ORIGINAL ARTICLE

To Determine Frequency of Dyslipidemia in Primary Hypothyroid Cases of Local Community

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ABSTRACT

Background: Hypothyroidism is associated with dyslipidemia in form of raised total cholesterol (TC), low density lipoprotein (LDL-C) Apo-lipoprotein (A and B), triglycerides and high density lipoprotein cholesterol (HDL-C)[1,] thus associated with cardiovascular morbidity and mortality[2]. Dyslipidemia is a potent risk factor for atherosclerosis and coronary artery disease (CAD), which in turn is the most common cause of death worldwide[3].

Aim: To determine frequency of dyslipidemia in primary hypothyroid cases" of local community.

Place and duration of study: Study conducted at Atomic energy Centre(outpatient) JPMC, Karachi in six months duration form 25th May 2006 to 24th November 2006.

Methods: The study is performed on 100 newly diagnosed cases of primary hypothyroidism between ages 25 to 55 years (for male 45) years, having no history of Ischemic Heart Disease (IHD) or family history of premature CAD, diabetes mellitus (DM), hepatic or renal disease, not on drugs which could alter serum lipids. Selected case undergone 14 hours fasting lipid profile check.

Results Frequency of dyslipidemia was high in hypothyroid cases, 91% had raised triglyceride levels more common in male hypothyroids and directly proportional to severity of hypothyroidism.

Conclusion Hypothyroidism is associated with high frequency of dyslipidemia and thus higher risks of CAD.

Keywords: Primary Hypothyroidism, thyroid hormones, thyroid stimulating hormone, lipoproteins

INTRODUCTION

Thyroid disease and lipid disorders; in terms of hypercholesterolemia, was described more than 70 years ago. Since then the association between thyroid disease and lipid disorders has been well-established[4]. Thyroid hormone TH (T3 and T4) have profound effects on development, differentiation, growth, and metabolism of body, required for the normal function of nearly all tissues. Disorders of the thyroid gland are among the most common endocrine maladies. According to one estimate, 15/1000 females and 01/1000 males are affected worldwide.[5] In Pakistan thyroid diseases are common and incidence of hypothyroidism is twice that of hyperthyroidism, but exact burden of the disease cannot be estimated due to lack "of available data[6]. Hypothyroidism is a clinical syndrome, which results from deficient secretion of thyroid hormone(TH). Primary hypothyroidism results from decrease in thyroid hormone secretion caused by damaged, defective, or absent thyroid gland, autoimmune thyroiditis is the commonest cause, others include iodine deficiency, previous thyroid surgery, irradiation and drugs. Secondary hypothyroidism results from deficiency of pituitary or hypothalamic stimulus. Most serious complication of hypothyroidism in elderly is cardiovascular complications. These cardiovascular complications occur by multiple mechanisms, including effects of thyroid hormone on lipid metabolism, homeostatic mechanisms, and homocysteine levels, effects on cardiac and vascular smooth muscles. Thyroid hormones regulate the activity of some key enzymes in lipoprotein transport including LPL, HDL and LDL receptors and it has been proved that thyroid hormone have significant effects on synthesis mobilization and metabolism of lipids. Absence of these hormones lead to abnormally raised serum lipids[7]. Dyslipidemia which is defined as "Disorder of lipoprotein metabolism including it's over production or deficiency, manifested by elevation of TC, LDL and TGs concentration and decrease in HDL-C concentration. It is of two types primary and secondary. Primary dyslipidemia results from genetic abnormalities and presents as familial hypercholesterolemia. Secondary dyslipidemia results from metabolic syndromes like DM, hypothyroidism, smoking, hepatic, renal diseases and drugs like statins, oral contraceptive pills, beta-blockers, diuretics and thyroxine[8]. Dyslipidemia is a potent risk factor for atherosclerosis and CAD and thus cardiovascular deaths[9]. It has been reported that the prevalence of clinically significant vascular disease is four times greater in patients with

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dyslipidemia than in normal subjects, thus increase in lipid levels has been recognized as an independent and direct risk factor for CAD and most important modifiable risk factor where early diagnosis and therapy are concerned[10].

MATERIALS & METHODS

This cross sectional study was conduceted during six months from 25th May 2006 to 24th November 2006 on patients attending thyroid clinic (outpatient) of Atomic energy Centre. JPMC Karachi. The atomic energy Centre ran thyroid clinic thrice a week on outpatient basis. On average 2150 patents reported for thyroid related complaints in six months duration from 25-5-2006 to 25-11-2006 out of which 200 patients were newly diagnosed cases of primary Hypothyroidism for study 100 patients fulfilling Inclusion and exclusion criteria selected for study. Non – probability purposive sampling technique was used. All newly diagnosed, untreated cases of primary hypothyroidism males from 25 to 45 years age and female from 25 to 55 years of age were included in the study.

