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Thyroid function profile and differential serum lipid and lipoproteins in Africans with endemic goitre.

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Summary

Serum total thyroxine (TT4), total triiodothyronine (TT3), thyrotrophine (TSH), thyroxine binding globulin (TBG), total lipids, triglycerides, total cholesterol, beta lipoprotein and beta lipoprotein cholesterol level were measured in 68 goitrous subjects and 4 agoitrous cretins by the techniques based on enzyme immunoassay (ELISA) (for thyroid parameters) and enzyme substrate principle (for lipid and lipoproteins) using commercial test kits (Boehringer Mannheim, W. Germany) and the results were matched with those derived from 59 clinically normal control subjects. The mean values of serum TT3, TBG, TSH and T3/T4 ratio showed positive correlations with the goitre size ($r > 0.8$, $P < 0.005$) while mean serum TT4 was negatively correlated ($r > -0.9$, $P < 0.005$). Typical biochemical features of hypothyroidism on serum lipid and lipoprotein profile were seen throughout, the changes being more marked in cretins. However, the serum lipid and lipoproteins were also, to some extent, found to be positively related to the thyroid size. In addition, a number of patients also showed variations in the serum lipid and lipoprotein levels appropriate to their compensated thyroid functional status in endemic goitre (as reflected by low TT4, raised TT3 and raised T3/T4 quotients).

Resume

Les niveaux de sérum thyroxine totale (TT4), de triiodothyronine total (TT3), de thyrotrophine (TS4), de globulin fixé de thyroxine (TBG), de lipides totals, de triglycérides, de cholestérol total, de bêta lipoprotéin et de bêta cholestérol lipoprotéin étaient mesurés dans 68 patients du goitre et 4 crétins non-goitreux au moyen technique basé sur l'immunotitrage diastase (ELISA) (en ce qui concerne les parametres thyroíde) ainsi que sur le principe du substrat de diastase (en ce qui concerne des lipides et des lipoprotéins), à partir des sacs réactifs médicaux (Boehringer Mannheim, W/Germany), et les résultats ont été appariés avec ceux obtenus à partir d'un groupe de 59 sujets normals, cliniquement contrôlés. Les valeurs moyennes des proportions de sérum TT3, TBG, TSH et de T3/T4 ont révélé des corrélations positives de la taille du goître ($r > 0.8$, $P < 0.005$), alors que le moyen du sérum TT4 était de corrélation négative ($r > 0.9$, $P > 0.005$). Les traits biochemiques typique de hypothyroiidisme sur le sérum lipide et sur le profil de lipoprotéin étaient entièrement aperçus, la variation étant plus marqués dans les crétins. Toutefois, les niveaux du sérum lipide et du lipoprotéin étaient aussi, dans une certaine mesure, positivement relatifs à la taille du thyroîde. En plus, quelques patients goîtreux qui ont été examiné, ont révélé des variations au niveau de leur sérum lipide et de leur lipoprotéin propres, au titre du fonctionnement de leur thyroíde dans des régions endémiques (comme c'est révélé par les quotients abaissés respectivement augmentés de TT4 et de TT3, T3/T4).

Introduction

Although the changes which occur in the major plasma lipid fractions in specific thyroid dysfunctions are fairly well established[1-6], the information on the variations which occur in endemic goitre do not appear to have received sufficient attention. The biochemical changes which occur in endemic goitre are complex and affect thyroid function, which in turn partly determines the state of the serum lipids. A reduction in serum total thyroxine (T4) to subnormal or hypofunctional levels is accompanied by increased thyroid size and a rise in

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the more potent serum triiodothyronine (T3). A persistently normal serum T4 level may be seen in the presence of clinical hypothyroid state, due to the increase in thyroxine binding globulin (TBG) which is characteristic of endemic goitre[7,8]. This discrepancy may be misleading in the evaluation of lipid profile of patients with endemic goitre. Moreover, in the past certain thyrolipid fractions were incriminated as causative factors in the pathogenesis of Hashimoto's disease and certain other forms of goitre[9,10]; besides they were also said to be involved in the synthesis of thyroxine in normal subjects[11,12]. The significance and role of lipids in the aetiology of coronary heart disease are well known. Endemic goitre is still a major health problem in many parts of the world, especially in the developing countries. An evaluation of serum lipid fractions and lipoprotein levels in this groups was therefore considered necessary. This paper describes the changes which occur in beta-lipoprotein, beta-lipoprotein cholesterol, total cholesterol, triglycerides and total lipids in the serum of patients with varying grades of thyroid enlargement and degrees of functional states as determined by alterations in serum T4, T3, TSH and TBG levels.

