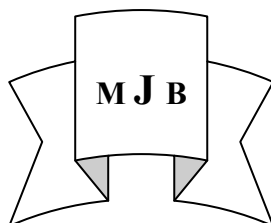


Physiological Changes in Patients with Hyperthyroidism

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Abstract

The present study was designed to investigate changes occurring in hematological, and biochemical changes in patients suffering from hyperthyroidism. A total number used was 170, patients and healthy subjects of both sexes, males and females. The total number of patients was 130; 100 females and 30 males, while the number of control subjects was 40. The ages of all subjects ranged between 20 years to 55 years. It was also found that percentage of affected females (76.93%) more than that of affected males (23.07%).

Concerning haematological changes, studying red blood corpuscles count (RBCs), hemoglobin concentration (Hb), and packed cell volume (PCV) showed a significant increase ($P<0.01$) when compared with healthy subjects. In addition, values of hemoglobin electrophoresis which included adult hemoglobin (HbA), adult hemoglobin2 (HbA2), and fetal hemoglobin (HbF) showed non significant difference when compared with control subjects. Results of erythrocyte sedimentation rate (ESR) and white blood cells count (WBCs) were also recorded non significant difference in a comparison with those healthy subjects.

Biochemical changes in serum, total serum protein (TSP) and serum albumin levels pointed out significant decrease ($P<0.01$) in hyperthyroid subjects, while serum globulin values showed non significant decrease when compared with those control subjects. More over, the present study was also involved determination of sodium (Na^+) and potassium (K^+) levels in both serum and urine samples of hyperthyroid patients. Sodium values showed significant increase ($P<0.01$) in both serum and urine samples. While , results of potassium showed non significant decrease in both serum and urine samples of hyperthyroid subjects when compared with control subjects. Total serum cholesterol levels showed significant decrease ($P<0.01$) in comparison with control subjects. In addition, results of serum triglycerides showed significant decrease ($P<0.01$) when compared with those healthy subjects . In view of the changes summarized, the increase or decrease in some hematological and biochemical parameters may be attributed to hyper metabolic state which arise due to higher production of thyroid hormones which, in turn, affect most of body tissues.

الخلاصة

تضمنت هذه الدراسة معرفة تأثير فرط إفراز هرمونات الغدة الدرقية على بعض صفات الدم والتي تضمنت المتغيرات الدموية والكيميوحيوية. شملت هذه الدراسة فحص (١٧٠) شخص من المصابين بفرط إفراز هرمونات الغدة الدرقية وغير المصابين (الأصحاء) ومن كلا الجنسين الذكور والإناث . حيث كان عدد الإناث المصابات (١٠٠) أنثى وعدد الذكور المصابين (٣٠) ذكراً أما أشخاص السيطرة (الأصحاء) فقد كان عدد الإناث الأصحاء (٢٠) أنثى وعدد الذكور الأصحاء (٢٠) ذكراً. حيث تراوحت أعمارهم بين (٢٠) سنة إلى (٥٥) سنة. بينت نتائج هذه الدراسة بأن نسبة الإناث المصابات (76.93%) أكثر من نسبة الذكور المصابين (23.07%). أما بالنسبة للمتغيرات الدموية فقد لوحظ ارتفاع معنوي بمستوى ($P<0.01$) لكل من العدد الكلي لكريات الدم الحمراء (RBCs) وتركيز خضاب الدم (Hb) وحجم الخلايا المضغوطة (PCV) للأشخاص المصابين عند مقارنتها بالأشخاص غير المصابين . كذلك لوحظ بأن قيم أنواع خضاب الدم (HbA, HbA2, HbF) والعدد الكلي لخلايا الدم البيض (WBCs) ومعدل سرعة ترسيب كريات الدم الحمراء (ESR) لم تسجل فروقاً معنوية عند مقارنتها بالأشخاص الأصحاء.

