DISCUSSION

After diabetes mellitus, thyroid disease represents the most common endocrine disorder (Ian D. Hay, 1988). A summary of goiter prevalence in Gujarat is shown in Table-12.

TABLE-12 : THE SUMMARY TABLE SHOWING GOITER PREVALENCE RATE IN DIFFERENT DISTRICTS DURING VILLAGE SURVEY

Sr. No.	District	Population (1981)	Population examined	Prevalence rate (%)
1.	Ahmedabad	3875724	14525	4.85
2.	Amreli	1079097	10029	14.00
3.	Banaskantha	1667914	23922	6.90
4.	Bharuch	1296451	14898	31.4
5.	Bhavnagar	1879340	29736	4.2
6.	Dang	113664	2711	44.4
7.	Gandhinagar	289088	2717	2.36
8.	Jamnagar	1393076	13105	2.19
9.	Junagadh	2100709	21222	3.1
10.	Kheda	3015027	24066	4.91
11.	Kutch	1060161	13961	1.01
12.	Mehsana	2548787	22486	3.47
13.	Panchmahal	2321689	15016	22.40
14.	Rajkot	2093094	21698	5.62
15.	Sabarkantha	1502284	14615	25.80
16.	Surat	2493211	25258	22.7
17.	Surendranagar	1034185	8378	4.48
18.	Valsad	1774136	Not stated	38.30

Table-13 shows the number of patients with thyroid disorder at the S. S. G. Hospital. Out of the 1400 patient samples analysed, 415 (29.64%) were males and 985 (70.36%) were females. Out of the total patients 531 (37.93%) were hypothyroid, out of which 139 (9.93%) were males and 392 (28%) were females, this indicates that it is more prevalent in females than males. The total number of hyperthyroid patients were 237 (16.93%), out of which 102 (7.29%) were males and 135 (9.64%) were females. Out of the total 632 (45.14%) were euthyroid.

Out of the 28% of hypothyroid females, 168 (12%) were in the age group of 31-40 years.

Table-13 : SHOWING THE NUMBER OF PATIENTS WITH THYROID DISORDER IN THE S. S. G. HOSPITAL, BARODA

Sex/Age	Hypothyroid	Hyperthyroid	Euthyroid	TOTAL
MALE (YEARS)				
< 20	39 (2.79%)	05 (0.36%)	41 (2.93%)	85 (6.07%)
21-30	18 (1.29%)	21 (1.50%)	37 (2.64%)	76 (5.43%)
31-40	39 (2.79%)	50 (3.57%)	50 (3.57%)	139 (9.93%)
41-50	21 (1.50%)	18 (1.29%)	16 (1.14%)	55 (3.93%)
51-60	16 (1.14%)	05 (0.36%)	16 (1.14%)	37 (2.64%)
> 60	06 (0.43%)	03 (0.21%)	14 (1.00%)	23 (1.64%)
TOTAL	**139 (9.93%)**	**102 (7.29%)**	**174 (1.00%)**	**415 (29.64%)**
FEMALE (YEARS)				
< 20	55 (3.93%)	06 (0.43%)	55 (3.93%)	116 (8.29%)
21-30	30 (2.14%)	31 (2.21%)	110 (7.86%)	171 (12.21%)
31-40	168 (12.00%)	45 (3.21%)	166 (11.86%)	379 (27.07%)
41-50	98 (7.00%)	38 (2.71%)	72 (5.14%)	208 (14.86%)
51-60	24 (1.71%)	10 (0.71%)	35 (2.5%)	69 (4.93%)
> 60	17 (1.21%)	05 (0.36%)	20 (1.43%)	42 (3.00%)
TOTAL	**392 (28.0%)**	**135 (9.64%)**	**458 (32.71%)**	**985 (70.36%)**
	531 (37.93%)	**237 (16.93%)**	**632 (45.14%)**	**1400**

Total number of samples analysed : 1400 (415 males and 985 females)

Total hypothyroid patients : 531 (139 males and 392 females)

Total hyperthyroid patients : 237 (102 males and 135 females)

Total euthyroid patients : 632 (174 males and 458 females)

According to Richard M. Jordan (1995), the calorigenic actions of thyroid hormones are mediated by nuclear receptors. A major effect is to stimulate the sodium pump via the cell membrane enzyme Na^+, K^+-ATPase. This process increases oxygen consumption and probably accounts for the characteristic increase in basal metabolic rate associated with thyroid hormone

administration. Mitochondrial metabolism also is influence by thyroid hormone; however, the mechanism by which this occurs is not clearly understood. This action also appears to increase oxygen consumption.

The studies we carried out in the bacterial system also supports the the fact that thyroid hormone increases the oxygen consumption, demonstrated using *E. coli* wild type.