Materials and methods

The present investigation is a controlled study spread over 131 subjects. Sixty eight patients with endemic goitre of varying degrees of thyroid enlargement and duration and four agoitrous cretins were selected for the study. The majority of the patients were selected from the Bassa Local Government Council of Plateau State, Nigeria which is a known endemic goitrous zone[11] (Fig. 1 and Table 1). A few cases with advanced goitre (Grade 4) were also selected from the referred hospital patients and included in the present investigation. The clinical examination and grouping of the patients (as shown below) were carried out during weekly field trips undertaken by our epidemiological survey team to the endemic zone. After a careful physical examination the patients were grouped according to the degree of thyroid enlargement into various grades as described by De Meyer *et al* [13].

Table 1A: Prevalence of endemic goitre in Bassa Local Government Council (L.G.C.) of Plateau State, Nigeria

Total number of subjects examined	= 1004
positive cases with goitre	= 249
%	= 24.8

Fig. 1: A middle aged male trader from Bassa district of Plateau State, Nigeria showing massive thyroid enlargement (Goitre grade 4). Blood biochemistry: Total T_4 = 4.5 ug/dl (55.3 nmol/l), Total T_3 = 1.71 ng/ml (2.63 nmol/l), TSH = 7.5 mu/l, TBG = 21 ug/ml (367.5 nmol/l), Total lipid = 712 mg/dl (7.12 g/l), triglycerides = 63 mg/dl (.72 nmol/l), Total cholesterol = 212 mg/dl (5.4 mmol/l), beta-lipoprotein = 406 mg/dl (4.06 g/l) and beta-lipoprotein cholesterol = 142 mg/dl (3.6 nmol/l).

Table 1B: Distribution of different grades of goitre in the same locality

Thyroid enlargement grade	*No.*	%
(Normal thyroid)	755	75.2
1a	147	15.00
1b	53	5.3
2	23	2.2
3	21	2.1
4 (Monstrous)	11	1.5
Total	1004	100

Degree of Thyroid Enlargement	No. of Patients
Grade — 1 (a + b)	12
Grade — 2	22
Grade — 3	19
Grade — 4 (Monstrous goitre)	15
Agoitrous Cretins	4
Total	72

(The grade 1 is inclusive of grades 1a and 1b).

A normal group consisting of 59 clinically healthy subjects of similar age range and sex were also assessed and used as the control. The latter were selected from the general population of Jos Metropolis which lies outside the endemic zone. About 10ml of blood was withdrawn from each subjects in fasting conditions and transferred into suitable containers. They were quickly sent to the research laboratory of the Department at the University Teaching Hospital, Jos. The clear serum samples obtained (from the disease and control groups) were subjected to various biochemical investigations for the determination of total thyroxine (T4), triiodothyronine (T3), thyroid stimulating hormone (TSH), thyroxine binding globulin (TBG), total lipids, triglycerides, total cholesterol, betalipoprotein and beta-lipoprotein cholesterol. Serum total T4, T3, TSH and TBG levels were determined with commercial test kits based on ELISA (Enzyme linked immunosorbent assay) technique[14]. Serum lipids and lipoprotein fractions were determined with commercial test kits based on enzyme — substrate principle: Total lipids were determined by the test combination colorimetric method (Cat. No. 124303), triglycerides by peridochrome (R) GPO - PAP (Cat. No. 701904), total cholesterol by monotest (R) CHOD - PAP (Cat. No. 237574) and beta-lipoprotein and its cholesterol by test combination enzymatic method (Cat. No. 123931)[15]. The kits used were supplied by the Boehringer Mannheim GmbH Diagnostica, Munich, West Germany. All investigations were carried out in batches and the accuracy of the results were checked by the inclusion of control sera "Precipath U" (for the lipid and lipoprotein profiles) and "Precinorm U" (for hormones and carrier protein determinations) supplied by Boehringer Mannheim Diagnostica, Munich) in each batch of samples processed. The factors which are known to influence plasma T4 or cholesterol levels such as pregnancy, prolonged use of contraceptive pills, nephrotic syndrome etc, were not common among the subjects assessed and were ruled out by taking proper history and carrying out detailed clinical examination before selecting the patients to the investigations.