أما بخصوص التغيرات الكيميوحيوية فقد أثرت قيم البروتين المصلي الكلي (TSP) والألبومين (Albumin) انخفاضاً معنوياً بمستوى ($P<0.01$) عند مقارنتها بالأشخاص الأصحاء كذلك لوحظ انخفاض غير معنوي في قيم الكلوبيولين عند مقارنتها

بالأشخاص الأصحاء. كذلك لوحظ بان قيم الصوديوم (Na^+) قد سجلت ارتفاعاً معنوياً بمستوى ($P<0.01$) في عينات المصل والإدرار عند مقارنتها بالأشخاص الأصحاء. أما قيم البوتاسيوم (K^+) فأنها قد سجلت انخفاضاً غير معنوي في عينات المصل والإدرار في الأشخاص المصابين عند مقارنتها بالأشخاص الأصحاء. وبيئت قيم كل من الكوليسترول الكلي والترايكليسرايد انخفاضاً معنوياً بمستوى ($P<0.01$) في عينات المصل عند مقارنتها بالأشخاص الأصحاء. أن التغييرات الحاصلة في المعايير الدموية والكيموحيوية يمكن أعزؤها بصورة رئيسة إلى ارتفاع معدل الايض بسبب الإفراز العالي لهرمونات الغدة الدرقية .

Introduction

Hyperthyroidism occurs when tissues expose to excess amount of the thyroid hormones, and describes as the clinical syndrome[1]. Thyroid stimulating hormone (TSH), the main stimulus for thyroid gland to enhance iodide uptake and stimulates the manufacture and release of T3 and T4 [2]. Hyperthyroidism resulted from several causes such as: Graves' disease (diffuse goiter) is an auto immune thyroid disease and comprises 80% of hyperthyroidism. In this auto immune disease, auto antibodies bind with TSH receptors to activate thyroid. TSH becomes suppressed because of negative feed back mechanism of T3 and T4[3]. Hyperthyroidism is also called thyrotoxicosis, a general term, refers to hypermetabolic state that results because of excess thyroid hormones[4]. This disorder had also been found to affect women five times more than men[5]. Clinical features of hyperthyroidism include nervousness, tachycardia, weight loss, profuse sweating, heat intolerance, diarrhea, muscular weakness, emotional excitement, and irregular menses[6]. Hormone-sensitive lipase, the other enzyme, acts inside fat cells to release free fatty acids from triglycerides. This enzyme is stimulated by epinephrine, cortisol, and thyroxine hormone[7]. Finally, the other miscellaneous causes represent a little incidence in hyperthyroidism such as metastatic thyroid carcinoma, and struma ovarii[8]. Thyroid hormones play essential roles in regulation the metabolism of major nutrient biomolecules such as carbohydrates,

lipids, and proteins[9]. Synthesis, mobilization, and degradation of lipids are controlled by thyroid hormones, because lipids are the major calorigenic molecules[10]. Moreover, thyroid hormones are important factors for the other physiological phenomena such as growth, puberty, and mental development[11].

Materials and Methods

(A):-Materials

Subjects of Study

The subjects of the study were 170 ; patients and healthy subjects of both sex, males and females. The total number of patients were 130 (100 females and 30 males). Forty subjects were used as control group. Their ages ranged between 20 years to 55 years. This study was carried out before doing treatment for all patients. Women of this study were non pregnant and no contraceptive drugs were used. All patients were attending to the hospital for laboratory diagnosis and treatment, while the control subjects were attending to the public health laboratory in the hospital. (B):-

Methods

(1):-Blood collection

The collection of blood was performed in Hilla teaching hospital. Two groups of labeled tubes were used ; the first tubes contain EDTA as anti-coagulants to prevent clotting of blood to be used for hematological studies. The second group of tubes were without anti-coagulant as plain tubes, for blood to be used for preparing sera for subsequent biochemical tests. The blood is allowed to clot for 45 minutes, and serum can be obtained by

centrifugation and precautions were taken to avoid hemolysis. The serum samples were liquated in sterile test tubes using micropipette with sterile disposable tips. Each sample was labeled and given a serial number together with the patient name, the serum samples were frozen at (-20°C) for biochemical analysis[12].

(2):-Urine analysis

The collection of urine samples was done on random samples of urine freshly voided by patients. Urine samples were diluted with distilled water (1:5) and then urinary K⁺, and Na⁺ concentrations were done as described in their corresponding estimation in serum. Estimation was carried out by using colorimetric and flame photometric method. (According by Phosphorus kit from spinreact).

