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CHANGES IN ELECTROLYTE AND LIPID PROFILE IN HYPOTHYROIDISM

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ABSTRACT

Hypothyroidism is known to affect electrolyte levels as well as lipids in circulation. Though the effect of deficiency of thyroid hormones on the lipid profile has been well established, the effect on electrolytes and certain minerals like calcium, phosphorus, magnesium is not clear and the underlying mechanisms responsible for these changes not well understood. The objective was to find out the effect of hypothyroidism on certain electrolyte & mineral levels and also on lipid profile.140 cases of overt hypothyroidism were chosen, 140 age and sex matched controls were chosen. Blood samples were collected from them and T3, T4 and TSH levels were measured. Also, Cholesterol, triglycerides, LDL, HDL, calcium, phosphorus, magnesium, sodium, potassium levels in blood was measured. It was found that cholesterol, triglyceride, LDL, HDL, magnesium and phosphorus levels were significantly elevated in hypothyroidism cases than the controls. The levels of calcium, sodium and potassium levels were significantly decreased in cases than controls.
It was also found that there was a significant positive correlation between serum TSH values and total cholesterol, triglyceride, LDL, HDL, magnesium, and phosphorus levels. At the same time, there was a significant negative correlation between serum TSH values and serum sodium, potassium and calcium levels. From this study, we were able to conclude that higher the TSH levels, higher will be cholesterol, triglyceride, LDL, HDL, magnesium and phosphorus levels in blood, and lower will be the values of serum calcium, sodium and potassium levels.

Keywords: Dyslipidemia, electrolytes, hypothyroidism, total cholesterol, triglycerides.

INTRODUCTION

Hypothyroidism is a clinical entity resulting from the deficiency of thyroid hormones or from their impaired activity (Hallengren B, 1998). Hypothyroidism is a common metabolic disorder in the general population. In India, 42 million people are suffering from thyroid diseases; hypothyroidism being the commonest thyroid disorder (Unnikrishnan AG and Menon UV, 2011). Thyroid hormones perform a wide array of metabolic functions including regulation of lipid, carbohydrate, protein and electrolyte and mineral metabolisms.

The most important effect on lipid metabolism includes mobilization of triglycerides from the adipose tissue causing increased concentration of free fatty acids in plasma. In patients with overt hypothyroidism there is an increase in serum total cholesterol (TC), Low Density Lipoproptein cholesterol (LDL-C),

Apolipoprotein B, Lipoprotein(a) levels and possibly triglyceride (TG) levels (Pearce EN, 2004).

The changes in protein metabolism include increased protein breakdown resulting in loss of muscle protein. The changes in carbohydrate metabolism include increased gluconeogenesis and glycogenolysis so as to generate free glucose. Thyroid hormone increases basal metabolic rate.

The dyslipidemia in hypothyroidism is accompanied by significantly elevated phosphate level (Al-Tonsi AA et al, 2004). Thyroid hormones are also believed to influence calcium metabolism (Begic-Karup S et al, 2001). Tereshchenko IV has analyzed the causes for Magnesium deficit in cases with hypothyroidism (Tereshchenko IV, 2008). Several studies have suggested that hypothyroidism could be a cause of hypokalemia (Kinoshita I et al, 1990). Schmitz PH et al have suggested that hyponatremia in hypothyroidism is due to a pure renal mechanism (Schmitz PH, 2001).

While the effect of thyroid hormones on lipid metabolism is well known, the effect on electrolytes and minerals has not been well established and also the underlying mechanisms not well understood. In this background the present study was undertaken to assess the dyslipidemia, alterations in the levels of serum electrolytes and the levels of calcium, phosphate, and magnesium levels in hypothyroidism. We also investigated the correlation between TSH levels and the serum concentration of lipids, electrolytes and minerals.

MATERIALS AND METHODS

140 cases of clinically established hypothyroidism were chosen. Biochemically, hypothyroidism was established based on low T3, low T4 and high TSH values in serum.

Inclusion criteria:

Age group: 18 – 75yrs

Exclusion criteria:

Pediatric age group
Renal disorders
Hepatic disorders
Bone diseases
Patients on medications such as diuretics, calcium, iron tablets, (anemics)
Diabetes Mellitus

Controls: 140 age and sex matched healthy controls were included in the study.

Method Of Analysis: 3ml of fasting venous blood sample was drawn from the cases and controls. Serum was separated and immediately tested for total cholesterol, triglycerides, LDL, HDL, sodium, potassium, calcium, phosphorus and magnesium.

