DEMOGRAPHIC FEATURES OF HYPOTHYROID PATIENTS: IS HIGH DENSITY LIPOPROTEIN CHOLESTEROL (HDL-C), AN INDICATOR OF DISEASE OR TREATMENT EFFECTIVENESS?

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ABSTRACT

Objective: To study demographic features of patients with hypothyroidism.

Place and duration of study: Department of medicine KRL Hospital, Islamabad from January 2017 to June 2017.

Methodology: It is a prospective observational study. Forty patients with age ranging from 17-65 years were included. Fourteen patients were hyperthyroid, thus excluded from study. Out of remaining twenty-six patients (92%) were females while (8%) were males. Serum triiodothyronine (T3), thyroxine (T4) and thyroid stimulating hormone (TSH), anti-thyroid peroxidase antibodies, total cholesterol (TC), triglycerides (TG), high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C) were measured. Routine laboratory tests including blood complete picture, liver function tests, and renal function tests were also performed.

Result: Current study included 40 patients of thyroid disease. Among them 26 were hypothyroid and 14 were hyperthyroid. Among hypothyroid patients 92.3% (n=24) were females and 7.6% (n=2) were males. Female to male ratio was (12:1). Mean age was 45.38 ± 9.97 years with age ranging from 26 to 64 years. Average weight was 74.13 ± 13.4 kg with weight ranging from 42 to 110 kg. Family history was positive in 27% (n=7) of hypothyroid patients. Co-existing diabetes mellitus was present in 15.38% (n=4). 19.23% (n=5) had previous exposure to interferon and 15.38% (n=4) had thyroidectomy. 7.69% (n=2) had goitre. Anti-Thyroid Peroxidase (TPO) antibodies were present in 14 patients. 30.76% (n=8) patients had serum cholesterol >200 mg/dl, 34.61% (n=9) had serum triglycerides >170 while Serum HDL was > 65 mg/dl in 57.69% (n=15) patients. Serum LDL remained normal in all patients as per our laboratory reference. Lethargy and weight gain was found in 100% and 92.3% respectively.

Conclusion: Female to male ratio was 12:1. High density lipoprotein cholesterol was found to be raised in 57.69% patients. Anti-thyroid peroxidase antibody was the commonest antibody detected. About one fifth of patients had interferon induced hypothyroidism.

Key Words: Serum total cholesterol (TC); triglycerides (TG); high density lipoprotein cholesterol (HDL-C); low density lipoprotein cholesterol (LDL-C); triiodothyronine (T3); thyroxine (T4); thyroid stimulating hormone (TSH).

INTRODUCTION

Thyroid disease, namely hypothyroidism and hyperthyroidism, constitutes the most common endocrine abnormality in recent years. It can present as overt disease or subclinical. Thyroid disease is associated with various metabolic abnormalities because of the effects of thyroid hormones on nearly all major metabolic pathways. Thyroid hormones regulate the basal energy expenditure through their effect on protein, carbohydrate and lipid metabolism. This might be a direct effect or an indirect effect by modification of other regulatory hormones such as insulin or catecholamines.[1] Dyslipidemia is a common metabolic abnormality which in association with other coexisting metabolic abnormalities and thyroid hormone-induced hemodynamic alterations, explain the high risk for cardiovascular disease.[2-5]

Lipoproteins are classified into 5 major categories: chylomicrons, very low density lipoprotein (VLDL), intermediate density lipoprotein (IDL), low density lipoprotein (LDL) and high density lipoprotein (HDL). Thyroid hormones influence all aspects of lipid metabolism including synthesis, mobilization, and degradation.[6] Thyroid hormones stimulate cholesterol synthesis by inducing 3-hydroxy-3-methyl-glutaryl coenzyme A reductase in the liver.[7] They also affect lipoprotein lipase activity. In hypothyroidism, lipoprotein lipase activity in the adipose tissue and liver is decreased, resulting in normal or high levels of triglycerides.[8-10] In hyperthyroidism lipoprotein lipase activity usually remains normal[9-11] but fatty acid synthesis and oxidation in liver increase due to enhanced Acetyl-CoA carboxylase 1 and carnitine palmitoyl transferase activity leading to increased VLDL biosynthesis.[12-14]

Thyroid hormones, especially triiodothyronine (T3), induce low density lipoprotein (LDL) receptor

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gene expression in the liver, enhancing LDL clearance and explaining the decreased or increased LDL levels observed in hyperthyroidism and hypothyroidism respectively.[6]

