

DYSLIPIDEMIA IN HYPOTHYROIDISM PATIENTS: A HOSPITAL BASED CASE AND CONTROL STUDY.

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Abstract

Objectives: This present study was to evaluate the incidence and abnormalities in lipid profile in patients with hypothyroidism.

Methods: A detail history, clinical examinations and relevant investigations were performed to all subjects. Serum free T₃ (fT₃) and T₄ (fT₄) were measured by competitive enzyme-linked immunosorbent assay (ELISA) method. Serum TSH was measured by sand-witch ELISA method. Serum cholesterol was measured by cholesterol oxidase-peroxidase (CHODPAP) method. Serum triglyceride was measured by glycerol-3-phosphate oxidase (GPO) method. Serum VLDL (in mg/dl) was calculated by dividing the value of TG by 5. Serum LDL value was calculated by Fried-Wald equation. And serum HDL level was calculated by precipitation method.

Results: Data was analysed by using software SPSS 15.0. Independent t-test was applied. Mean and standard deviations were observed. P-value was taken equal to or less than 0.05 for significant differences (p≤0.05).

Conclusions: Hypothyroidism was commonly seen in elderly age group subjects. Females were more preponderance than males. Hypercholesterolemia, hyper triglyceridemia and increased LDL-cholesterol & VLDL-Cholesterol were extremely significant associated with hypothyroidism. Hence, hypothyroidism has an importantly associated with abnormal lipid profile. Therefore, biochemical screening for thyroid dysfunction should be perform in all dyslipidemic patients. Early diagnosis should be made for proper treatment of dyslipidemia in hypothyroidism patients.

Keywords: hypothyroidism, dyslipidemia, age, sex.

Introduction:

Hypothyroidism is a condition of thyroid dysfunction in which less amount of thyroid hormones are produced by thyroid gland, such subjects eventually will lead to have lower metabolic rate and clinical manifestation such as overweight, fatigue, hypotension and depression [1,2]. The serum TSH assay is an accurate test for detecting out of range circulating levels of thyroid hormones for either of hypothyroidism and hyperthyroidism [3]. The prevalence of thyroid dysfunction is determined by testing patients in geo-graphic areas, primary care clinics, and in populations that have not been screened previously [4]. Thyroid function significantly affects lipoprotein metabolism as well as some cardiovascular disease (CVD) risk factors [5]. Thyroid hormones can influence HDL metabolism by increasing cholesteryl ester transfer protein (CETP) activity, which exchanges cholesteryl esters from HDL to VLDL and Tg to the opposite direction [6]. 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 [7,8]. Another effect of T3 is the up-regulation of apolipoprotein AV (ApoAV), which plays a major role in Tg regulation [9]. Indeed, increased levels of ApoAV have been associated with decreased levels of Tg [10]. Thyroid hormones are the principal regulators of energy balance. Their role in obesity has been the focus of various scientific studies. The unfavourable effects of high levels of serum TSH on the lipid metabolism have been reported and follow-up studies have shown an increase in the risk of development of atherosclerosis and cardiovascular manifestations in clinical hypothyroid subjects with high normal serum TSH levels [11,12,13]. Objectives of our study was to evaluate the lipid profile abnormalities in patients with hypothyroidism.

Material & Methods

This present study was conducted in Department of Biochemistry, with the collaboration of Department

of Medicine, Katihar Medical College and Hospital, Katihar, Bihar, India during a period from November 2018 to July 2019.

Attendants/patients signed an informed consent approved by institutional ethical committee of Katihar Medical College, Katihar, Bihar, India was sought.

Data was collected with irrespective of age and sex by simple random methods. This present study had categorised into two groups (case & control). Case group had 50 patients of hypothyroidism. And control group had 50 normal euthyroid subjects. And it was assured that selected control group subjects were not suffered from any endocrine or metabolic disorders.