(3):-Hematological studies

(a):-Red blood corpuscles count (RBCs count)

Blood was diluted with formal citrate solution (1% formalin in 38 gram /liter(gm/L)tri-sodium citrate).A twenty microliter of blood was added into four ml of diluting fluid, the counting chamber (Neubaur hemocytometer) was filled before being examined under the microscope [13].

(b):-White blood cells count (WBCs count):-

A twenty microliter of blood was diluted with 0.4 ml of Turk's solution; the counting chamber a(Neubaur hemocytometer) was filled before being examined under the microscope[13].

(c):-Erythrocytes sedimentation rate (ESR):-

Westergren method was used to determine the ESR. Blood was diluted with tri-sodium citrate solution 3.8%. 0.5 ml of diluted solution was used for 2 ml of blood. Westergren tube up to the zero mark and tube set upright in a stand position. The level of the top of

the red blood corpuscles column is read at the end of one hour[14].

(d):-Determination of packed cells volume (PCV):-

Microhematocrit method was used to determine PCV. Heparinized capillary tubes used, and blood was permitted be fill to approximately three quarters of their lengths then the unmarked end is closed with modeling clay and put in the microhematocrit centrifuge[13].

e)Estimation of hemoglobin (Hb):-

A cyanomethemoglobin method was used to estimate the hemoglobin contents of the blood. The results were estimated by using Hb meter at 540 nm wave length [15].

(f):-Hemoglobin electrophoresis

Cellulose acetate electrophoresis method was used to determine hemoglobin quantitation (HbA, HbA₂, and HbF). Electrophoresis is the name given to the movement of charged particles through on electrolyte subject to an electric field. If these are differently, they will move in apposite direction. The rate of migration of particles of like charge will depends among other thing on the number of charges each carrier. Hb will migrate from cathode to the anode in the following order. First hemoglobin constant spring, then HbA₂,C,and E migrate in the same band, next HbS and Lepore, again in the same band next hemoglobin F followed by Hb A then Hb Bart's and last HbH[14].

(4):-Biochemical studies:-

(a):-Measurement of total serum protein:-

Proteins are given an intensive violet-blue complex with copper salts in alkaline medium. Iodide is included as an antioxidant. The intensity of the color formed is proportional to the total protein concentration in sample. The intensity of color was measured photometrically at 450 nm wave length, by using spectronic 21[16].

(b):-Determination of serum albumin:-

Albumin in the presence of bormocresol green at slightly acid pH, produces a color ,the intensity of color was measured by using spectronic 21 at 630 nm wave length. (according by albumin kit from spinreact).

(c):-Determination of serum globulin:-

Serum globulin was determined by subtracting albumin from total serum protein and the results represented the values of serum globulin.[12]

(d):-Determination of total serum cholesterol:-

The cholesterol is determined after enzymatic hydrolysis and oxidation. The quantity indicator of red dye quinoneimine formed is proportional to the cholesterol concentration, and was measured photometrically by using spectronic 21 at 505 nm wave length (according by cholesterol kit from Biomagreb).

(e):-Determination of triglycerides:-

The triglycerides are enzymatically hydrolyzed to glycerol and fatty acids. The reagents were mixed and incubated for 5 minutes at 37C°, and then measured photometrically by using spectronic 21at 505 nm wave length. (according by triglycerides kit from Biomagreb).

(f):-Determination of potassium and sodium in both serum and urine samples

Flame emission photometer was used to determine sodium and potassium in both serum and urine samples .Serum samples were diluted(1:4),where as urine samples diluted(1:5);and then samples injected into sample cup of the system to measure emitted lights., Standard curve were made for both sodium and potassium. [12].

Statistical analysis

All values were expressed as means $\pm$ SE. The data were analyzed by using of computer SPSS program.

Student's t-test was used to examine the differences between different groups^[17].

Results**(1):-Relationship between hyperthyroidism and sex :-**

The results which are shown in figure (1) show that the number of affected females was 100(76.93 %)out of 130 and the number of affected males was 30(23.07%).