The thyroid profile of the control group had mean TSH value of 2.77 μIU/ml while the T_3 mean was 1.28 ng/ml, and the mean T_4 levels were 9.67 μg/dl. In group-I consisting of hyperthyroid patients, the mean TSH, T_3, T_4 levels were 0.143 μIU/ml, 4.244 ng/ml and 17 μg/dl respectively (Z = 7.2, 7.6 and 7.9; $P < 0.001$).

In group-II, patients with T_3 toxicosis the mean TSH, T_3, T_4 levels were 0.213 μIU/ml, 5.49 ng/ml, 9.51 μg/dl respectively (Z = 6.9, 7.54, 0.23 respectively; $P < 0.001$; $P<0.001$; $P > 0.05$) indicating that the change in TSH and T_3 is statistically significant, whereas that of T_4 is insignificant in patients with T_3 toxicosis.

In group-III, the hyperthyroid follow up patients had the mean TSH, T_3, T_4 as follows : 3.722 μIU/ml, 1.4 ng/ml and 8.65 μg/dl respectively (Z = 10.22, 7.31, 9.14; $P < 0.001$) was statistically significant.

In patients with hyperthyroid over-treatment of group-IV, the mean TSH, T_3, T_4 levels were 9.56 μIU/ml, 0.666 ng/ml, 3.1 μg/dl respectively (Z = 10.34, 9.29, 16; P < 0.001). In group-V of hypothyroidal patients with hypercholesterolemia the mean TSH, T_3, T_4 levels were 15.67 μIU/ml, 0.935 ng/ml and 3.33 μg/dl respectively (Z = 9.28, 8.68, 9.8; P < 0.001).

Group-VI, hypothyroidal patients with type IIB hyperlipoproteinemia, the mean TSH, T_3, T_4 levels were 11.67 μIU/ml, 0.922 ng/ml, 4.25 μg/dl (Z = 11.9, 8.68, 9.4; P < 0.001) they were statistically significant.

While group-VII of severe hypothyroid of severe hypothyroid with type III hyperlipoproteinemia had mean TSH, T_3, T_4 levels of 19.25 μIU/ml, 0.371 ng/ml and 1.8 μg/dl respectively (Z = 21.1, 10.99, 14.3; P < 0.001) were found to be significantly increased as compared to normal.

In group-VIII, having hypothyroid follow up patients had mean TSH, T_3, T_4 levels as 3.63 μIU/ml, 1.236 ng/ml, 8.14 μg/dl respectively (Z = 19.18, 10.29, 12.3; P < 0.001), the changes were statistically significant.

Group-IX, hypothyroid over-treatment patients had mean TSH, T_3, T_4 values of 0.449 μIU/ml, 2.058 ng/ml and 14.3 μg/dl respectively (Z = 25.96, 11.93, 17.9;

P<0.001) all were significantly decreased compared with the severe hypothyroid.

In group-X, patients with thyroid disorder secondary to liver disease had mean TSH, T_3, T_4 values of 8.25 μIU/ml, 0.713 ng/ml, 5.97 μg/dl respectively (Z = 8.72, 5.66, 3.7; P < 0.001), the TSH levels were significantly increased as compared to normal.

In group-XI, patients with thyroid disorder secondary to renal disease had mean TSH, T_3, T_4 levels as 6.97 μIU/ml, 0.635 ng/ml, 6.51 μg/dl respectively (Z = 8.0, 8.18, 4.6; P < 0.001).

MECHANISM FOR PLASMA LIPOPROTEIN ALTERATIONS IN THYROID DYSFUNCTION

HYPOTHYROIDISM

The increased concentrations of plasma cholesterol and triglyceride in hypothyroidism seem to result of defect return rather than from increased production. Thus, kinetic cholesterol transport studies in hypothyroid patients have shown only alterations in cholesterol synthesis and intestinal absorption. Similarly, synthesis of VLDL triglyceride seems to be essentially normal in hypothyroid (Nikkila and Kekki, 1972). Kinetic studies have demonstrated impaired elimination of VLDL-TG and decreased catabolic rate of LDL

markedly affected. However, the pronounced changes in the HDL subclasses, with a relative increase. In HDL_2, emphasize the pathophysiological importance of the lowered activity of HL.

It is suggested that the decreased activity of HL can indeed contribute to the accumulation of lipoprotein particles in the IDL fraction. The IDL fraction can, as a matter of fact, be regarded as a result of a back up in the flux of surface components from the VLDL-LDL system through HDL to the liver. The significance of such a mechanism is indicated by comparison with conditions associated with an isolated impairment of LPL or LDL receptor activity, which lead to accumulation of triglyceride-rich lipoproteins or LDL, respectively, but not of IDL (Fredrickson et al, 1967).

In short, we propose that decreased activities of HL, LPL and LCAT lead to an impairment, at multiple interacting sites in the elimination routes for cholesterol and triglyceride from plasma in hypothyroid patients. Along with an alteration of the LDL receptor function, these enzymes mediated effect would largely explain the plasma lipoprotein changes seen in hypothyroidism.