Thyroid hormones were measured by Chemiluminescence Immunoassay method on Beckman Coulter Access 2 autoanalyzer. The lipids and minerals were analyzed on Beckman Coulter DXC autoanalyzer.

Results were tabulated. The Statistical software namely SAS 9.2, SPSS 15.0, Stata 10.1, MedCalc 9.0.1, Systat 12.0 and R environment ver.2.11.1 were used for the analysis of the data. The results of cases and controls were compared by student't' test. A p value of <0.05 was considered significant. A p value of < 0.01 was considered highly significant. All the parameters were compared with TSH levels. Pearson's correlation and t test of coefficient were calculated.

RESULTS

Clinical data was studied to find out the age and sex distribution of hypothyroidism in the selected population. It was observed that a highest number (32.1%) of patients belonged to the age group of 31-40 yrs. (Table I, Fig 1). We also observed that majority of the patients (75.7%) were females and 24.3% of the patients were males (Table II, Fig 2).

Table I: ***Age distribution***

Age in years	Cases		Controls	
	No	%	No	%
1-10	1	0.7	1	0.7
11-20	11	7.9	11	7.9
21-30	35	25.0	35	25.0
31-40	45	32.1	45	32.1
41-50	22	15.7	22	15.7
51-60	16	11.4	16	11.4
61-70	8	5.7	8	5.7
71-80	2	1.4	2	1.4
Total	140	100.0	140	100.0
Mean ± SD	37.77±14.01		37.82±13.34	

Samples are age matched with P=1.000

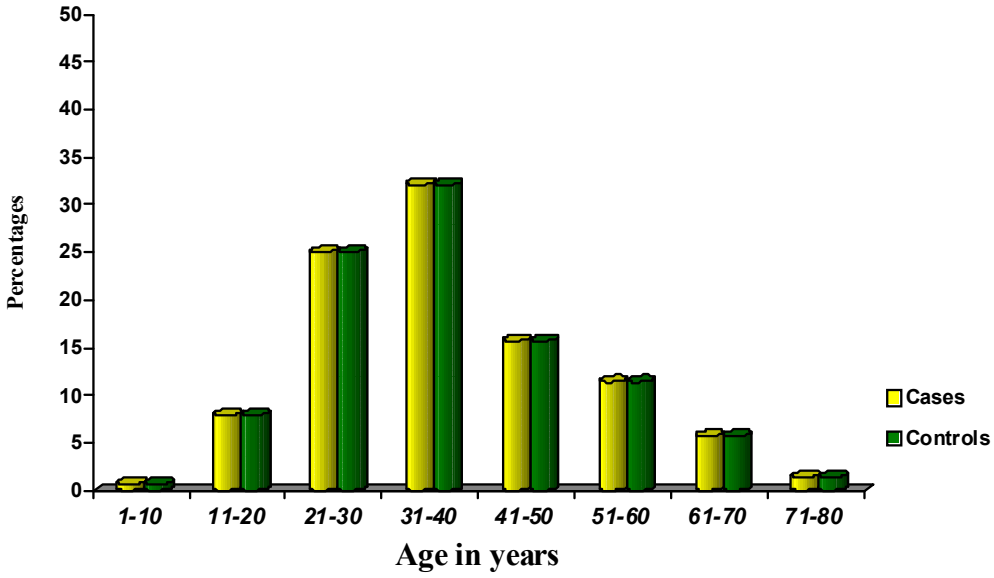

Fig 1: ***Graphical representation of distribution of age groups.***

Table II: ***Gender distribution***

Gender	Cases		Controls	
	No	%	No	%
Male	34	24.3	31	22.1
Female	106	75.7	109	77.9
Total	140	100.0	140	100.0