(2):-Hematological studies:-**(a):-RBCs count, Hb concentration , and PCV :-**

Results of RBCs count ,Hb concentration , and PCV of both males and females affected with hyperthyroidism are illustrated in table (means $\pm$ SE) (1).

(i):-RBCs count :-

Results of RBCs count of hyperthyroid in males and females groups (5.520 ± 0.164 ; 5.100 ± 0.169 million/mm³, respectively) which was a significant increase ($P < 0.01$) higher than control subjects, of males and females(4.610 ± 0.159 ; 4.000 ± 0.113 million /mm³,respectively)

(ii):-Hb concentration :-

Results of Hb concentration of both affected males and females groups (15.106 ± 0.384 , 14.066 ± 0.318 gm/dL, respectively) were significantly($P < 0.01$) higher than control males and females (13.380 ± 0.243 ; 12.164 ± 0.246 gm/dL, respectively).

(iii):-PCV :-

Results of PCV in hyperthyroid patients, males and females groups (0.458 ± 0.025 , $0.42 \pm 0.011\%$, respectively) which were significantly ($P < 0.01$) higher than healthy males and females (0.421 ± 0.032 ; $0.40 \pm 0.021\%$, respectively).

(b):-Hb electrophoresis :-

Results of HbA, HbA2 , and HbF of males and females groups affected

with hyperthyroidism are explained in table (2) .

(i):-HbA :-

Values of HbA for hyperthyroid in males and females groups (98.08 ± 0.216 ; 98.211 ± 0.228 %, respectively) which non significantly different in a comparison with those control male and female, (98.00 ± 0.207 ; 98.260 ± 0.348 %, respectively).

(ii):- HbA2 :-

Results of HbA2 of hyperthyroid, males and females were 1.48 ± 0.112 ; 1.56 ± 0.174 %, respectively ,these values were non significantly different in a comparison with control, males and females (1.54 ± 0.168 ; 1.72 ± 0.123 %, respectively).

(iii):-HbF :-

Values of HbF of hyperthyroid groups, males and females (0.742 ± 0.113 , 0.881 ± 0.103 %, respectively) which were non significantly different when compared with those for healthy males and females (0.752 ± 0.123 ; 0.780 ± 0.074 %, respectively) .

(c):-Total WBCs count and ESR :-

Results of WBCs count and ESR of both hyperthyroid patient groups, males and females are depicted in table(3).

(i):-Total WBCs count :-

Results of WBCs count of hyperthyroid, males and females (5160 ± 0.451 ; 4810 ± 0.226 cell/mm³, respectively) were non significantly different when compared with control, males and females (5090 ± 0.351 ; 4680 ± 0.184 cell/mm³, respectively).

(ii):-ESR:-

Values of ESR of both hyperthyroid males and females (4.22 ± 0.666 ; 6.00 ± 1.07 mm/h, respectively) were non- significantly different in a comparison with those healthy control groups (4.02 ± 0.894 ; 7.610 ± 1.077 mm/h, respectively).

(3):-Biochemical studies:-

(a):-Total serum protein, albumin, and globulin:-

Results of total serum protein, albumin ,and globulin of both hyperthyroid groups males and females are shown in table (4).

(i):-Total serum protein :-

Values of total serum protein of both hyperthyroid groups, males and females (4.90 ± 0.335 ; 5.623 ± 0.241 g/dL, respectively), these results were significantly ($P < 0.01$) lower than control males and females (6.75 ± 0.338 ; 7.010 ± 0.204 g/dL, respectively).

(ii):-Serum albumin :-

Results of serum albumin value of both hyperthyroid males and females were (3.50 ± 0.171 , 3.685 ± 0.158 g/dL, respectively). These results pointed with significant decrease ($P < 0.01$) when compared with those healthy control males and females (4.44 ± 0.257 ; 4.480 ± 0.175 g/dL, respectively).

(iii):-Serum globulin :-

Values of serum globulin of both hyperthyroid males and females were (1.708 ± 0.163 , 1.985 ± 0.139 g/dL, respectively). These results were in significant decrease in a comparison with control, males and females (2.050 ± 0.160 ; 2.270 ± 0.145 g/dL , respectively) .