HYPERTHYROIDISM

Kinetic studies demonstrate only minor changes in the synthesis of cholesterol, while the products of VLDL-TG are increased in hyperthyroid patients. The

removal of triglyceride from the circulation, the catabolism of LDL cholesterol and the excretion of neutral steroid seem to be increased in hyperthyroids. The main effect of excess of thyroid hormones on the transport of lipids therefore, seems to be to promote their elimination from the circulation.

In vitro studies have shown that triiodothyronine can increase the number of LDL receptors in cultured fibroblasts (Chait A. et al, 1979). An enhanced elimination of LDL particles via the LDL receptor pathway may therefore explain the lowered levels of LDL cholesterol in hyperthyroid patients.

The surface components, released at an increased rate during the accelerated degradation of VLDL through the LPL reaction, can readily be accepted by the HDL fraction in hyperthyroid patients. The markedly increased activity of HL enhances the elimination of surface components in the liver and provide a HDL_2/HDL_3 ratio which is favourable for the LCAT activity.

We suggest that the hepatic elimination of cholesterol is accelera ed more than the input of cholesterol to HDL, providing an explanation for the low HDL cholesterol concentration in these patients. This is in agreement with the finding of a selective reduction of the HDL_2 subclass seen in zonal ultracentrifugation (Lisch et al, 1982).

In short, we propose that the increased activity of HDL is of major importance for the enhanced elimination of cholesterol from the circulation in hyperthyroid patients. Along with alterations in LDL receptor activity, the elevated HL activity would largely explain the changes in plasma lipoproteins seen in hyperthyroidism.

It has been known for many years that thyroid hormones play a role in lipid metabolism since in hypothyroidism there is an increase in most of the serum lipids and in thyroid hormone excess a decrease in serum lipids is seen. Serum cholesterol (free and esterified), phospholipids and low density β-lipoprotein of serum are increased in hypothyroidism and reduced in hyperthyroidism. Serum free fatty acids, however, vary in the opposite direction, being increased in hyperthyroidism and depressed in hypothyroidism. Hypothyroidism, however, does not prevent the rise in free fatty acids produced by growth hormone. The fatty acid composition of the triglyceride, cholesterol ester, and phospholipid fractions of serum has also been studied, and a trend toward greater saturation was found in hypothyroid compared to normal subjects.

Cornwell et al (1961) also found moderate decreases in both LDL and HDL in thyrotoxicosis as was reported by Walton K. W. (1965) and also reported by us. The data presented by Cornwell et al (1961), do in fact, show somewhat lower

mean levels of cholesterol and phospholipid in their hyperthyroid cases than in their euthyroid controls, though these changes were not statistically significant.

In the light of the observation that the extent of the change in the lipoproteins correlates with the severity of thyroid dysfunction, it seems probable that this slight discrepancy with our findings may merely reflect differences in the severity of the cases selected for study.

The inverse relation between LDL levels and the basal metabolic rate suggested that serum lipoprotein levels might be influenced primarily by the level of protein metabolism in general, which is known to be markedly affected by thyroid dysfunction.

The metabolism and turn over of LDL is affected in a manner similar to that of serum albumin and gamma-globulin by altered thyroidal activity.

In hypothyroidism, for example, raised serum levels of LDL might result from a long standing positive metabolic balance due to decreased degradation and utilization of LDL outweighing even the reduced protein synthesis known to be characteristic of myxedema (Crispel et al, 1961).

The changes in the lipid parameters in the various groups were found to vary considerably in various disease states. The mean triglyceride levels in the normal group was 92.3 mg/dl, whereas in hyperthyroid patients of group-I it is

64.893 mg/dl (Z = 7.2; P < 0.001), the mean levels in group-II, of patients with T_3 toxicosis it was 60.643 mg/dl (Z = 9.9; P < 0.001), the mean levels in hyperthyroid follow up cases of group-III was 99.503 mg/dl (Z = 7.9; P < 0.001), whereas the mean level for patients with over-treatment with antithyroid drugs of group-IV was 191.9 mg/dl (Z = 9.9; P < 0.001). The mean levels of triglyceride in patients of hypothyroidism with hypercholesterolemia of group-V was 103.01 mg/dl (Z = 1.66; P > 0.05) these variations were statistically insignificant. The mean levels in hypothyroid patients with hyperlipoproteinemia (type IIb) were 171.32 mg/dl (Z = 18.23; P < 0.001). The patients of severe hypothyroidism of group-VII had a mean of 204.33 mg/dl (Z = 15.4; P < 0.001), hypothyroid follow up patients of group-VIII had a mean of 93.463 mg/dl (Z = 18.5; P < 0.001), whereas those with over-treatment in group-IX had mean levels of 62.85 mg/dl (Z = 5.4; P < 0.001). The mean TG levels in patients with thyroid disorders secondary to liver disease of group-X was 167.2 mg/dl (Z = 12.22; P < 0.001), whereas in those with secondeary renal disease it was 158.55 mg/dl (Z = 13.2; P < 0.001).