HDL particles can be subcategorised into 47 subclasses based on physiochemical properties quantified by nuclear magnetic resonance (NMR) spectroscopy.[15,16] HDL transports cholesterol mostly to the liver by direct or indirect pathway. HDL is removed by HDL receptor B1 which mediates the selective uptake of cholesterol from HDL. In humans probably the most relevant pathway is indirect one which is mediated by cholesterol ester transfer protein (CETP). This protein exchanges the triglycerides of VLDL against cholesterol esters of HDL. The triglycerides are not stable in HDL but are degraded by hepatic lipase so that finally small HDL particles are left which restart the uptake of cholesterol from cells. These changes are thought to be mediated by the effect of thyroid hormones on hepatic lipase (HL) and cholesterol ester transfer protein (CETP). HDL levels have been reported to be normal or decreased in hyperthyroidism where as in hypothyroidism HDL has been increased or remain normal and several studies have examined the effect of T4 replacement therapy on HDL sub fractions.[4,6,8,9]

Several steps in the metabolism of HDL can participate in the transport of cholesterol from lipid-laden macrophages of atherosclerotic arteries, termed foam cells, to the liver for secretion into the bile. This pathway has been termed reverse cholesterol transport and is considered as the classical protective function of HDL toward atherosclerosis. HDL and its protein and lipid constituents help to inhibit oxidation, inflammation, activation of the endothelium, coagulation and platelet aggregation. It has been postulated that the concentration of large HDL particles more accurately reflects protective action, as opposed to the concentration of total HDL particles. In clinical practice it is the HDL cholesterol that is measured rather than LDL to risk stratify the patient. Based on data from Framingham heart study the risk for myocardial infarction increases by about 25% for every 5 mg/dl decrement in serum HDL-C below median values for men and women.[17] While many autoimmune diseases share genetic risk factors, there is evidence that these diseases form separate clusters based on genetics. For example, the 620W allele of PTPN22 has a protective effect in Crohn's disease but is the risk allele for type 1 diabetes and hypothyroidism. SH2B3 also shows opposite directions of effect in multiple sclerosis and celiac compared to rheumatoid arthritis, psoriasis, type 1 diabetes, and hypothyroidism.[25-27] Medications associated with the onset of autoimmune thyroid disease include lithium, amiodarone, interferon α, interleukin 2, campath-1h, and highly active anti-retroviral therapy.[28]

MATERIALS AND METHODS

It was a prospective observational study. Data was collected from 40 patients of thyroid disease presenting to medicine outpatient of Khan Research Laboratory (KRL) Hospital, Islamabad. Hyperthyroid patients were excluded from the study. A detailed questionnaire was made; including age, gender, weight, duration of disease, etiological risk factors, comorbid conditions, clinical symptoms and signs of disease. The Institutional ethical review committee approved the study and informed consent was obtained from all patients. Special emphasis was laid on thyroid function tests and lipid profile. Cut off values of different lab parameters were as follows: serum cholesterol > 200 mg/dl, serum triglycerides > 170 mg/dl, serum LDL >150 mg/dl and serum HDL > 65 mg/dl. Serum TSH > 4.2 μIU/ml. Those patients who were acutely ill or were on lipid lowering drugs were excluded from the study. Laboratory tests including blood complete picture, liver and renal function tests were also performed.

RESULTS

Current study included 40 patients of thyroid disease. Among them 26 were hypothyroid and 14 were hyperthyroid. Among hypothyroid patients 92.3% (n=24) were females and 7.6% (n=2) were males. Female to male ratio was (12:1). Mean age was 45.38 ± 9.97 years with age ranging from 26 to 64 years. Average weight was 74.13 ± 13.4 kg with weight ranging from 42 to 110 kg. Family history was positive in 27% (n=7) of hypothyroid patients. Co-existing diabetes mellitus was present in 15.38% (n=4). 19.23% (n=5)

Table 1: Characteristics of study group

Characteristics	No. of Patients	
Total patients	26	
Age	Mean ± SD	45.38 ± 9.97
	Max. Age	64
	Min. Age	26
Gender	Female	24
	Male	02
Weight	Mean ± SD	74.13 ± 13.4
	Max. Weight	110
	Min. Weight	42
Family history	Positive	07
	Negative	19
Risk factors	Thyroidectomy	04 (15.38%)
	Interferon treatment	05 (19.23%)
Lipid Profile Abnormalities	Serum cholesterol >200 mg/dl	8 (30.76%)
	Serum triglycerides >170 mg/dl.	9 (34.61%)
	Serum HDL-C >65 mg/dl.	15 (57.69%)
	Serum LDL-C > 150 mg/dl.	0

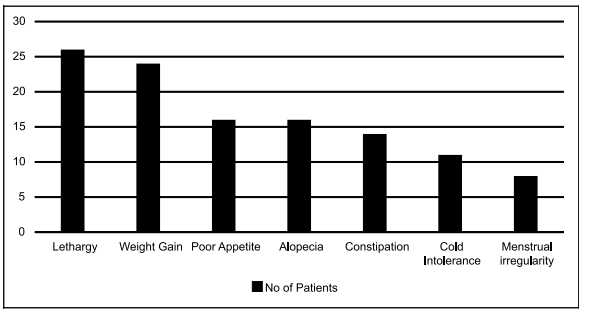

Figure 1: Frequency of symptoms.