(b):-Sodium and potassium:-

Results of sodium and potassium in serum and urine samples of hyperthyroid, males and females were illustrated in table (5) .

(i):-Sodium:-

Values of serum sodium of affected, males and females were 150.500 ± 3.55 ; 151.700 ± 1.989 mmol/L, respectively .These results were significantly increase ($P < 0.01$)when compared with healthy subjects of both sex (137.400 ± 1.58 ; 139.900 ± 1.876 mmol/L, respectively). Values of urine sodium were (65.300 ± 4.839 ; 58.5100 ± 3.685 mmol/L, respectively) showed significant increase ($P < 0.01$) in a

comparison with control males and females (33.501 ± 4.349 ; 27.272 ± 2.966 mmol/L, respectively).

(ii):-Potassium :-

Results of serum potassium of hyperthyroid groups ,males and females were (3.670 ± 0.134 ; 3.870 ± 0.413 mmol/L, respectively) which showed non significant decrease in comparison with control males and females (4.14 ± 0.163 ; 4.190 ± 0.179 mmol/L, respectively). Moreover, values of urine potassium of affected males and females were (5.810 ± 0.256 ; 5.631 ± 0.425 mmol/L, respectively). These results were non significant decrease when compared with healthy control males and females (6.470 ± 0.397 ; 6.231 ± 0.455 mmol/L, respectively).

(c):-Cholesterol and triglycerides :-

Values of serum cholesterol and triglycerides of hyperthyroid males and females are illustrated in table (6).

(i):- Cholesterol :-

Results of cholesterol of affected males and females were 155.871 ± 8.730 ; 148.23 ± 5.103 mg/dL, respectively. These results pointed out significant decrease ($P < 0.01$) in a comparison with control males and females (183.98 ± 3.600 ; 181.294 ± 3.437 mg/dL, respectively).

(ii):- Triglycerides:-

Values of triglycerides of hyperthyroid males and females (86.200 ± 6.719 ; 80.000 ± 7.766 mg/dL respectively) were significantly ($P < 0.01$) lower than control males and females (112.500 ± 5.325 ; 101.600 ± 6.172 mg/dL, respectively).

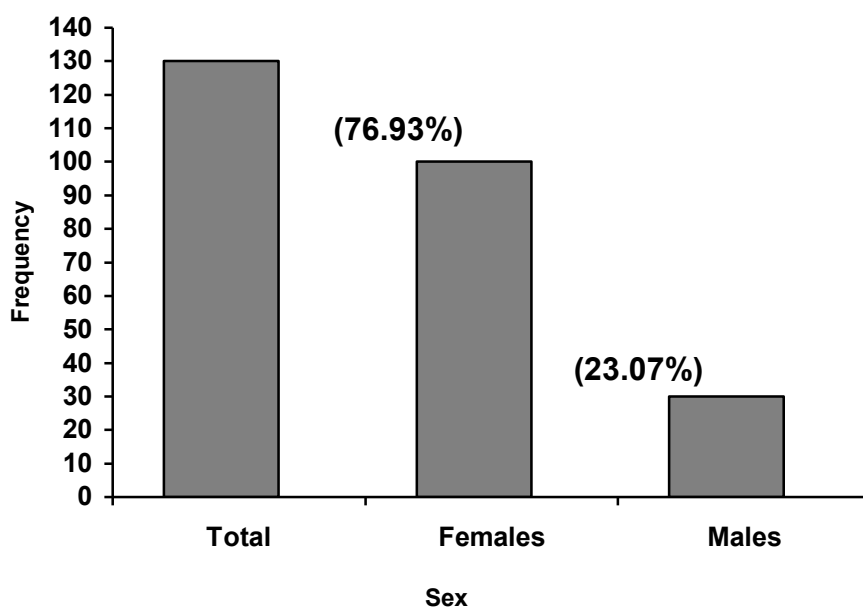


Figure 1 The relationship between sex and the frequency of hyperthyroidism.