The mean VLDL values in the control group was 18.46 mg/dl, whereas that in hyperthyroid patients of group-I, it was 12.96 mg/dl (Z = 7.25; P < 0.001), the mean VLDL value in patients with T_3 toxicosis of group-II was 12.13 mg/dl (Z = 9.78; P < 0.001), the mean levels in hyperthyroid follow up patients of group-

III were 19.9 mg/dl ($Z = 7.8$; $P < 0.001$), whereas the mean levels in hyperthyroid over-treatment group-IV were 38.41 mg/dl ($Z = 9.85$; $P < 0.001$).

The mean VLDL levels in hypothyroid patients of group-V were 20.6 mg/dl ($Z = 1.66$; $P > 0.05$) was statistically insignificant, whereas, the mean levels in group-VI hyperthyroid patients with type IIb hyperlipoproteinemia was 34.26 mg/dl ($Z = 18.35$; $P < 0.001$), and the mean levels in severe hypothyroid patients of group-VII were 40.87 mg/dl ($Z = 15.35$; $P < 0.001$), whereas that of hypothyroid follow up cases of group-VIII was found to be 18.69 mg/dl ($Z = 13.24$; $P < 0.001$) and the mean in hypothyroid patients with over-treatment was 12.57 mg/dl ($Z = 5.3$; $P < 0.001$). The mean VLDL levels in patients with thyroid disease secondary to liver disease 33.43 mg/dl ($Z = 11.9$; $P < 0.001$) and the mean in patients with renal disease is 31.71 mg/dl ($Z = 13.3$; $P < 0.001$).

The mean LDL level in normal persons was 124.29 mg/dl, while the mean levels in hyperthyroid patients of group-1 was 72.591 mg/dl ($Z = 9\ 78$; $P < 0.001$), the mean levels in patients with T_3 toxicosis of group-II were 80.632 mg/dl ($Z = 9.4$; $P < 0.001$), whereas that in the hyperthyroid follow up cases of group-III were 119.3 mg/dl ($Z = 9.16$; $P < 0.001$) and that in the hyperthyroid patients with over-treatment group-IV, it was 205.34 mg/dl ($Z = 9.1$; $P < 0.001$). In the hypothyroid patients of group-V the mean LDL level was 277.14 mg/dl ($Z = 14.8$; $P < 0.001$), whereas the mean LDL level in hypothyroid

patients with type IIb hyperlipoproteinemia of group-VI was 209.56 mg/dl (Z = 13.4; P < 0.001) and the mean levels in severe hypothyroid patients of group-VII was 233.61 (Z = 12.98; P < 0.001), whereas that in hypothyroid follow up cases of group-8 was 126.58 mg/dl (Z = 11; P < 0.001) and in patients over-treated for hypothyroidism it was 84.78 mg/dl (Z = 6; P < 0.001). The mean level in patients with thyroid disorder secondary to liver disease was 191.45 mg/dl (Z = 11.6; P < 0.001) and whose patients with secondary renal disease had mean LDL level of 178.39 mg/dl (Z = 5.27; P < 0.001).

The mean HDL level in normal group was 43.17 mg/dl, whereas the mean level in hyperthyroid patients of group-1 was 35.68 mg/dl (Z = 6.14; P < 0.001) and that in patients with T_3 toxicosis was 37.21 mg/dl (Z = 4.95; P < 0.001) whereas the mean level in the hyperthyroid follow up cases was 43.6 mg/dl (Z = 6.6; P<0.001) and patients with over-treatment in group-IV had a mean of 48.7 mg/dl (Z = 2.5; P < 0.001), patients with hypothyroidism of group-V had a mean HDL level of 44.9 mg/dl (Z = 0.89; P > 0.05) which did not vary significantly from the normal group. The mean levels in group-VI comprising of patients with hypothyroidism with type IIb hyperlipoproteinemia were 40.08 mg/dl (Z = 1.7; P > 0.05) which was not statistically significant. The mean levels in group-VII of severely hypothyroid patients was 59.2 mg/dl (Z = 11.4; P < 0.001) which increased significantly from the normal. In the hypothyroid

follow up cases of group-VIII had mean levels of 47.4 mg/dl which decreased significantly from the severe hypothyroid patients ($Z = 7.9$; $P < 0.001$). The levels in over-treated patients of group-IX were 36.35 mg/dl ($Z = 7.9$; $P < 0.001$) whereas those with thyroid disorder secondary to liver disease of group-X had mean levels of 37.15 mg/dl ($Z = 4.21$; $P < 0.001$) in these with secondary to renal disease had mean 39.55 mg/dl ($Z = 4.46$; $P < 0.001$).