Results

Table 1a represents a part of the results of epidemiological survey carried out by the authors and shows the percentage distribution of endemic goitre in the community of Bassa Local Government Council of Plateau State, Nigeria. Out of 1004 subjects screened, 249 had visible goitre, a prevalence of 24.8% which suggests that the above region from where the majority of the patients were selected is highly endemic. Table 1b shows the prevalence of various grades of goitre in the same locality. Out of 249 goitrous patients examined, 147 had grade 1a thyroid enlargement (15%), 53 with grade 1b (5.3%), 23 with grade 2 (2.2%), 21 with grade 3 (2.1%) and 11 with huge monstrous goitre of grade 4 category (1.1%) (see Fig. 1).

Table 2: The mean serum lipid fractions found in endemic goitre compared with those derived from a group of normal subjects used as a control. (Values in brackets are in S.I. Units)

Diagnosis	No. of cases	Age range (Yrs)	Sex	Place of residence	Goitre grade	Serum lipid and lipoprotein fractions mg/100ml (Mean + SE) Total lipids (g/l)	Triglycerides (mmol/l)	Total cholesterol (mmol/l)	Beta-lipo-protein (g/l)	Beta-lipo-protein cholesterol (mmol/l)
Control	59	5 - 65	M-32 F-27	Jos Township (Non-goitrous zone)	Grade "0"	452 ± 14 (4.52 ± 14)	53 ± 3.57 (0.6 ± .04)	136 ± 6.6 (3.4 ± .07)	251 ± 7 (2.51 ± .07)	84.8 ± 3.12 (2.19 ± .08)
Endemic Goitre (including 4 ageitrous cretin)	72	22-72 (for goitrous subjects) 8-16 (for the cretins and some with mild goitre	M-12 F-60	Binci/Zagun market Bassa L.G.C. (Goitrous Zone)	Grade (1-4)	659 ± 25 (6.58 ± .25)	68 ± 5.29 (0.77 ± .05)	185 ± 8.59 (4.74 ± 0.22)	348 ± 21 (3.48 ± .21)	126.6 ± 6.5 (3.23 ± .17)
Significance of difference between means						t=3.21, df=129 P < .01	t=2.77, df=129 P < .01	t=4.46, df=129 P < .01	t=5.73, df=129 P < .01	t=5.19, df=129 P < .01

Table 2 shows a comparision of the results of serum lipid and lipoprotein analysis between the patients with endemic goitre and the normal subjects used as the control. It is evident from the table that all the serum lipid fractions determined in the present investigation were significantly raised in the patients of endemic goitre compared to the corresponding mean values seen in the control group ($p < 0.01$ in all fractions).

Table 3: Classification of the subjects into various functional groups based on their serum levels of T4/TBG ratio, T4, T3 and TSH

Diagnosis	No. of subjects	Age range (Yrs)	Sex	T4/TBG	Serum Hormones (Mean + SE) T4 ug/dl (nmol/l)	T3 ng/dl (nmol/l)	TSH mu/l
Control	59	5 - 60	M - 32 F - 27	3.2 ± 2.1	7.6 ± 0.19 (97.8 ± 2.4)	98.0 ± 3.7 (1.41 ± 0.06)	1.96 ± 0.13
Hypothyroid	14	6 - 45	M - 4 F - 10	1.8 ± 0.16	3.9 ± 0.23 (50.2 ± 3.0)	58 ± 2.1 (0.89 ± 0.03)	26 ± 7.1 (primary = 10) (0.4 ± 0.02) (Secondary = 4)
(agoitrous cretins)	(4)	6 - 16	M - 2 F - 2	1.6 ± 0.11	3.5 ± 0.31 (45 ± 3.9)	25 ± 2.7 (0.38 ± 0.04)	0.4 ± 0.02 (Secondary = 4)
Euthyroid goitrous	35	12 - 48	M - 8 F - 27	2.9 ± 0.27	6.06 ± 0.13 (78 ± 1.67)	154 ± 4.9 (2.4 ± 0.07)	4.6 ± 1.8
Hyperthyroid	23		M - 1	4.7 ± 0.12	12.0 ± 0.42	182 ± 6.7	0.1 ± 0.04
T4 Elevation	19	35 - 65	F - 18		(154.4 ± 5.4)	(2.79 ± 0.1)	
T3 Toxicosis	4	28 - 41	M - 0 F - 4	3.4 ± 0.19	7.6 ± 0.21 (97.8 ± 2.7)	289 ± 11.3 (4.44 ± 0.17)	0.1 ± 0.02