Table 1 The means of red blood corpuscles count (RBCs), hemoglobin concentration (Hb), and packed cell volume (PCV) in hyperthyroid males and females .

Parameter	Males		Females	
	Control groups	Patient groups	Control groups	Patient groups
RBCs million/mm³	4.610 ± 0.159	** 5.520 ± 0.164	4.000 ± 0.113	** 5.100 ± 0.169
Hb gm/dL	13.380 ± 0.243	** 15.106 ± 0.384	12.164 ± 0.246	** 14.066 ± 0.318
PCV %	0.421± 0.032	* 0.458 ± 0.025	0.40 ± 0.021	* 0.42 ± 0.011

-Values are means ± SE.

-Means with two asterisk are significantly different at P<0.01.

Table 2 The means of values of adult hemoglobin (HbA), adult hemoglobin2(HbA2),and fetal hemoglobin (HbF)in hyperthyroid males and females.

Parameter	Males		Females	
	Control groups	Patient groups	Control groups	Patient groups
HbA %	98.00 ± 0.207	98.08 ± 0.216	98.260 ± 0.348	98.211 ± 0.228
HbA2 %	1.54 ± 0.168	1.48 ± 0.112	1.72 ± 0.123	1.56 ± 0.174
HbF %	0.752 ± 0.123	0.742± 0.113	0.780 ± 0.074	0.881 ± 0.103

-Values are means ± SE .

Table 3 The means of erythrocytes sedimentation rate (ESR)and total white blood cells count (WBCs) in hyperthyroid males and females.

Parameter	Males		Females	
	Control groups	Patient groups	Control groups	Patient groups
ESR mm/h	4.0 ± 0.894	4.22 ± 0.666	7.610 ± 1.077	6.00 ± 1.07
WBCs cell/mm³	5090 ± 0.351	5160 ± 0.451	4680 ± 0.184	4810 ± 0.226

Values are means ± SE .

Table4 The means of total serum protein, albumin, and globulin values in hyperthyroid males and females .

Parameter	Males		Females	
	Control groups	Patient groups	Control groups	Patient groups
Total serum protein g/dL	6.75 ± 0.338	** 4.90 ± 0.335	7.010 ± 0.204	** 5.623 ± 0.241
Albumin g/dL	4.440 ± 0.257	** 3.500 ± 0.170	4.480 ± 0.175	** 3.685 ± 0.158
Globulin g/dL	2.310 ± 0.160	1.408 ± 0.163	2.530 ± 0.145	1.938 ± 0.139

- Values are means ± SE .

-Means with the two asterisks are significantly different at p<0.01

Table 5 The means of sodium and potassium levels in both serum and urine samples of hyperthyroid patients, males and females.

Parameter	Males		Females	
	Control groups	Patient groups	Control groups	Patient groups
Serum sodium mmol/L	137.400 ± 1.58	** 150.500 ± 3.55	139.900 ± 1.876	** 151.700 ± 1.989
Urine sodium mmol/L	33.501 ± 4.349	** 65.300 ± 4.839	27.272 ± 2.966	** 58.500 ± 3.685
Serum potassium mmol/L	4.14 ± 0.163	3.670 ± 0.134	4.190 ± 0.179	3.870 ± 0.413
Urine potassium mmol/L	6.470 ± 0.397	5.810 ± 0.256	6.231 ± 0.455	5.631 ± 0.425

-Values are means ± SE .

-Values with two asterisks are significantly different at P<0.01 .

Table 6 The means of cholesterol and triglycerides levels in hyperthyroid males and females .

Parameter	Males		Females	
	Control groups	Patient groups	Control groups	Patient groups
Cholesterol mg/dL	183.98 ± 3.600	** 155.87 ± 10.730	181.294 ± 3.437	** 148.23 ± 4.103
Triglycerides mg/dL	112.500 ± 5.325	** 86.200 ± 6.719	101.600 ± 6.172	** 80.00 ± 7.766

-Values are means ± SE .

-Values with two asterisks are significantly different at $P < 0.01$.

Discussion

The present study of this thesis concentrated on hyperthyroidism to analysis some of the hematological and biochemical parameters in both males and females which are associated with such disorder.

