elements (TREs)⁽⁵⁾. Furthermore, T3 controls the sterol regulatory element-binding protein-2 (SREBP-2) which in turn regulates LDL receptor's gene expression⁽⁶⁾. T3 has also been associated with protecting LDL from oxidation⁽⁷⁾. Thyroid hormones can influence HDL metabolism by increasing cholesterol ester transfer protein (CETP) activity, which exchanges cholesteryl esters from HDL₂ to the very low density lipoproteins (VLDL) and TGs to the opposite direction⁽⁸⁾. In addition, thyroid hormones stimulate the lipoprotein lipase (LPL), which catabolizes the TG-rich lipoproteins, and the hepatic lipase (HL), which hydrolyzes HDL₂ to HDL₃ and contributes to the conversion of intermediate-density lipoproteins (IDL) to LDL and in turn LDL to small dense LDL (sdLDL)^(9,10). Another effect of T₃ is the up-regulation of apolipoprotein AV (ApoAV), which plays a major role in TG regulation⁽¹¹⁾. Indeed, increased levels of ApoAV have

been associated with decreased levels of TGs⁽¹²⁾. Proposed mechanisms for the effect include the decrease of hepatic VLDL-TG production and the increase of plasma LPL levels and activity, resulting in increase of lipoprotein remnant generation due to enhanced LPL-mediated lipolysis of VLDL-TG⁽¹²⁾. Beyond their effect on lipid profile thyroid hormones can equally affect a number of other metabolic parameters related to CVD risk. Indeed, thyroid function can influence adipocyte metabolism and the production of adipokines⁽¹³⁻¹⁵⁾. Furthermore, endothelial⁽¹⁶⁾ and cardiac function as well as atherosclerosis⁽¹⁷⁾ have been positively associated with thyroid hormone levels. Hypothyroidism is a common metabolic disorder in the general population. Indeed, data from the third National Health and Nutrition Examination Survey (NHANES III) showed a 4.6% prevalence of hypothyroidism in the general population, while 9.5% of the Colorado prevalence study participants had elevated levels of TSH⁽³⁾. Thyroid failure is more common in women and its prevalence rises with age. Hypothyroid patients have increased levels of TC and LDL-C⁽³⁾. Indeed, hypothyroidism is a common cause of secondary dyslipidemia^(18,19). Although decreased thyroid function is accompanied by reduced activity of HMG-CoA reductase, TC and LDL-C levels are increased in patients with overt hypothyroidism⁽²⁰⁻²⁴⁾. This is due to the decreased LDL-receptors' activity, resulting in decreased catabolism of LDL and IDL⁽²⁵⁻²⁷⁾. Moreover, a decrease in LPL activity is found in overt hypothyroidism, decreasing the clearance of TG-rich lipoproteins⁽²⁸⁾. Therefore, overt hypothyroidism patients may also present with elevated TG levels associated with increased levels of VLDL and occasionally fasting chylomicronemia^(22-24,27). The VLDL and IDL particles in hypothyroidism are rich in cholesterol

and apolipoprotein E, thus resembling β -VLDL particles of type III.

The association between overt hypothyroidism and coronary heart disease has been repeatedly observed (Becker 1985⁽²⁹⁾). It was shown that even subclinical hypothyroidism independently doubled relative risk of myocardial infarction in females⁽³⁰⁾. The most frequent cause of hypothyroidism is the autoimmune thyroid disease (AITD) manifested by elevated thyroid antibodies, namely thyroid peroxidase antibodies⁽³¹⁾. Thus, a sole increase in thyroid antibodies may potentially influence the coronary risk.

MATERIALS & METHODS

Study sample consisted of patients with acute ischemic heart disease. Briefly, study sample selection was conducted by review of 50 patients were recruited to Ibn ALnafes Hospital records for acute ischemic heart disease (31 males with age range from 35–70 years) average (50 years) and 19 females with age range from (40 -60) years, average (52 years) . Information on personal and demographic characteristics, personal and family history of coronary heart disease, lifestyle, and current pharmacotherapy were obtained at interview. The history of these patients was showed in table(1).