Reference range values
Serum Total T4 = 4.5 - 9.7 ug/dl (58 - 125 nmol/l)
Serum Total T3 = 67 - 115 ug/dl (0.9 - 2.4 nmol/l)
Serum TSH = 0.5 - 4.0 uU/ml (0.5 - 4.0 mu/l)
Serum T4/TBG = 2.2 - 4.3

Table 3 shows the classification of the patients into different functional groups (hypothyroid, euthyroid and hyperthyroid groups) based on their serum levels of T4:TBG ratios (taken as an indicator of serum free thyroxine index), total thyroxine (T4), triiodothyronine (T3) and thyrotropin (TSH) and a comparision of the results with those from the control group. Out of 72 patients selected for study 14 were hypothyroid (4 agoitrous cretins in secondary hypothyroidism and 10 goitrous subjects in primary hypothyroid state), 23 were in hyperthyroid (19 with T4 elevation and 4 with typical biochemical findings consistent with T3 thyrotoxicosis) and remaining 35 in the goitrous euthyroid group. The overall Male/Female distribution of the subjects in the disease group was 1.5: 5.

The impact of thyroid functional status of the entire group of patients assessed (n = 72) and that of the degree of thyroid enlargements of 35 goitrous euthyroid subjects (eliminating the functional hypo & hyperthyroid groups) on serum lipid fractions and lipoprotein levels are shown in Tables 4 and 5 respectively (See Fig. 2). The later allows one to examine the effect of thyroid size alone on the changes in serum lipid and lipoprotein fractions in goitrous euthyroidism.

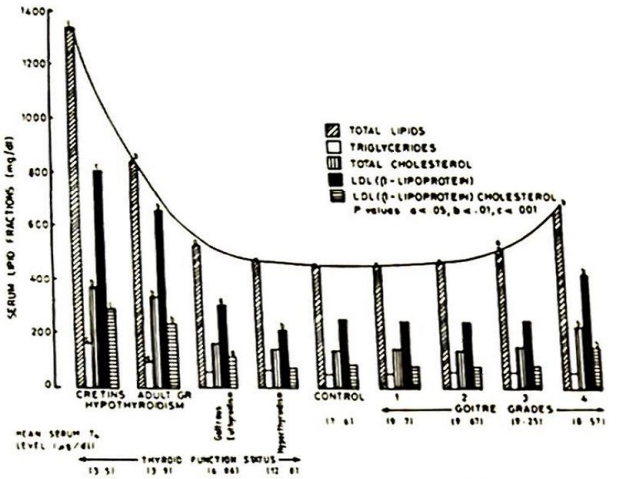

Fig. 2: Shows the impact of thyroid functional states (entire patient group n = 72) and the degree of thyroid enlargement (of 35 euthyroid goitrous subjects) on the serum lipid and lipoprotein values in the subjects with endemic goitre including 4 agoitrous cretins. (Conversion factors to S.I. Units: Serum total T_4 x 12.87 = nmol/l, total lipids + 100 = g/l, triglycerides + 88 = mmol/l, total cholesterol + 39 = mmol/l, beta-lipoprotein + 100 = g/l and beta-lipoprotein cholesterol + 39 = mmol/l).

Total lipids: Compared to the mean value seen in the control group, there was a highly significant rise in its mean level in the patients of hypothyroid group (t = 5.27, df = 71, P < 0.01) followed by a moderate but significant elevation in the goitrous euthyroid group (t = 2.82, df = 92, P < 0.02). The hyperthyroid group however did not show any significant changes in this respect (Table 4). Similarly a significant rise was also seen in the subjects with grade 4 goitre (t = 3.66, df = 66, P < 0.01) as well as in the group with grade 3 thyroid enlargement (t = 3.07, df = 67, P < 0.01).