The mean cholesterol level in normal subjects was 189 mg/dl, while that in hyperthyroid patients of group-1 it decreased with a mean of 121.95 mg/dl ($Z = 13.75$; $P < 0.001$) and in patients with T_3 toxicosis the mean level was 130.07 mg/dl ($Z = 14.22$; $P < 0.001$). In patients with hyperthyroid follow up cases of group-III had mean level were 182.8 mg/dl which had increased appreciably from the hyperthyroid patients, which was statistically significant ($Z = 11.58$; $P < 0.001$), whereas that in hyperthyroid over-treatment patients of group-IV, had mean level had 296.25 mg/dl ($Z = 9.96$; $P < 0.001$), the mean levels in hypothyroid patients with hypercholesterolemia of group-V were 342.84 n g/dl ($Z = 15.7$; $P < 0.001$), the mean levels of hypothyroid patients of group-VI were 283.9 mg/dl ($Z = 16.5$; $P < 0.001$), whereas the mean levels in severe hypothyroid patients of group-VII were 333.67 mg/dl ($Z = 16.34$; $P < 0.001$) and that in the follow up group-VIII mean levels were 192.7 mg/dl ($Z = 13.5$; $P < 0.001$), the mean levels in hypothyroid over-treated patients of group-IX were

133.7 mg/dl ($Z = 13.5$; $P < 0.001$). The mean levels in patients with thyroid disorder secondary to liver disease the values were 262.02 mg/dl ($Z = 12.96$; $P < 0.001$) whereas those in patients secondary to renal disease the mean levels were 247.15 mg/dl ($Z = 5.44$; $P < 0.001$).

According to Mazzaferri E. L. (1997), thyroid disorders are very common in women and are especially important around the time of pregnancy and after menopause when the consequences of thyroid disease are quite different.

Vahab Fatourechi (1988) reported of hyperthyrodism following hypothyroidism, stating that hypothyroidism complicated by spontaneous hyperthyroidism is an interesting but rare occurance in the spectrum of autoimmune thyroid disorder. Although autoimmune mechanisms and variations in thyroid blocking and stimulating antibodies are considered important in the pathogenesis of this phenomenon, no definite explanation is provided. Vahab commented that Grave's disease, thyroiditis and hypothyroidism are now considered autoimmune in origin, representing the spectrum of the same pathogenic mechanisms. Grave's disease may occur in histologically proved Hashimoto's thyroiditis (Fatourechi V. et al, 1971), and hypothyroidism often develops spontaneously after hyperthyroidism (Wood L.C. et al, 1979).

Reviewing the literature of other cases of hyperthyroidism after hypothyroidism, Vahab Fatourechi (1988) found 39 case reports of this phenomenon. Certain findings strongly suggest that autoimmune mechanisms are important in the pathogenesis of this syndrome.

The exact mechanism by which hypothyroidism transforms into clinical and biochemical hyperthyroidism is unclear, although several explanations are possible. Because most of the patients have been treated with thyroxine, the thyroid hormone itself is considered to be a possible factor in the pathogenesis. This might occur through a direct or an indirect effect of the thyroid hormone on suppressor T-lymphocyte function.

Alternative pathogenic explanation might include Jod Basedow syndrome, which is a phenomenon of hyperthyroidism fueled by iodine replacement in hypothyroid patients living in iodine-deficient areas. Further possibility may be Hashimoto's toxicosis in either chronological order : lymphocytic infiltration resulting in suppression of thyroid function or stimulation of it or both in varied sequence.

According to Aglio Dall etal (1988) Janaka and Starr in 1959, described the deficiency of thyroxine binding globulin (TBG). The prevalence of familial TBG deficiency has been estimated to range between 0.06% and 0.006%. Reduction of TBG capacity can be due to either an inherited defect in TBG

synthesis, or to an acquired diminution of TBG concentration. It is generally accepted that inherited TBG deficiency is due to a decreased liver synthesis of the protein.

Since TBG has a binding capacity for T_4 five-fold higher than for T_3 patients with TBG deficiency and thyrotoxicosis are expected to have a decreased or a normal serum T_4 concentration, and an increased serum T_3 concentration.

Miskel M. A. (1977) stated that although an elevated plasma cholesterol level has long been described as a metabolic accompaniment of primary hypothyroidism, the frequency of combined hypercholesterolemia and hypertriglyceridemia has not been emphasized in the literature. The association of various types of hyperlipoproteinemia with hypothyroidism has been well discussed, but data about the relative and absolute frequency of the various forms of hyperlipoproteinemia are not available. Miskel M. A. (1977) showed that type II B hyperlipoproteinemia accounts for 50% of the cases of hyperlipidemia in primary hypothyroidism.