(a):-Sex:-

Hyperthyroidism and its relationship with sex in this study is shown in figure (1).The results showed that the number of affected females was 100 (76.93%) out of 130 patients, while the number of affected males was 30 (23.07%). From the above results, it was appeared clearly that females were more susceptible to such disease than males and that agrees with several studies [3; 18 ;19]. The reasons which may assist or exacerbate the female to acquire this disease could be due to sex hormones imbalance such as estrogen hormone which are normally elevated in females during puberty and pregnancy. This suggestion was supported by Woeber and Ingher[20]who suggested that high levels of estrogens in euthyroid females increase the total T3 and T4 concentration to about 1.5–2 time above their normal levels. Lahita *et al* [21]who reported that the capacity of sex hormones to influence the functions of immune system and the development of auto immune disease has been firmly established, in general,

estrogen hormones were found to stimulate immunity, while testosterone has the opposite effect. Also Smyth[22] and Ganong[23]reported that elevation of total serum T4 and T3 without alteration in thyroid status are a consequence of estrogen induced increase in thyroxin binding globulin. On the other hand, the effect of androgen hormone has a reversible effect than estrogen, but the male's hormone (androgens) play important role in exhibiting hyperthyroidism but the frequency in females remained higher than that observed in males[24].

(b):-Hematological Studies:-

Concerning red blood corpuscles count in hyperthyroidism which are illustrated in table(1) they showed significant increase in hyperthyroid males and females when compared with control groups. Oxygen is of vital importance for the metabolism and function of all cells in the human body. Thyroid hormones have been found to augmented oxygen capacity of blood by increasing the production of erythropoietin. Erythropoietin levels are induced by 50 to 100 fold in vitro by physiologically relevant level of hypoxia[25]. Thyroid hormones are required in nearly all tissues, with major effects on oxygen consumption and metabolic rate. Adaptation to this increased metabolic demand is partly achieved by potent effects of thyroid

hormones on erythropoiesis and thus blood oxygen capacity increased[26]. At the same time, thyroid hormones directly increase the proliferation of erythroid progenitor[27]. Data of the present study may be attributed to high level of thyroid hormones which in turn stimulate bone marrow and lead to increase number of red blood corpuscles and this suggestion is agree with other previous studies [28,29]. Results of hemoglobin concentration which are presented in table (2) showed a significant increase in hyperthyroid patients, males and females. Over production of thyroid hormones maintains a higher level of hypoxia, and stimulates respiratory center. Also, it increases cellular demands for oxygen because of hyper metabolic rate. Hemoglobin is a major oxygen transporter in blood to meet body requirements of oxygen[30]. As explained in RBCs count, thyroid hormones stimulate erythropoietin production which in turn stimulates erythropoiesis in bone marrow. In addition, thyroid hormone itself stimulate erythrocyte precursors by beta-adrenergic receptors to enhance RBCs production[26]. One of thyroid hormones actions is increased synthesis of multiple enzymes which are responsible for manufacturing of several proteins. Hemoglobin is considered as an intracellular protein, therefore, increasing erythrocytes production in hyperthyroidism is essentially associated with an increase in hemoglobin synthesis[31]. These results may be attributed to direct effects of thyroid hormones excess on bone marrow to increase hemoglobin synthesis within red blood corpuscles [28]. Results of packed cell volume in table(1) recorded a significant increase in subjects with hyperthyroidism of both sexes. Data of the present study agree with previous studies[32,28]. As mentioned previously that, PCV test