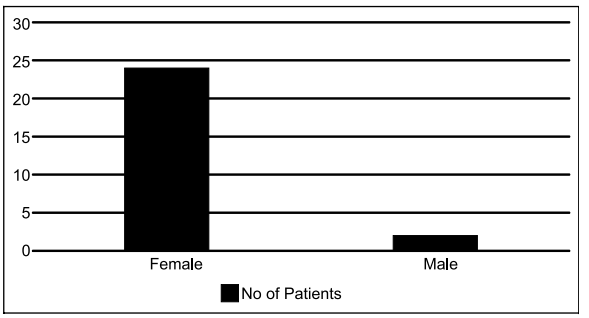

Figure 2: Gender distribution.

had previous exposure to interferon and 15.38% (n=4) had thyroidectomy. 7.69% (n=2) had goitre. Anti-Thyroid Peroxidase (TPO) antibodies were present in 14 patients. 30.76% (n=8) patients had serum cholesterol >200 mg/dl, 34.61% (n=9) had serum triglycerides >170 mg/dl while Serum HDL was > 65 mg/dl in 57.69% (n=15) patients. Serum LDL remained normal in all patients. This is shown in Table 1. Symptoms of hypothyroidism in order of frequency were lethargy 100% (n=26), weight gain 92.30% (n=24), poor appetite 61.53% (n=16), constipation 53.84% (n=14), cold intolerance 42.30% (n=11), alopecia 61.53% (n=16), menstrual irregularities 30.76% (n=8). This is shown in Figure 1.

DISCUSSION

This study showed higher prevalence of thyroid disease in females as compared to males, more common in middle age group. A study in Pakistan revealed that more females were affected as compared to males with a ratio of 3:1.[18] Another study showed that thyroid diseases are more common in middle aged and older people.[19] Prevalence of most of the symptoms of thyroid disease were observed in females of age range 31-40 years. Our study revealed that predominant of our patients were having lethargy and weight gain while some local studies showed that maximum patients were suffering from depression and weakness.[18]

In our study; Co-existing diabetes mellitus was present in 15.38%, 19.23% had previous exposure to interferon and 15.38% had thyroidectomy. In a study it was found that the frequency of another autoimmune disorder was 9.67% in Graves' disease and 14.3% in Hashimoto's thyroiditis index cases (P = .005). Rheumatoid arthritis was the most common coexisting autoimmune disorder (found in 3.15% of Graves' disease and 4.24% of Hashimoto's thyroiditis cases). Relative risks of almost all other autoimmune diseases in Graves' disease or Hashimoto's thyroiditis were significantly increased (>10 for pernicious anemia, systemic lupus erythematosus, Addison's disease, celiac disease, and vitiligo).[30] Pearce EN et al reported that interferon use was associated with development of thyroid disease.[28] In a study it was reported that after thyroid lobectomy; 64.2% patients develop hypothyroidism, mostly subclinical hypothyroidism while only 1.5% patients developed overt hypothyroidism.[31]

Thyroid hormones play an important role in lipid metabolism because they regulate the expression of enzymes involved in metabolism, resulting in decreased level of lipid in serum. Thyroid diseases, specifically hypothyroidism is associated with dyslipidaemia. An association between thyroid dysfunction and dyslipidaemia was first reported in 1930.

Overt hypothyroidism is associated with an altered lipid profile[20,21]. However, the relationship between subclinical hypothyroidism and abnormal lipid profile is still unclear. Our main focus in this study was to look for alteration in lipid profile in thyroid disease, particularly HDL cholesterol in hypothyroidism. Results revealed that almost 58% patients had HDL-C higher than normal. Other lipid parameters like total cholesterol and triglycerides were high in 30.76% and 34.61% patients respectively. Serum LDL-C levels remained within normal limits. Several cross-sectional studies with large sample sizes had been carried out in different countries to study the relationship between hypothyroidism, either overt or subclinical, and altered lipid profile. The Colorado, USA study showed that subclinical hypothyroid patients had higher TC and LDL-C level compared with euthyroid populations.[22] Another study in Austria did not find these differences.[23] In a meta-analysis of sixteen studies most of the studies reported increased levels of TC, LDL-C and TG in hypothyroid patients with statistically significant results. Among sixteen studies only one reported higher levels of HDL-C while in three studies HDL-C levels were lower and results were not statistically significant.[24] In another study it was found that HDL cholesterol was significantly decreased in subclinical hypothyroidism compared to the controls (P<0.01). With thyroxine therapy, normalization of serum TSH was associated with (1) no significant change in total cholesterol and triglycerides, (2) an increase of HDL cholesterol (P<0.01) and apoprotein A1 (P<0.05) levels.[29]

CONCLUSION

Female to male ratio was 12:1. High density lipoprotein cholesterol was found to be raised in 57.69% patients. Anti-thyroid peroxidase antibody was the commonest antibody detected. About one fifth of patients had interferon induced hypothyroidism.

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