Samples are gender matched with p=0.671

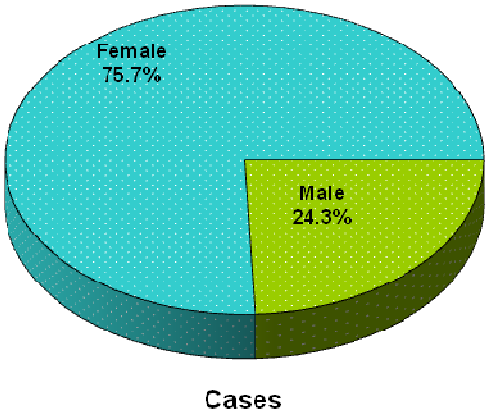

Fig 2: ***Diagramatic representation of gender distribution***

When the cases and controls were compared, there was a significant variation in the values between the two groups. All the lipids measured, namely total cholesterol, triglycerides, LDL and HDL were found to be significantly elevated in hypothyroid patients when compared to the controls ($p<0.001$). Figures 3 & 4 show graphical representations of serum total cholesterol and triglycerides levels respectively in hypothyroid cases in comparison with controls. Among the minerals, phosphorus and magnesium levels in serum were significantly elevated in patients with hypothyroidism when compared to controls ($p<0.001$). The levels of calcium and sodium were significantly decreased in cases when compared to controls ($p<0.001$) (Table III). However, serum potassium levels in hypothyroid patients were found to be less than that of controls but the difference was not statistically significant. Figures 5 & 6 show graphical representations of serum sodium and phosphorus levels respectively in hypothyroid cases in comparison with controls.

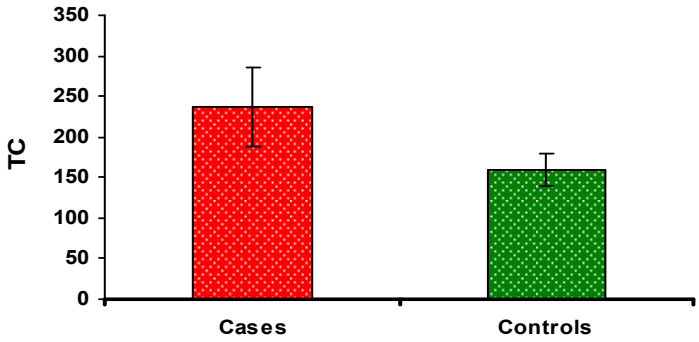

Fig3: ***Graph showing the comparison between serum Total cholesterol (TC) levels in cases and controls.***

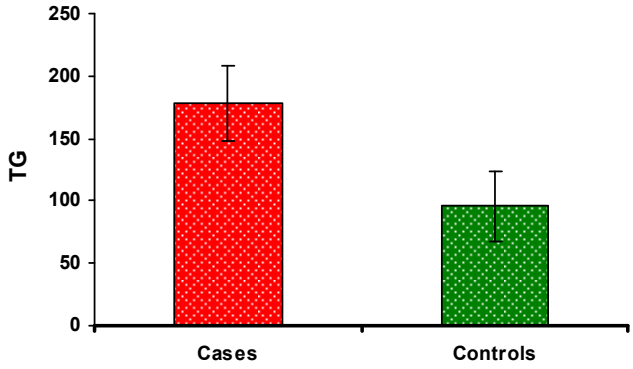

Fig4: ***Graph showing the comparison between serum Triglycerides (TG) levels in cases and controls.***

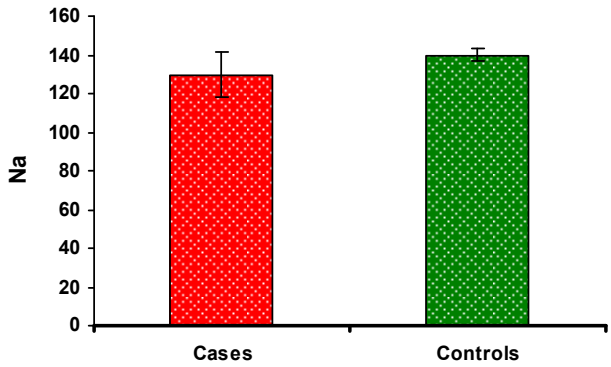

Fig5: ***Graph showing the comparison between serum sodium (Na) levels in cases and controls.***

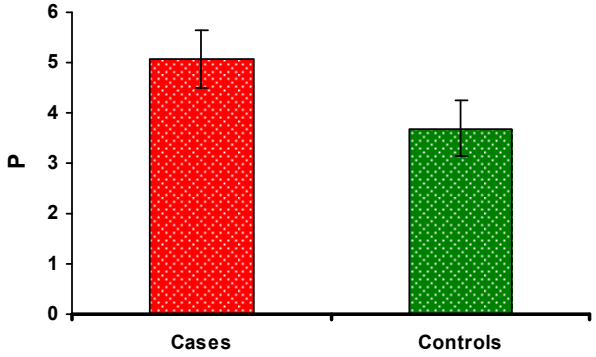

Fig6: ***Graph showing the comparison between serum phosphorus (P) levels in cases and controls.***