Methods:

Blood was drawn from antecubital vein after overnight fasting from both the cases and controls. Serum was prepared and was made ready for measurement of following parameters: -

Serum free T_3 (fT_3) and T_4 (fT_4) were measured by competitive enzyme-linked immunosorbent assay (ELISA) method. Serum TSH was measured by sandwich ELISA method. Serum cholesterol was measured by cholesterol oxidase-peroxidase (CHODPAP) method. Serum triglyceride was measured by glycerol-3-phosphate oxidase (GPO) method. Serum VLDL value (in mg/dl) was calculated by dividing the value of TG by 5. Serum LDL value was calculated by Fried-Wald equation. And serum HDL value was assessed by precipitation method.

Normal range of free T_3 (fT_3) in adult and pregnant women are 1.4-4.2 pg/ml and 1.8-4.2 pg/ml respectively. Normal Range of free T_4 (fT_4) [105] in adult and pregnant women are 0.8-2.0ng/dl and 0.76-2.24ng/dl respectively. Normal range of TSH [108] is 0.39- 6.16 μ IU/ml. Reference range of total cholesterol concentration in serum (mg/dl) [110, 113] are as desirable : <200, borderline high : 200-239, high risk: \geq 240. Reference range of HDLs concentration in serum (mg/dl) are as low risk: \geq 60, high risk \leq 40. Reference range of triglyceride [113] concentration in mg/dl are as normal :< 150' borderline high: 150-199, high: 200-499 and very high: \geq 500.

Statistical Analysis

Data was analysed by using software SPSS 15.0. Independent t-test was applied. Mean and standard deviations were observed. P-value was taken equal to or less than 0.05 for significant differences ($p \leq 0.05$).

Observations

Table 1: Showing the age distribution in cases of hypothyroidism and controls.

Age Interval	Cases		Control	
	Frequency	%	Frequency	%
20 – 40	57	57	72	72
41 – 65	43	43	28	28
TOTAL	100	100	100	100

In this present study, majorities of patients in case (57%) and control (72%) were belonged in age group of 20-40 years.

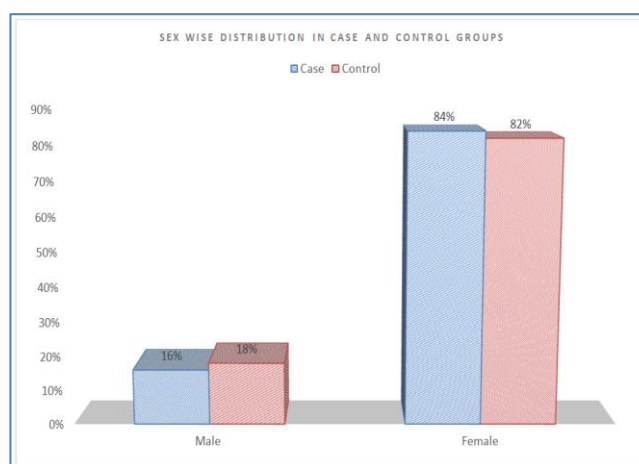


Figure 1: Showing the sex distribution in frequency and in percentage between the cases of hypothyroidism and controls.

In this study majorities of cases were females in both case 42(84%) and control 41(82%) groups.

Table 3: Various parameters of cases in case and control groups.

Parameters	Case group (mean \pm S.D.)	Control group (mean \pm S.D.)	t-value	p-value
Age	47.44 \pm 8.725	39.12 \pm 9.299	4.614	<0.0001
fT_3	2.149 \pm 0.547	2.206 \pm 0.552	0.521	0.6036
fT_4	0.957 \pm 0.241	1.288 \pm 0.253	6.680	<0.0001
TSH	34.038 \pm 13.002	1.758 \pm 0.671	17.532	<0.0001
T CHOL	327.834 \pm 47.512	137.388 \pm 12.569	27.401	<0.0001
HDL CHOL	53.746 \pm 6.710	42.240 \pm 5.385	9.456	0.0001
Triglyceride	298.706 \pm 77.298	148.366 \pm 12.259	13.583	<0.0001
VLDL CHOL	59.122 \pm 15.818	30.311 \pm 2.559	12.714	<0.0001
LDL CHOL	215.147 \pm 42.355	65.564 \pm 11.549	24.093	<0.0001

And mean age of cases and control was 47.44 ± 8.725 and 39.12 ± 9.299 years respectively. P -value was found to be <0.0001 . Which is extremely significant?