Table 4: The serum lipid and lipoprotein values in the normal subjects of control group and in the patients with various categories of thyroid dysfunction. (This includes 4 cretins), (Figures in S.I. Units are shown in brackets)

			Plasma lipids and lipoprotein mg/dl (Results are in mean ± SE)						
Diagnosis	No. of cases	Age range (Yrs)	Sex	Thyroid enlargement grade	Total lipids (g/l)	Triglycerides (mmol/l)	Total cholesterol (mmol/l)	Beta-lipoprotein (g/l)	Beta-lipoprotein cholesterol (mmol/l)
Control	59	5 - 60	M - 32 F - 27	"0"	452 ± 14 (4.52 ± 0.14)	53 ± 3.57 (0.58 ± 0.04)	136 ± 6.6 (3.4 ± 0.17)	251 ± 7 (2.51 ± 0.07)	84.8 ± 3.12 (2.19 ± 0.08)
Hypothyroidism Agoitrous Cretins	4	8 - 16	M - 2 F - 2	Agoitrous Cretins	1322 ± 45*** (13.22 ± 0.45)	160 ± 45*** (1.82 ± 0.05)	370 ± 59*** (9.5 ± 1.5)	808 ± 71*** (8.08 ± 0.71)	283 ± 25*** (7.3 ± 0.64)
Entire hypothroid group	14	8 -45	M - 4 F - 10	4 agoitrous cretins +10 adults with massive (grade 3-4) enlargement	977 ± 100.9** (9.77 ± 1.0)	92 ± 18** (1.05 ± 0.2)	331 ± 36.6** (8.49 ± 0.94)	655 ± 96.9** (6.55 ± 0.97)	230 ± 40.4** (5.9 ± 1.04)
Euthyroidism	35	12 - 48	M - 8 F - 27	Grade 1-4	496 ± 27 (4.94 ± 0.27)	57.6 ± 5.5 (0.65 ± 0.06)	159 ± 8.87 (4.07 ± 0.23)	304 ± 1.5* (3.04 ± 0.2)	113 ± 8.62 (2.89 ± 0.2)
Hyperthyroidism	23	35 - 65	M - 1 F - 22	Grade 1-4	482 ± 24.7 (4.82 ± 0.25)	58 ± 3.6 (0.77 ± 0.4)	137 ± 11.3 (3 5 ± 0.29)	210 ± 13** (2.1 ± .13)	78 ± 7.0 (2 ± 0.18)

P values: * < .05, ** < .01, *** < .001.

Table 5: Impact of the degree of thyroid enlargement on the serum lipids and lipoprotein fractions. (Excluding those with hyper & hypothyroidism) (Values in brackets are in SI Units)

				Serum lipids and lipoprotein mg/dl (Result are in mean + SE)				
Thyroid enlargement grades	No. of cases	Age range (Yrs)	Sex	Total lipids (g/l)	Triglycerides (mmol/l)	Cholesterol (mmol/l)	B-lipoprotein (g/l)	B-lipoprotein cholesterol (mmol/l)
0 (Control)	59	5-65	M - 32 F - 27	452 ± 14 (4.52 ± 0.14)	53 ± 3.57 (0.58 ± 0.04)	136 ± 6.6 (3.4 ± 0.17)	251 ± 7 (2.51 ± 0.07)	84.8 ± 3.12 (2.19 ± 0.08)
Grade 1	6	11-22	M - 2 F - 4	458 ± 21 (4.58 ± 0.21)	54 ± 6.1 (0.6 ± 0.06)	142 ± 12.7 (3.64 ± 0.37)	247 ± 17 (2.47 ± 0.17)	83.6 ± 11.2 (2.14 ± 0.28)
Grade 2	10	15-70	M - 2 F - 8	466 ± 11.88 (4.66 ± 0.12)	58.4 ± 4.33 (0.66 ± 0.05)	140 ± 8.9 (3.6 ± 0.23)	240 ± 12.85 (2.4 ± 0.13)	84.3 ± 7.86 (2.16 ± 0.2)
Grade 3	10	35-67	M - 1 F - 9	494 ± 13.65* (4.94 ± 0.14)	59 ± 9.87 (0.6 ± 0.06)	152 ± 9.87 (3.9 ± 0.25)	249 ± 12.22 (2.49 ± 0.12)	85 ± 8.09 (2.18 ± 0.2)
Grade 4	9	36-72	M - 1 F - 8	663 ± 60** (6.63 ± 0.06)	58.6 ± 7 (066 ± 0.08)	222 ± 23.10** (5.7 ± 0.6)	423 ± 42** (4.23 ± 0.42)	148 ± 19** (3.79 ± 0.49)

P values: * < 0.05, ** < 0.01.