Table III: ***Comparison of Variables in two groups studied***

Lab variables	Cases	Controls	P value
T3	1.04±0.43	2.43±13.93	0.241
T4	6.42±3.14	8.61±1.91	<0.001**
TSH	25.65±27.4	2.85±1.20	<0.001**
Na	129.66±11.83	139.86±3.23	<0.001**
K	3.93±0.31	5.92±17.34	0.174
Ca	8.72±0.41	9.61±0.56	<0.001**
P	5.07±0.56	3.69±0.56	<0.001**
Mg	2.19±0.33	1.27±0.28	<0.001**
TC	236.78±49.49	158.75±19.85	<0.001**
TG	178.25±29.96	95.83±28.01	<0.001**
LDL	155.85±29.86	89.15±17.91	<0.001**
HDL	42.52±5.16	30.12±4.64	<0.001**

The serum TSH values of patients were studied in relation to the values of serum lipids, sodium, potassium, calcium, magnesium and phosphorus. On analyzing the values, a statistically significant positive correlation between serum TSH and cholesterol, triglyceride, HDL, LDL, magnesium and phosphorus levels was noticed ($p<0.001$). At the same, a statistically significant negative correlation between serum TSH and calcium, sodium and potassium levels was observed (Table IV).

Table IV: ***Correlation of TSH with other lab parameters***

Lab variables	Cases	
	r value	p value
Na vs TSH	-0.257	0.004**
K vs TSH	-0.274	0.002**
Cavs TSH	-0.862	<0.001**
P vs TSH	0.940	<0.001**
Mg vs TSH	0.789	<0.001**
TC vs TSH	0.920	<0.001**
TG vs TSH	0.846	<0.001**
LDL vs TSH	0.841	<0.001**
HDL vs TSH	0.871	<0.001**

DISCUSSION

Hypothyroidism is a condition in which the body suffers from insufficient thyroid hormone. Since thyroid hormones are involved in controlling various metabolisms, more importantly lipid metabolism and that of various electrolytes, the hypothyroid patient generally suffers from a slow metabolism resulting in dyslipidemias and electrolyte disturbances. Hypothyroidism is a very common condition and seen more in women than in men. Our study also indicates that majority of our patients were women and in the age group of 31 to 40 years.

Earlier statistics also have suggested that hypothyroidism is six times more common in women than in men. The higher prevalence of thyroid disease in women suggests that estrogen might be involved in the pathophysiology of thyroid dysfunction. Estradiol has an antagonistic effect on the hormones T3 and T4. The reason being, estradiol competes with T3 and T4 for binding sites on the receptor proteins (Vasudevan N et al, 2002). Moreover, estradiol also limits the thermogenic action of T4 and promotes storage of fat.

Gantus MA et al studied the effects of estrogen on a homogeneous stromal cell population (TS7 cells) of rat thyroid gland. Their results point to the cytokine transforming growth factor beta-1 (TGF-ß1) / transcription factor Smad-2 signaling pathway as a putative target of estrogen actions on thyroid stromal cells (Gantus MA et al, 2011).

Thyroid hormones have a significant role to play in metabolism of lipids. Any deficiency of thyroid hormones tends to cause hyperlipidemia, which is a known risk factor for development of atherosclerotic disease. In this study, we discuss the role of thyroid hormones on the levels of cholesterol, LDL-C, HDL-C and triglycerides and the pathogenic mechanisms underlying the same.

From our study it was observed that total cholesterol and LDL-C are elevated in cases of overt hypothyroidism. This finding supports other studies such as the one done by Chan Hee Jung et al in Seoul, Korea (Jung CH et al, 2003)**.** This is due to the fact that expression of LDL receptor is modulated by thyroid hormones. In a study done by Scarbottolo et al in experimental hypothyroid rats, it was demonstrated by ligand binding analysis that of a decreased expression of

lipoprotein receptors by the liver (Lia Scarabottolo et al, 1986). In another study done by Jiskra et al in 2007, the mechanism of dyslipidemia in hypothyroidism has been explained. In overt hypothyroidism, the number of LDL receptors in

the liver decreases and as a result, there is an increase in overall cholesterol and LDL cholesterol (Jiskra J et al, 2007). We also observed the elevation of triglycerides in overt hypothyroidism. This is due to the fact that there is poor clearance of endogenous and exogenous triglycerides from circulation in hypothyroidism (Tulloch BR, 1973).