Hypothyroidism is accompanied by overt hypercholesterolemia, reflected in human by raised low density lipoproteins (LDL) and occasionally raised very low density lipoprotein (VLDL) concentrations, whereas apolipoprotein-E (apo-E)-rich larger high density lipoprotein (HDL), β-VLLL and LDL particles

accumulate in plasma (Staeb Bart et al, 1991). According to him, the decrease in plasma HDL_2 cholesterol observed in L-T_4 treated hypothyroid humans can be explained by an increased post-heparin plasma hepatic triglyceride lipase (HTGL) activity. The clearance of plasma LDL has been shown to be delayed in hypothyroid subjects due to decreased LDL receptor activity, a situation readily reversed by thyroid hormone treatment.

The study by Wahlquist M. L. (1977) confirms that hypercholesterolemia and hypertriglyceridemia are frequently observed in association with hypothyroidism. In type III hyperlipoproteinemia in which there is increasing evidence for the accumulation of a VLDL remnant or intermediate lipoprotein possibly involved in the conversion of VLDL to LDL. Thus, the study by Wahlquist M. L. et al appears to provide some support for the view that thyroid hormones act, at least in part, at the level of lipoprotein interconversion.

According to Tulloch B. R. et al (1973), plasma triglyceride levels are increased in hypothyroid subjects and after thyroxine therapy the fell towards the normal range. In untreated thyrotoxicosis, fasting plasma triglyceride values were subnormal or low normal. The triglyceride levels therefore, change with the thyroid function in a similar manner to cholesterol.

The rise in fasting triglyceride levels could be caused either by decreased clearance, or by increased hepatic production of VLDL from circulating FFA or by both mechanisms.

According to Hanna Engler et al (1990), thyroid hormones not only influence LDL-C and apo-B concentrations, they also clearly show an effect on Lp (a) concentration. The effects in hyperthyroidism were more pronounced than those in hypothyroidism mean increase of 60% during treatment of hyperthyroidism versus a decrease of 10% during T_4 substitution or hypothyroidism.

Thyroid hormones appear to be involved in the metabolism of a rather large number of mineral elements. Byrom, however, in a study reported that in the hypothyroid or normal man, thyroxine (in a massive dose) caused a loss of both these elements (Na^+ and K^+). In the hypothyroid subjects the loss of sodium, was much greater than that of potassium, whereas in the normal subjects more potassium was lost. They suggested that this meant that the fluid accumulated by the myxedematous patient was largely extracellular but that in the normal subject an intense thyroxine effect could cause loss of intracellular water and salts.

Thyroid hormone has a profound effect on water, however, in myxedematous patient given thyroxine or triiodothyroxine, there is a marked diuresis, and one report shows an increase in the level of sodium and chloride in serum,

suggesting that enough water was excreted to cause a relative concentration of extracellular fluid. According to Mahajan K. K. et al (1983) red cell sodium and plasma tyrosine levels are raised in hyperthyroid and lowered in hypothyroid cases.

The characteristic increase in metabolic rate appears to be due to the induction of key enzymes regulating metabolism. Thyroid hormones potentiate the calorigenic effects of other hormones such as catecholamines, probably by increasing the synthesis of the enzyme Na-K-ATPase. The adenosine diphosphate (ADP) produced by hydrolysis of adenosine triphosphate (ATP) stimulates mitochondria and increases the rate of oxidative phosphorylation.

According to L. Gavin (1991), patients suffering from myxedema coma, the end point of chronic thyroid hormone deficiency, exhibit wide spread organ dysfunction. Myxedema coma adversely affects vital functions such as respiration, cardiac performance, mental status, and thermoregulation. In addition, myxedema is associated with a spectrum of hematologic, biochemical and immunologic derangements. This condition is seen most often in elderly women who have chronic hypothyroidism from a spectrum of causes. Myxedema coma is complex, because apart from thyroid hormone deficiency, the syndrome is frequently associated with cardiorespiratory dysfunction (hypoxemia, hypercapnia), hyponatremia, hypoglycemia and hypothermia.

Renal and Electrolyte Alterations according to L. A. Gavin (1991) hyponatremia is a frequent finding and is reflective of the increase in total body water (dilutional). The hyponatremia results from a combination of events; diminished glomerular filtration, decreased delivery of water to the distal tuble, and a consequent impaired water diuresis. Patients with hypothyroid coma may suffer from the syndrome of inappropriate ADH (SIADH) secretion and a deficiency of atrial natriuretic factor (ANF). Both aggravate the salt and water abnormalities. The hyponatremia will compound the patients mental confusion and when severe, may be responsible for the eventual decompensation into coma.

Sodium regulation (Jordan R. M., 1995 MCNA) states that renal blood flow and glomerular filtration are reduced in hypothyroidism. Despite this, renal tubular sodium resorption is reduced. The decreased sodium resorption may, in part, be due to effects of thyroid hormone on Na^+, K^+-ATPase described previously. Also, hypothyroid patients cannot excrete a water load normally, and urine osmolarity is not appropriately dilute despite hypoosmolarity of the serum. Some patients have an inappropriately elevated plasma vasopressin level despite the low serum osmolarity.