Venous blood samples drawn in fasting state were used for biochemical laboratory analysis. The laboratory examinations included estimation of total cholesterol (TCHOL) and high density cholesterol (HDL) ,triglycerides (TG) by enzymatic colorimetric methods and tri-iodothyronine (T3), thyroxine (T4), and thyroxine stimulating hormone (TSH) by gamma counter methods.

Methods: TSH IRMA KIT

Principle of the assay

The immune radiometric assay of thyroid stimulating hormone (TSH) is a sandwich type assay. Mouse monoclonal antibodies directed against two different epitopes of TSH and hence not competing are used. The samples or calibrators are incubated in tubes coated with the first monoclonal antibody in the presence of the second monoclonal antibody labeled with iodine 125. After

incubation, the content of tubes is aspirated and the tubes are rinsed so as to remove unbound I (125-labeled antibody. The bound radioactivity is then determined in a gamma counter. The TSH concentrations in the samples are obtained by interpolation from the standard curve. The concentration of TSH in the samples is directly proportional to the radioactivity.

Total T4 RIA KIT:

Principle of the assay

The radioimmunoassay of total thyroxine (TT4) is a competition assay. Samples and calibrators are incubated with I125-labeled T4. As tracer, in antibody-coated tubes. After incubation, the liquid content of tubes is aspirated and the bound radioactivity is determined in a gamma counter. A standard curve is constructed and unknown values are obtained from the curve by interpolation.⁽³²⁾

Total T3 RIA KIT: The principle is the same as in the total T4 assay by gamma counter.

RESULTS

A total of 50 patients (31 males) age range from 35-70 years (average 50 years) and (19 females) age range from 40- 60 years (average 52 years) (table 1) were analyzed in the present study. The prevalence of various forms of thyroid disorder is given in (table2, 3, and 4). Prevalence of hypothyroidism was significantly higher in females than males. Hypothyroid females were also more often substituted with thyroid hormones than males in present study 14 patients out of 50 show low T3 concentration (28%) and 8 patients out of 50 with high TSH concentration (16%) and 5 patients out of 50 with high T4 concentration (10%) of patients. Prevalence of hypothyroidism was more than 3 times higher in subjects in both genders and also significantly higher in females with total cholesterol levels greater than7 mmol/L. We compared a large set of coronary risk factors by thyroid status and presence of positive TPO (table 5). As expected, males and females with hypothyroidism (without L-thyroxin substitution) had significantly higher TSH and TPO Tch, while lower T4concentration, than control groups.

TABLE 1: History of patients with acute ischemic heart disease at the time of admission.

Patients	Males N=31	Females N=19
Age	35 -70 years	40 -60 years
Average age	(50)	(52)
Smoking	All of them	12 out of 19
Traponin +ve	11 out of 31	7 out of 19
Diabetes	10 out of 31	6 out of 19
Increased serum urea	6 out of 50	
Increased serum of creatinine	5 out of 50	
Polycythemia	7 out of 50	

TABLE 2: Concentration of Triiodothyronin (T3) in acute ischemic heart disease and normal subjects

Variable	N	Mean Nmol/L	Sd. Deviation	Sd. Error mean	P value
T3	50	1.4792	0.52896	0.07481	0.05 Significant
Control	20	1.8042	0.47598	0.10920	

TABLE 3: Concentration of Thyroxine (T4) in acute ischemic heart disease and normal subjects

Variable	N	Mean Nmol/L	Sd. Deviation	Sd. Error mean	P value
T4	50	121.04	35.75595	5.05666	No Significant
Control	20	111	21.25535	4.75284	

TABLE 4: Concentration of Thyroid stimulating hormone (TSH) in acute ischemic heart disease and normal subjects

Variable	N	Mean mIU/ml	Sd. Deviation	Sd. Error mean	P value
TSH	50	4.8824	1.329553	1.88027	0.05 Significant
Control	20	2.1330	1.0335	0.2311	

TABLE 5: Total cholesterol (TC), Triglyceride (TG) and Low density lipoprotein (LDL) in acute ischemic heart disease and normal subjects.