Exclusion criteria:

1. All patients with secondary hypothyroidism (low levels of both TSH and FT3 and FT4)
2. All patients with diabetes mellitus.
3. All patients with nephrotic syndrome.
4. All patients with IHD and family history of premature CAD.
5. All patients with three months history of use of pharmacological agents as levothyroxine, B-blockers, anabolic steroids, diuretics, oral contraceptives and statins. .

Data collection procedure: Newly diagnosed, untreated but registered cases of primary hypothyroidism fulfilling inclusion exclusion criteria included in study. Diagnostic criteria of primary hypothyroidism was taken as TSH level >4.05mlU/L, and FT4 level <0.89 mlU/L, according to values recommended by laboratory of Atomic Energy Centre, JPMC, by using Kit of Immunotech Backman Coulter Company. Immuno-radio metric assay in vitro was the method applied for. Upper age limit of the patients was chosen to avoid age related dyslipidemia. Secondary hypothyroidism was excluded on basis of TSH and FT4 levels. Diabetes mellitus was excluded out by checking fasting sugar as per American Diabetic Association (ADA) criteria. Nephrotic syndrome was excluded on basis of negative history and examination and 24 hour urinary protein loss in suspected cases. IHD and family history of premature coronary heart disease was excluded on basis of history and ECG findings.

In all selected cases 14 hours fasting lipid profile including TC, LDL-C, HDL-C and TGs checked in mg/dl of serum. Informed consent was taken from all patients. Information regarding variables: age, gender, smoking status, BMI, serum TSH, FT4 levels in mlU/L and serum lipid profile level were collected on proforma.

Data analysis procedure: The filled on proforma were converted into database on SPSS number 10.0. For description purpose variables were divided into categories. Hypothyroidism divided into mild, moderate and severe groups, on basis of TSH in mlU/L as: mild (4.05-13), moderate (14-24) and severe (>24). Serum. TC, LDL-C, HDL-C and TGs levels were classified into desirable, near optimal, borderline, high and very high levels. Significance of this classification was to highlight the association or risk of CAD. Patients were labeled as dyslipidemia whose two or more than two values of lipid profile were raised (above desirable or near optimal values).Thus results were analyzed in the form of qualitative variables. Serum. TC, LDL-C, HDL-C and TGs levels were classified into desirable, near optimal, borderline, high and very high levels according to the classification given by National Cholesterol Education Program, adult Panel III (NCEP ATP III) which is based on the role of abnormal lipid profile as a risk factor of CAD.

The total dyslipidemia was presented by theirs frequencies and percentages and with 95% confidence interval patterns of dyslipidemia were presented as frequencies and percentages and Mean + SD. P-value and Chi- square test were applied for al variables to achieve the objective of study. In all statistical analysis, only P-value < 0.05 considered as significant.

RESULTS

In our study, patients selected according to inclusion and exclusion criteria. Total number of patients was 100. Results were divided into two main parts, first part is showing frequency of dyslipidemia in study population and second part shows its patterns especially with respect to age, gender, smoking, BMI and severity of hypothyroidism.

Out of 100 cases 91(91%) cases had dyslipidemia. Cases having dyslipidemia were those in which two out of four lipid categories including TC, LDL-C, HDL-C, and TGs, were found to be above desirable or near optimal values. The upper and lower limits of these values were set according to classification given by NCEP adult panel III

Patterns of Dyslipidemia: According to chronological order of distribution of dyslipidemia, out of 100 cases of primary hypothyroidism; 97% had raised TGs levels, 75% had raised HDL-C levels,

74% had raised TC levels, and 34% had raised LDL-C levels, irrespective of their age, gender, smoking status, BMI and severity of hypothyroidism.

Risk of cardiovascular disease is directly proportional to raised levels of above lipids. Thus above results support the hypothesis that hypothyroidism is associated with higher degree of dyslipidemia, which indirectly makes hypothyroidism a strong risk factor for CAD and "atherosclerosis.

Out of 100 cases f hypothyroidism 97(97%) cases had raised TGs levels, 3 (3%) had desirable, 20 (20%) had borderline, 76(76%) had high and 1(1%) had very high TGs levels. Out of 82 women 79 (96.3%) and out of 18 males 18(100%) had raised TGs levels irrespective of serum TSH levels. Mean raised TGs level out of 97 cases was 360.4±77.3mg% for males and 290.14±78.5mg% for female, statistically significant raised levels in males than females. (P-value 0.002) (Table 2).