The present study control group had mean sodium level of 140.2 mEq/L and potassium level of 4.18 mEq/L. In patients of group-I the hyperthyroids mean

Na^+ was 131.2 mEq/L and K^+ levels 5.173 mEq/L ($Z = 8.72$ and 7.13; $P < 0.001$), the group-II of patients with T_3 toxicosis had mean Na^+ levels of 135.6 mEq/L ad K^+ levels of 5.257 ($Z = 5.1$ and 7.05; $P < 0.001$). The group-III comprised of the follow up cases of hyperthyroid patients with mean Na^+ level of 140.4 mEq/L and K^+ level 4.353 mEq/L ($Z = 6.3$ and 5.5 respectively; $P < 0.001$). The group-IV of hyperthyroid patients with over-treatment had Na^+ levels of 129.8 mEq/L and mean K^+ levels of 3.96 mEq/L ($Z = 5.39$, 3.44; $P < 0.001$). In group-V comprising hypothyroid patients with hypercholesterolemia had mean Na^+ levels 132.6 mEq/L ($Z = 7.56$; $P < 0.001$) and mean K^+ levels 4.01 mEq/L ($Z = 1.49$; $P > 0.05$) which was not statistically significant. In group-VI of hypothyroid with type IIb hyperlipoproteinemia the mean Na^+ levels were significantly decreased, with a mean of 131.7 mEq/L ($Z = 9.2$; $P < 0.001$) while there was [redacted] significant change in the mean K^+ levels of 3.913 mEq/L ($Z = 2.3$; $P < 0.001$). In group-VII comprising hypothyroid patients with type III hyperlipoproteinemia had a significant decrease in mean Na^+ levels of 127.9 mEq/L ($Z = 10.9$; $P < 0.001$), whereas there was, statistically significant change in mean K^+ levels of 4.287 mEq/L ($Z = 0.8$; $P > 0.05$). In group-VIII, hypothyroid follow up cases, the mean Na^+ was 139.7 mEq/L and mean K^+ level was 3.847 mEq/L ($Z = 8.03$, 4.2; $P < 0.001$). In hypothyroid patients with over-treatment the mean Na^+ level was 133.9 mEq/L and mean K^+ level was 4.0 mEq/L ($Z = 2.6$, 1.81; $P < 0.001$, $P > 0.05$) which was statistically significant

only for the sodium levels. In group-X, patients suffering from thyroid disorder secondary to liver disease mean Na^+ levels were 131.8 mEq/L and K^+ levels were 3.275 mEq/L ($Z = 8.6, 9.4$; $P < 0.001$) which were statistically significant.

In group-XI of patients with thyroid disorder secondary to renal disease, the mean Na^+ level was 157.7 mEq/L and mean K^+ levels were 3.32 mEq/L ($Z = 9.12, 8.83$; $P < 0.001$) they were statistically significant.

These data suggest that there is hyponatremia in patients suffering from hypothyroidism. Hyponatremia accompanying myxedema coma is a management challenge. In most instances, the hyponatremia is mild to moderate and is due to diminished free water clearance. It can be managed by mild fluid restriction (1000 m/day) and is corrected once thyroid hormone replacement is started.

According to Jordan R. M. (1995) ancillary laboratory testing that supports the values are often greater than 500 U/L and may exceed 1000 U/L. The predominate CPK isoenzyme is the MM fraction, which comes from skeletal muscle. This occurs because the muscle cell membrane becomes increasingly permeable in hypothyroidism with accumulation of glycogen, mitochondria and type II muscle fibre atrophy. Study carried out by Paul De Weer et al (1988), Am. Rev. Phys. Demonstrates that the Na-K pump rate is voltage dependent. A

large body of evidence indicates that Na^+ and K^+ activated adenosine triphosphate (ATP phosphohydrolase, EC 3.6.1.3) is the enzymatic equivalent of the system responsible for active transmembrane sodium transport (Sinha S. K. et al, 1981). According to Dahl J. L. et al (1974), the active transport of sodium and potassium is a fundamental and major energy requiring cellular process underlying the maintenance of cell volume absorption process in kidney and intestine and excitability in nerve and muscle.

A variety of biochemical abnormalities reflecting hepatic, adrenal and renal decompensation characterize patients with thyroid disorders. According to Laurence A. Gavin (1991), the liver function tests in thyroid storm often reveal an elevated serum bilirubin, a prolonged prothrombin time, and elevated AST and ALT. Both hypercalcemia and hyperglycemia may occur. Hypoglycemia, an ominous finding, results from depletion of hepatic glycogen, high peripheral utilization of glucose, and decreased gluconeogenesis due to hepatic failure. The presence of an abnormal adrenal status should be prompted by the electrolyte triad of hyperkalemia, hyponatremia, and hypercalcemia. Finally, rising levels of serum blood urea nitrogen (BUN) and creatinine indicate a decreased creatinine clearance and pre-renal azotemia secondary to dehydration and obtundation.