Variables	Mean normal	Mean abnormal
	No=20	No=50
TC mg/dL	155 ± 27	229 ± 26
TG mg/dL	117 ± 42	285 ± 70
LDL mg/dL	93 ± 22	155 ± 21
Significant difference	P < 0.05	

DISCUSSION

The above abnormalities of lipid metabolism associated with overt hypothyroidism predispose to the development of atherosclerotic coronary artery disease (CAD)^(33,34). Moreover, hypothyroidism can adversely affect other C.V.D. risk factors, further contributing to increasing C.V.D. risk. Decreased thyroid function not only increases the number of LDL particles, but also promotes LDL oxid ability⁽³⁵⁾. Furthermore, hypothyroidism increases plasma homocysteine levels⁽³⁶⁻³⁹⁾ which can attributed to the hypothyroidism-induced decline of kidney function⁽⁴⁰⁾ as well as impaired methylene tetra -hydro folate reductase activity⁽⁴¹⁾.

In addition, thyroid failure is strongly associated with arterial hypertension (especially diastolic⁽⁴²⁻⁴⁴⁾ via sympathetic and adrenal activation and increased vascular stiffness.^(45,46) Subject with overt hypothyroidism also exhibit impaired endothelial function⁽⁴⁷⁾ that lead to increased uric acid,⁽⁴⁸⁾ and phosphate levels⁽²²⁾, all of which are associated with increased C.V.D risk⁽⁴⁹⁾. In addition, an increase in carotid intima media thickness (CIMT) has been observed in hypothyroid by increased prevalence of metabolic syndrome.⁽⁵⁰⁾ In our sample of patients with manifest coronary heart disease we found the overall prevalence of hypothyroidism 11.5%. It was 4 times more prevalence in females, than in males (23.4% vs. 6.9%, respectively). This result is agreed with result of (Mayer et al 2005).⁽⁵¹⁾ Prevalence of hypothyroidism was shown to gradually increase between age 45 and 60 years and to be higher in females, than in males^(52,53). In contrast to these findings, the prevalence of hypothyroidism in females was in our sample similar in both, aged >55 or younger than 55 years. Therefore, the screening of thyroid functions seems to be warranted in female coronary patients without regard to age.

Hypothyroidism has been generally considered as cardiovascular risk factor in majority of studies, because of its association with elevated serum total and LDL cholesterol. Hypercholesterolemia in hypothyroidism probably results from reduced catabolism of lipoproteins, a phenomenon that may be explained by decreased

expression of lipoprotein receptors^(54,55). We found that females with untreated hypothyroidism had significantly higher total and LDL cholesterol.

Females with total cholesterol greater than 7mmol/L had about 7 times higher risk of hypothyroidism.

CONCLUSION

Although it is clear that thyroid replacement therapy has beneficial effects on serum lipid profile and cardiovascular risk in overt hypothyroid patients. It seems that thyroid substitution, if used, would be most beneficial in patients with prominent thyroid dysfunction (TSH levels >10 miu/L), higher initial cholesterol levels, and smokers. Furthermore, when treating people with angina pectoris or heart disease, one should be very caution because thyroxin therapy may exacerbate angina or promote cardiac arrhythmia. Overall, measurement of serum TSH levels should be included in the screening of patients with dyslipidemia. In conclusion, thyroid dysfunction has to be considered a highly prevalent condition, mainly in females, which could potentially contribute to the overall coronary risk and may be amenable to secondary preventive intervention. The evidence of benefit of L-thyroxine substitution in addition to conventional therapies on morbidity and mortality of coronary patients remains to be elucidated by randomized pharmacological trials.

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