HDL level was found to be increased in hypothyroid cases when compared to controls. The cause of normal or elevated levels of HDL in hypothyroid cases is due to reduced activities of Cholesterol Ester Transfer protein (CETP) and hepatic lipase (Jiskra J et al, 2007). This results in reduced transport of cholesteryl esters from HDL-2 to very low-density lipoproteins (VLDL) and intermediate density lipoprotein (IDL) (Leonidas HD, 2002).

Total calcium levels in serum were found to be significantly lowered in hypothyroid patients when compared to controls. Thyroxine normally regulates blood calcium levels by releasing calcium from the cells. In hypothyroidism, there is less thyroxine in the bloodstream; thus less thyroxine enters the cells and less calcium is released.

Our hypothyroid patients in the study exhibited significantly elevated levels of serum magnesium compared to the controls ($p<0.001$). The levels of magnesium also showed a significant negative correlation with the levels of TSH ($p<0.001$).

In a study done by Frizel et al, both plasma ionized magnesium and total magnesium levels were increased in hypothyroidism (Frizel D et al, 1967).

McCaffrey et al studied renal Calcium and Magnesium handling in rats with chronic thyroid hormone deficiency or excess. According to their study thyroid deficient rats reabsorbed 15-30% more of the filtered magnesium at any given plasma concentration because the thyroid hormone has a direct effect on the tubule which if chronically absent results in renal retention of magnesium (McCaffrey C and Quamme GA, 1984).

In the present study the serum phosphate levels were markedly increased in cases of hypothyroidism as compared to healthy controls (p value<0.001). There was a significant positive correlation between TSH and serum phosphate levels.

Al-Tonsi et al investigated the occurrence of dyslipidemia and altered serum phosphate concentrations in patients with thyroid disorders. Their results also indicated a significantly elevated serum cholesterol, triglyceride and phosphate levels in the hypothyroid patients (Al-Tonsi AA et al, 2004).

Hypothyroidism is one of the most prevalent endocrine diseases. It can lead to a variety of clinical situations, including congestive heart failure, electrolyte disturbances and coma. Hyponatremia is the most common electrolyte abnormality encountered in clinical practice (Kargili A et al, 2010).

In our study the serum sodium levels in cases was markedly decreased as compared to healthy controls. The result obtained in Table 3 indicates that the mean serum sodium levels in cases was 129.66+/-11.83, while in controls the mean serum sodium levels was 139.86+/-3.23 (p value < 0.001) There was a significant negative correlation between TSH levels and serum sodium levels in cases.

According to Saruta T et al Plasma Renin Activity (PRA) and Plasma Aldosterone (PA) may be suppressed in hypothyroidism probably due to dysfunction of juxtaglomerular cells and glomerulosa cells respectively and the possibility that suppression of PRA and PA in patients with hypothyroidism is related to exaggerated sodium excretion and decrease in potassium excretion cannot be ruled out (Saruta T et al, 1980).

Serum potassium levels were found to be decreased in hypothyroid patients when compared to controls, though it was statistically significant. But when potassium values were studied in relation to serum TSH values, a significant negative correlation was found (p= -0.002). Higher the value of TSH, lower was the level of serum potassium.

Sodium and potassium are important components of the enzyme Na-K ATPase, which is an enzyme on the cell membrane that helps in the transport of water and nutrients across the cell membrane. Thyroid hormones regulate the activity of sodium potassium pumps in most of the tissues (Ismail Beigi F and Edelman IS, 1971). In

hypothyroidism, because of low potassium levels, and because of deficiency of thyroid hormones, this enzyme is affected, resulting in accumulation of water inside the cells and causing edema. This is said to be one of the mechanisms responsible for weight gain seen in hypothyroid patients.

CONCLUSION

It has been shown in our study that hypothyroid patients have elevated atherogenic parameters and are at high risk for developing cardiovascular disorders. They also exhibited serum electrolyte disturbances such as low sodium, low potassium, low calcium levels and high magnesium and phosphorus levels.

Hence monitoring of serum levels of these electrolytes and lipid profile parameters during the follow up of hypothyroid patients will be of great benefit.

Also, electrolyte disturbances need to be monitored and treated appropriately in conditions such as myxedema coma to avoid the ill effects resulting from the changes in the serum levels of these cations.

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