In secondary hypothyroidism, hyperkalemia may reflect adrenal insufficiency. Liver enzymes (AST, ALT, and LDH) may be abnormal (L. A. Gavin, 1991) and a modest increase in CPK-MB has been described.

According to Jane T. Gaede (1977), recognition of a pattern of elevations in commonly measured serum enzymes (creatine phosphokinase [CPK], lactic dehydrogenase [LDH] and glutamate oxaloacetate transaminase [SGOT] can facilitate the diagnosis of hypothyroidism.

The first chemical correlation of enzyme abnormality with hypothyroidism was reported by Graig and Ross in 1963. They found a significant elevation of serum CPK activity in 10 of 15 hypothyroid patients, and noted that the CPK level returned to normal after thyroid replacement therapy.

An extensive study of serum CPK, LDH and SGOT in 120 patients with myxedema was reported by Fleisher et al in 1965. They found elevations of LDH and SGOT in addition to CPK. They suggested skeletal muscle as the most likely source for the elevation of these three enzymes.

A smaller series of 66 patients reported by Griffiths (1965) yielded similar results for CPK and SGOT; in addition, 60 per cent had elevated levels of serum aldolase. Griffiths, however, favoured cardiac muscle as the source of the increased CPK.

By electromyogram, however, Scarpalezos et al were able to detect abnormalities in only 18 of 51 patients with adult onset hypothyroidism (Scarpalezos S. et al, 1973). This might be explained by greater sensitivity of the enzyme test to early muscle damage. Muscle biopsy performed on a severely hypothyroid patient with enlarged muscles, as reported by Chowdhuri et al (1974), showed spotty atrophy of muscle fibers and oedema of the interstitial tissues. Although CPK was not determined, this patient did have a significantly elevated level of aldolase, which decreased by half after treatment with thyroxine. A serial muscle biopsy study in 6 hypothyroid patients was reported by McKeran et al (1975) who found a significantly lower percentage of type II muscle fibers in the hypothyroid subjects as compared to controls. The extent of the changes was well correlated with the serum CPK levels. During thyroid replacement therapy, the percentage of type II fibers approached normal again. The explanation suggested was that since thyroxine facilitates glycogen breakdown, and since type II muscle fibers are more dependent upon glycogenolysis and glycolysis for energy than are type I fibers, a state of thyroxine deficiency could be expected to lead to selective atrophy of type II fibers.

In addition to serum enzyme alterations (CPK, LDH, AST, aldolase) which can be explained on the basis of skeletal muscle involvement, some observers

(Chertow B. S. et al, 1974) have noted a downward trend in total protein, albumin and creatinine levels during the course of treatment of hypothyroidism.

In the present study, the mean levels of LDH and AST in normal subjects had a mean of 267.5 IU/L and 22.937 IU/L respectively, whereas, hyperthyroid patients had a mean level of 389.14 and 46.477 IU/L respectively ($Z = 6.9$; 13.1; $P < 0.001$) in patients with T_3 toxicosis, the mean LDH and AST levels were 354.7 and 36.793 IU/L respectively ($Z = 7.38$; 7.3; $P < 0.001$), the hyperthyroid follow up cases had a mean LDH and AST level of 310 IU/L and 32.133 IU/L respectively ($Z = 3.3$; 10.5; $P < 0.001$), in hyperthyroid over-treatment patients the mean levels were 429.4 and 34.045 IU/L respectively ($Z=9$; 1.9; $P < 0.001$; $P > 0.05$). The AST means in this group were statistically insignificant, whereas, that of LDH were statistically significant.

In hypothyroid patients with the mean LDH and AST levels were 434.43 IU/L and 68.95 IU/L respectively ($Z = 11.7$; 8.9; $P < 0.001$), whereas the mean in hypothyroid patients with type II b hyperlipoproteinemia the mean level was 461.55 and 54.863 IU/L respectively ($Z = 10.9$; 14; $P < 0.001$), whereas, the mean in group 7 of severely hypothyroid patients were 473.6 IU/L and 48.017 IU/L ($Z = 16$; 11.4; $P < 0.001$), in the hypothyroid follow up group 8, the mean LDH and AST levels were 314.65 and 28.027 respectively ($Z = 9.8$; 9.49; $P<0.001$).

In patients with hypothyroidism being over-treated had mean LDH and AST levels of 352.1 and 42.74 IU/L ($Z = 2.23; 4.28; P < 0.001$) whereas patients with thyroid disorder secondary to liver disease had mean LDH and AST levels of 434.35 and 42.737 IU/L respectively ($Z = 14.6; 36; P < 0.001$) whereas those with thyroid disorder secondary to renal disease had mean LDH and AST level of 452.5 and 44.745 IU/L respectively ($Z = 15.8, 8.72; P < 0.001$) all the values were statistically significant.