Mean fT3 level in case and control groups was 2.149 ± 0.547 and 2.206 ± 0.552 respectively. P value was found to be 0.6036. This is not statistically significant differences.

When mean \pm standard deviation of fT4 in case and control group was compared. P value was found to be 0.0001. it was seen that data was extremely significant difference.

When mean \pm S.D of TSH levels in case and control groups was compared. P value was found to <0.0001 . It shows that data is extremely significant.

When mean \pm S.D of total cholestrol levels in case and control groups was compared. P value was found to <0.0001 . It shows that data is extremely significant.

When mean \pm S.D of HDL CHOL levels in case and control groups was compared. P value was found to be 0.0001. It shows that data is significant difference.

When mean \pm S.D of triglyceride levels in case and control groups was compared. P value was found to <0.0001 . It shows that data is extremely significant.

When mean \pm S.D of VLDL-cholestrol levels in case and control groups was compared. P value was found to <0.0001 . It shows that data is extremely significant.

When mean \pm S.D of LDL-cholestrol levels in case and control groups was compared. P value was found to <0.0001 . It shows that data is extremely significant.

Discussions

Thyroid hormones play an important role in synthesis, mobilization and metabolism of lipids [14]. Therefore, hypothyroidism is a major cause of secondary dyslipidemia. Investigations report elevated levels of TC and LDL-C in patients with overt hypothyroidism. These patients may also present elevated to normal levels of TG and HDL-C [15]. In subclinical hypothyroidism (SCH), there is an elevation in thyroid stimulating hormone (TSH) with normal levels of thyroxine (T4) and triiodothyronine (T3) [16]. This condition which is more common in women and older populations may progress to overt hypothyroidism [17].

This present study had categorised into two groups (case and control). 50 patients with hypothyroidism

were enrolled in case group and 50 normal euthyroid subjects were enrolled in control group.

Mean age of patients with hypothyroidism was 47.44 ± 8.725 years. Mean age of euthyroid Controls group was 39.12 ± 9.299 years. An extremely significant differences was between mean age of case and control groups ($p < 0.0001$). And most of the cases were belonged in age group 20 to 40 years.

Our findings supported the findings of Sanjoy K Bhandopadyay et al [18]. In their study, mean age case was 38.56 years.

This present study showed female predominance with 84%. Only 16% of total study population was males. This was similar to the study by Sanjoy K Bhandopadyay et al [18] where females constituted 78% of study populations.

Cases had a mean total fT3 value of $2.149 \pm .547$ pg/ml and control had 2.206 ± 0.521 . p value was found to be 0.6036. It shows that fT3 levels between cases & controls is not statistically significant. This is an expected finding because; peripheral deiodination of T4 to T3 is unaffected in subclinical hypothyroidism. Study by Salmon Rizvi et al [19] has yielded similar results. This may be due to subjects of hypothyroidism were taken L-thyroxin. Mean fT4 levels among patients of hypothyroidism was 0.957 ± 0.241 ng/dl while the level of fT4 among normal subject were 1.288 ± 0.253 ng/dl. This increased value of fT4 among subjects was extreme statically significant with p-value < 0.0001 . fT4 levels in cases were towards the lower limit of normal range.

This was similar to a study by Krishnaveni. D.V [20] in their study the mean value of total T4 was 2.73 ± 1.88 μ g/dl as compared to their control group where it was 7.75 ± 1.72 μ g /dl. The changes were statistically significant with p-value less than 0.001.

In present study shows mean TSH values of cases was 34.038 ± 13.002 μ IU/ml while the value among control was remained 1.758 ± 0.671 μ IU/ml.

Mean value of Total cholesterol among the subjects of hypothyroidism was 327.834 ± 47.512 mg/dl and control was 137.388 ± 12.569 . This was highly increased to the normal levels and the elevation of Total cholesterol was statistically highly extreme significant when compared with their normal counterparts with p value < 0.0001 .