Triglycerides: The mean serum triglyceride level in the hypothyroid was significantly elevated compared to the mean value seen in the control group ($t = 2.24$, $df = 71$, $P < 0.02$). Although raised levels were seen in the other groups the rise was statistically not significant (Tables 4 and 5).

Total cholesterol: Similarly, the only significant changes seen with the mean serum total cholesterol levels were amongst the hypothyroid group, and in those with grade 4 thyroid enlargement. In both groups the mean levels were markedly elevated compared to the control group ($t = 5.4$, $df = 71$, $P < 0.01$ and $t = 3.72$, $df = 66$, $P < 0.01$, respectively). Other groups of patients however did not show any appreciable changes in their respective mean serum total cholesterol levels.

Beta-lipoprotein: Compared to the mean value seen in the control group, the mean serum level of beta-lipoprotein was markedly rised in hypothyroid patients ($t = 4.17$, $df = 71$, $P < 0.01$) and moderately but significantly depressed in the hyperthyroid group ($t = 3.18$, $df = 80$, $P < 0.01$). The level seemed to increase with increasing thyroid grade and so was the size compared to the control group ($t = 4.02$, $df = 66$, $P < 0.01$).

Beta-lipoprotein cholesterol: The changes in serum beta-lipoprotein cholesterol levels were almost identical with that seen in serum beta-lipoprotein fraction. Its mean levels were raised in the groups of hypothyroid as well as that of goitrous euthyroid subjects. Compared to the mean value seen in the control group that rise was more significant in the former group ($t = 3.57$, $df = 71$, $P < 0.01$) compared to the latter ($t = 2.66$, $df = 92$, $P < 0.01$). Similarly, the subjects with monstrous thyroid (grade 4) exhibited a markedly higher mean serum leves compared to the value observed in the control group ($t = 3.27$, $df = 66$, $P < 0.01$).

A serum lipid study was carried out on the four agoitrous cretins with secondary hypothyroidism (see Table 4 and Fig. 2). Lipid changes exceeding a three fold increase compared to normal subjects were seen which seemed to correlate very well with the functional state of their thyroid glands (Mean values: T4 = 3.5 µg/dl (45 nmol/l), T3 = 0.25ng/ml (0.38nmol/l), TSH = 0.04µU/ml. This finding suggests that hypofunctional rather than thyroid size accounts largely for the lipid changes which occur in the serum of patients with endemic goitre.

Table 6: Correlations between the goitre grades and the serum distribution of thyroxine, triiodothyronine, thyroid stimulating hormones and thyroxine binding globulin in the subjects with endemic goitre (Agoitrous cretins excluded). (Figures in brackets are in S.I. Units)

		Serum hormones and carrier protein (Means + SE)					
Goitre grades	No. of subjects	T4 ug/dl (nmol/l)	T3 ng/dl (nmol/l)	TSH uU/ml	T3/T4	TBG ug/ml (nnol/l)	T4/TBG
0 (Control)	59	7.6 ± 0.19 (97.0 ± 2.4)	98.0 ± 3.7 (1.5 ± 0.06)	1.96 ± 0.13	12.9	18.7 ± 1.3 (327.3 ± 22.8)	2.97
1.	12	9.7 ± 0.23 * (125 ± 3.0)	99.2 ± 4.1 (1.52 ± 0.06)	2.18 ± 0.35	10.2	24.8 ± 1.6* (434 ± 28)	2.89
2.	22	(9.65 ± 0.63* (124.2 ± 8.1)	103.7 ± 4.9 (1.59 ± 0.08)	2.85 ± 0.49**	10.75	27.6 ± 1.3** (483 ± 22.8)	2.57
3.	19	9.25 ± 0.56 (119.0 ± 7.2)	110.1 ± 6.2** (1.7 ± 0.13)	3.87 ± 0.63**	11.9*	26.2 ± 1.5** (458.5 ± 26.3)	2.60
4.	15	8.57 ± 1.25 (111.6 ± 16.1)	114.8 ± 9.9** (1.7 ± 0.15)	6.79 ± 1.7**	13.4**	28.2 ± 1.8** (495.3 ± 32)	2.25
Coefficient of linear correlation (r)		-0.975***	+0.93***	+0.94***	+0.81***	+0.79***	-0.623*