Out of 100 cases of hypothyroidism 75(75%) cases had raised HDL-C levels. Among which 60(73%) are female and 15(83%) are males. Mean raised HDL-C level out of 75 cases was 47.0±17.0 mg% in males and 39.7±8.1mg% in female, with statistically significantly raised levels in males than female (P-value 0.03) (Table 3). This favors the theory that male gender itself is a risk factor of IHD and is according to available literature.

Here it is important to mention that as HDL-C is cardio protective, risk of CAD is inversely proportional to HDL-C levels, less the level of HDL-C more will be the chances of CAD.

Out of 100 cases of hypothyroidism, 34(34%) had raised LDL-C levels out of which 28(34%) were female and 6(33%) were males. Mean LDL-C level was 166.8±37.1mg% in male and 166.8±26.9mg% in male. P-value was 0.99 showing no statistically significant gender different (Table 4).

Out of 100 cases, 74(74%) had raised TC levels. 16(88%) of them were male and 58(70%) of them were female. Mean raised TC out of 74 cases was 292.3±75.5 mg% in male and 273.0±46.21 mg% in female with value 0.2, showing no statistically significant gender difference in distribution (Table-5).

Out of 51 severely hypothyroidism cases 100% and dyslipidemia 88% of moderately hypothyroid cases had dyslipidemia while 75% of mildly hypothyroid cases had dyslipidemia. This shows that dyslipidemia in case of hypothyroidism was directly proportional to severity of dyslipidemia and is statistically significant (p-value=0.002) and chi-square test value was 12.82 (Table-6)

Table1: NCEP Adult panel III Classification of LDL, Total cholesterol, HDL Cholesterol and triglycerides (mg/dl)

Classification of lipids	**TC mg%**	**LDL-C mg%**	**HDL-C mg%**	**TGs mg%**
Desirable	<200	<100	>60	<150
Near optimal	-	100-129	Higher value is better	-
Borderline high	200-239	130-159	-	150-199
High	240 and above	160-189	59-40	200-499
Very high	-	190 and above	<40 major risk factor	500 and above

Table 2: Distribution of triglycerides in hypothyroid cases

Triglyceride (mg%)	**Male (n=18)**	**Female (n=82j**	**Total (n=100)**
Desirable (<150)	-	3 (3.7%)	3 (3%)
Borderline (150-199)	3 (16.7%)	17 (20.7%)	20(20%)
High (200-499)	14 (77.8%)	62 (75.6%)	76(76%)
Very high (500 & above)	1 (5.5%)		1(1%)
Raised TGs(mg %)	360.4±77.3 (n=15)	290.14±78.5 (n=69)	p=0.002 (t=3.14)

Table 3: Distribution of HDL-c in hypothyroid cases

HDL-C (mg %)	**Male (n=18)**	**Female (n=82)**	**Total (n=1**00)
Desirable (>60)	3(16.7%)	22 (26.8%)	25 (26%)
High (59-40) ,	3 (16 7%)	32 (39.0%)	35 (35%)
Very high (<40)	12 (66.7%)	28 (34.1%)	40 (40%)
Raised HDL-C(mg %)	34.3+9.8 (n=15)	39.7±8.1 (n=6)	**p**=0.03(t=2.22)

Table 4: Distribution of ldl-c in hypothyroid cases

LDL-C (mg %)	**Male (n=18)**	**Female (n*82)**	**Total** (n**=100)**
Desirable **(<100)**	4 (22.2%)	31 (37.8%)	**35 (35%)**
Near optimal **(100-129)**	8 (44.4%)	23 (28.0%)	31 (31%)
Borderline **(130-159)**	4(22.2%)	14(17.1%)	18 (18%)
High (160-189)	-	8 (9.8%)	8(8%)
Very high **(190** & above)	2(11.1%)	6(7.3%)	8 (8%)
Raised LDL-**C** cases(mg%)	**166.8**±37.l (n=6)	166.8±26.9 n=28	p=0.99 t=0.002

Table 5: Distribution of total cholesterol in hypothyroid cases

Total Cholesterol category	**Male (n=18)**	**Female (n*82)**	**Total** (n**=100)**
Desirable (<200mg%)	2(11.1%)	24 (29.3%)	26(26%)
Borderline (200-239mg%)	4 (22.2%)	18(22.0%)	22(22%)
High (240 & above rng%)	12 (66.7%)	40 (48.7%)	52(52%)
Raised TC (mg%):	292.3±75.54 (n=16)	273.0±46.21 (n=58)	p=0.21 (t=1.23)