This study was similar to the study by Krishnaveni. D. V [20] in their study Total Cholesterol level in cases of hypothyroidism was 266.50 ± 47.60 in mg% when compared to controls and in this group level of Total Cholesterol was 175 ± 17.62 in mg% . This was statistically very significant with P-value was less than 0.000.

In this present study, mean HDL-cholesterol levels in hypothyroid patients was 53.746 ± 6.710 mg/dl. While the level of HDL-Cholesterol among control group had 42.240 ± 5.385 mg/dl. This increase in HDL-Cholesterol was significant difference when compared with the normal subjects with p-value 0.0001.

Heimberg M. et. al., found that hypothyroid patients usually exhibits elevated levels of HDL-Cholesterol mainly due to increased concentration of HDL-2 particles [2]. In another study it was found that the decreased Activity of CETP results in reduced transfer of cholesteryl ester from HDL-Cholesterol to VLDL-Cholesterol, thus increasing HDL-Cholesterol level [22].

Kong et al [26] have shown mean HDL-cholesterol value was 39 mg/dl. Rajan et al [23] have shown HDL value of 41.5mg/dl which was not statistically significant.

In present study, the mean value of serum triglyceride in subjects with normal thyroid function (control group) was 148.366 ± 12.259 mg/dl. The levels were significantly increased and went up to 298.706 ± 11.37 mg/dl among the subjects with the hypothyroidisms. Which was statistically extreme significant as compared to controls with a p-value < 0.0001. In patients of hypothyroidism activity of lipoprotein lipase in adipose tissue has been found normal or decreased, in addition to decreased hepatic lipase activity resulting in normal or high levels of triglycerides [24,25]. In different study Kong et al [26] reported mean value of triglyceride was 159mg/dl. And William J. Hueston et al [21] have shown mean triglyceride value of 178.1mg/dl in their study. The value of LDL-Cholesterol was higher among the subjects with hypothyroidism as compared to control groups. Control group had mean LDL-cholesterol level was 65.564 ± 11.549 mg/dl which was elevated up to 215.147 ± 42.355 in the patients of hypothyroidism. This increase in LDL-Cholesterol level was extremely significant with p-

value less than 0.0001. This finding was similar to the study done by Krishnaveni.D. V [20] in their study level of LDL-cholesterol in cases of hypothyroid patient was 203.76 ± 50.11 in mg% as compared to control group which was 118.23 ± 15.46 mg%. This was very significant statistically with p-value was less than 0.00001.

Rajan et al [23] have shown mean LDL value of 134mg/dl with statistical significance. Tromso study [27] also demonstrated elevated LDL-cholesterol levels which came down after treatment. In Present study the value of VLDL-Cholesterol in subject without hypothyroidism was 30.311 ± 2.559 which was significantly increased to 59.122 ± 15.818 mg/dl in case of subjects with hypothyroidism with p-value less than 0.0001. Krishnaveni. D.V. [20] done a study on hypothyroid patients and in her study value of VLDL-cholesterol was statistically significant. Hypertriglyceridemia associated with increased levels of VLDL and occasionally fasting chylomicronemia are found less commonly in hypothyroidism these changes are attributable to the decreased activity of LPL. Decreased thyroid secretion greatly increases the plasma concentration of triglycerides [28]. Nikkila & Kekki [29] have stated that hypertriglyceridemia in hypothyroidism is due to decreased activity of lipoprotein lipase (LPL), which results in decreased clearance of triglyceride-rich lipoproteins.

Conclusions

This present study concluded that the hypothyroidism was commonly seen in elderly age group subjects. Females were more preponderance than males. Hypercholesterolemia, hyper triglyceridemia and increased LDL-cholesterol & VLDL-Cholesterol were extremely significant associated with hypothyroidism patients. Hence, hypothyroidism has an importantly associated with abnormal lipid profile. Therefore, biochemical screening for thyroid dysfunction should be perform in all dyslipidemic patients. Early diagnosis should be made for proper treatment of dyslipidemia in hypothyroidism patients.

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