P values: * < 0.05, ** < 0.01, *** < 0.005

Table 6 shows correlations between the degree of thyroid enlargements and the serum levels of thyroid hormones and its carrier proteins determined in the present investigation (total T4, total T3, TSH and TBG). The degree of thyroid enlargement appears to bear an inverse linear correlation with the mean serum total T4 levels ($r = -0.975$, $P < 0.005$), and direct linear correlations with the mean serum levels of total T3 ($R = 0.93$ $P < 0.005$) and TSH ($R = 0.94$, $P < 0.005$). The quotients of T3/T4 ratio was also found to be positively correlated with increasing goitre size ($R = 0.81$, $P < 0.005$) while T4/TBG ratio was negatively correlated ($r = -623$, $P < 0.05$). Similarly the mean serum TBG were positively correlated ($r = 0.79$, $P < 0.005$).

Discussion

Endemic goitre embodies a spectrum of changes in which varying degree of thyroid functional states are fully represented. This makes it a suitable model for studying the details which occur in serum lipids in thyroid disease. Hypercholesterolaemia is recognised as a biochemical feature of hypothyroidism; this was consistently seen in our present investigation in hypothyroid goitrous patients and in agoitrous cretins. Other lipid fractions were similarly markedly raised. Fig. 2 shows that there is an inverse relationship, though to a limited extent between serum lipids and serum total T4 levels. The biochemical changes which occur in endemic goitre are complex and affect serum lipids. Our investigation show with increasing goitre size a rise in TBG levels, a negative correlations between thyroid size and the mean serum T4 levels ($R = -0.975$) and positive correlation with the mean serum T3 level ($R = 0.93$) and consequently a gradual but progressive rise in T3/T4 ratio. These changes are physiological compensatory attempts by the enlarging thyroid in an iodine deficient environment to remain functionally in euthyroid state. The process of compensation is further evident in the gradual rise seen in the mean serum TSH with increasing thyroid size ($R = 0.94$) while serum T4 declines. These compensatory mechanisms which operate in endemic goitre, namely, increasing serum T3 and TBG levels as well as increasing thyroid size make their own contributions too as modifying and modulating factors which affect the serum lipids in endemic

goitre. Serum T3 levels may be considerably high in endemic goitre. In a previous investigation our studies showed that about 44 per cent of the patients with endemic goitre had hyperthyroid T3 values, due in part to some extent probably to the concomitant rise in TBG values[7,8]. The resulting increase in T3/T4 ratio which occurs with increasing thyroid enlargement, also alters the thyroid function to keep the gland as far as possible euthyroid, and which may modify the serum lipid levels. Accordingly our investigations show that several patients in this category have normal lipid values inspite of the fall in serum total T4 levels. The state of other organs indirectly connected with thyroid function make their own impact too. The conversion of T4 to the more potent T3 which occurs in the peripheral organs[16,17] e.g. liver, kidney, heart also help to determine the degree of thyroid function and therefore the serum lipid status. A patient with severe chronic liver, kidney or heart disease may therefore be hypothyroid with seeming lipid changes conforming with the hypothyroid state developing subsequently.

The mild to moderate rise in serum lipids seen in euthyroid patients with very large goitre of grades 3 and 4 categories suggests that the serum lipid changes which occur in endemic goitre may, in part, be related to goitre size (see Fig. 2).

The comment may be made here that increased serum lipids especially cholesterol, triglycerides (and phospholipids) are probably required for the increased glandular support for an expending thyroid frequently seen in endemic goitre environments. Whether this finding is related to this function or due to increased TSH levels frequently seen in euthyroid subjects with advanced goitre in endemic zones or purely coincidental cannot be affirmed by the evidence obtained from the results of the present investigation.

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