Table 6: Distribution of dyslipidemia according to severity of hypothyroidism

Hypothyroidism	**n**	**Dyslipidemia Case**
Mild	24	18(75.0%)
Moderate	25	22 (88.0%)
Severe	51	51 (100%)
Total	100	91

P-value= 0.002 Chi-square test=12.82

DISCUSSION

Hypothyroidism is a common disorder in general population and one of the most serious complications of hypothyroidism is cardiovascular diseases. There are multiple ways of developing these cardiovascular complications but most important of them is by producing atherosclerosis and CAD[9]. Atherosclerosis also occurs by multiple means but most important and highly studied mechanism is by causing dyslipidemia. Dyslipidemia in case of hypothyroidism needs only levothyroxine along with lifestyle changes to correct while dyslipidemia due to other causes like diabetes mellitus, renal and hepatic causes and genetic causes (primary dyslipidemia) need other interventions for correction. Thus, it is important to evaluate frequency of dyslipidemia in hypothyroid cases in our local population.

In this study, 100 cases of newly diagnosed, untreated cases of hypothyroidism were selected. Out of 100 cases, 91(91%) cases had dyslipidemia. These cases were labeled dyslipidemia on the basis of two or more than two raised levels of either of following four variables; (TC, LDL-C, HDL-C and TGs levels in mg%).

Out of 100 cases of hypothyroidism 97% had raised TGs levels. This is a large figure. Dyslipidemia is associated with hypothyroidism but such high number needs further studies in a relatively large population to justify and to detect some other possible explanations of such high levels of TGs in hypothyroid cases. In addition, mean raised TGs level among 97 cases was 360.4±77.3mg% for males and 290.14±78.5mg% for female, statistically significantly higher in males than females (P-value=0.002). It indicates that male gender has an association with raised TGs. How much hypothyroidism contributes in it, this needs some comparative studies to see serum TGs between normal males and hypothyroid males.

HDL-C has inversely proportional relation with CAD. Thus less the amount of HDL-C more is the chances of CAD. NCEP ATP III has classified its levels according to risk of CAD, according to which high and very high shows risk rather than actual serum levels. Thus according to that classification in our study out of 100 cases, 75% had raised HDL-C, mean raised HDL-C levels were (34.3+9.8mg%) among males and 39.7+8.1 among females with statistically significant gender difference (P-value=0.03) more significant among males than female.

Out of 100 cases 34%, cases had raised LDL-C, 18% had borderline high, 8% had high and 8% had very high LDL-C levels. Mean raised LDL-C among males was 166.88+37.1% and 166.8+26.9mg% among females with no statistical significant gender difference (P value = 0.99).

74% cases also had raised TC which is also high figure. Mean raised TC among 74 cases was 292.3 4±75.54mg% in males and 273.0+46.21 mg% in females. However statistically non-significant, but values show relatively higher levels in males than females. Statistically non-significant gender difference (P-value=0.21) but overall increased in males than female.

Except TGs, which turned to be very high in our study, rest of the results follows the available literature. We have got eye opening results through this study which shows a very high frequency of dyslipidemia in our cases. Possible explanation of this is that majority of cases had moderate and severe hypothyroidism (22% and 51%) respectively. According to literature available, more severe, the hypothyroidism more severe will be the dyslipidemia.

The overall impression of our study is that hypothyroidism is associated with high frequencies of dyslipidemia and its patterns are highly dependent upon severity of hypothyroidism as per literature10. This was a small sample size study; there is a need of large population based studies to justify the results and recognition of new aspects of dyslipidemia in these cases. We can prevent a large number of patients from having cardiovascular disease simply

by replacing thyroid hormone therapy and life style modification. Further research work is required to find new risk factors of cardiovascular disease in our community like hyperhomocystenemia, and hemostatic abnormalities in these cases.

CONCLUSION

Very high frequencies of dyslipidemia found in hypothyroidism directly proportional to severity of hypothyroidism and male predominance which increases the risk of atherosclerosis and CAD in these cases. Chronological order of commonest presentation of dyslipidemia was raised TGs, HDL-C, LDL-C and TG respectively. Frequency of dyslipidemia favors current literature however to study patterns of dyslipidemia in different communities, may need further studies on relatively larger sample sizes. We can prevent a large number of patients from having cardiovascular disease simply by replacing thyroid hormone. Further research work is required to find new risk factors of cardiovascular disease in our community like hyperhomocystenemia, and hemostatic abnormalities in these cases.

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