represents the ratio between cellular part and plasma volume. It is not surprising, that an increase in red blood cells resulted in an increase of packed cell volume. Increase in RBCs count because of thyroid hormones excess is the main reason in elevation of PCV in hyperthyroid patients [33]. Concerning the relationship between hyperthyroidism and hemoglobin electrophoresis which are shown in table(2). It appears that, results of HbA, HbA2 and HbF reported non significantly different in patients with hyperthyroidism of both males and females when compared with those of control subjects. Results of the present study do not agree with other previous studies [34,32]. These studies indicated that there was slight elevation in HbA2 and HbF level in hyperthyroidism, and these studies based on the fact that thyroid hormones modulate globin chains synthesis by affecting genes of these chains. In addition, these results were obtained at advanced stages of hyperthyroidism in which the effects of excess thyroid hormones on hemoglobin types become more prominent. In contrast, the present study was obtained at newly diagnosed hyperthyroid patients, thus, suggested that there was not enough time for excess thyroid hormones to exert its effects on hemoglobin types[34]. Results of erythrocytes sedimentation rate in table(3) showed non significant difference in hyperthyroid patients. Present results agree with previous studies [35,36] which indicated that ESR level remains within normal values in thyrotoxic patients. Also a study by Parmar and Sturge[37] indicated that increase in RBCs count in hyperthyroid patients reduces ESR level, at the same time, there was not any inflammatory complication within the body. Determination of total WBCs count in hyperthyroid patients

of both sexes which are shown in table(3) pointed out non significant differences. Previous studies had recorded different results. Such as Hrycek[38] who reported that in patients with hyperthyroidism, the number of leukocytes especially neutrophils was decreased. Tsidale and Kemp[39] who recorded increased granulocytes in hyperthyroid patients. In the present study, it appears that the effects of thyroid hormones on bone marrow are restricted on erythropoiesis process to increase RBCs which in turn will increase oxygen availability for tissue cells[29].

(c):-Biochemical Studies :-

The present study also involved study of the relationship between hyperthyroidism and total serum protein, albumin, and globulin which are shown in table (4). Results of total serum protein showed significant decrease in hyperthyroid subjects of both sex. The present results were consistent with previous studies[40,41]. Protein synthesis and degradation are stimulated by thyroid hormones, thus, excessive production of thyroid hormones accelerated protein catabolism, leading increased nitrogen excretion[42]. Moreover, over production of T3 and T4 resulted in elevation of body basal metabolic rate which in turn increase catabolism of nutrient molecules such as lipids, carbohydrates, and proteins to produce energy[41]. Results of serum albumin showed a significant decrease in hyperthyroid patients. Albumin represents the major component of serum proteins and perform several important physiological functions within the body. Among these functions, its ability to scavenge reactive oxygen species, where it is found to be an important anti-oxidant in plasma, by scavenging free radicals and then prevent their effects [43]. Concerning results of serum

globulin which showed non significant decrease in both affected males and female. As explained previously, globulin, the second important component of plasma proteins[44]. The present data may suggest that serum globulin also undergo catabolism and oxidative stress but in lesser extent than albumin [45].

The present study also included the relationship between excess thyroid hormones and levels of sodium and potassium in both serum and urine samples which are shown in table (5). Results of sodium reported a significant increase in both serum and urine samples of hyperthyroid groups. Whereas, potassium results recorded non significant decrease in both serum and urine samples of hyperthyroid patients, males and females. Sodium is the more cation presented in extracellular fluids, while potassium is the main intracellular cation. This distribution of both two ions is dependent essentially on cell membrane bound $\text{Na}^+\text{-K}^+\text{ATPase}$, which actively transports three sodium ions to the outside of cells simultaneously with the transport two potassium ions into inside of cells[46]. $\text{Na}^+\text{-K}^+\text{ATPase}$ had been found to be stimulated by several hormones. One of them, thyroid hormones, since, the metabolic and thermogenic effects of excess thyroid hormones are mediated by increasing $\text{Na}^+\text{-K}^+\text{ATPase}$ activity[47]. The effects of thyroid hormones on $\text{Na}^+\text{-K}^+\text{ATPase}$ appear by increasing the content of $\text{Na}^+\text{-K}^+\text{ATPase}$ subunit genes and increased mRNA of this enzyme (Awais *et al.*, 2000)[47]. Furthermore, excess thyroid hormones increase the number of beta adrenergic receptors in the cells of tissues[49], which in turn increase potassium uptake[50]. Insulin hormone had also been found to promote potassium transfer from extra cellular fluids to intra cellular fluids. Thus,

insulin hormone promotes uptake of potassium independently of cellular glucose uptake by increasing ATPase activity. Moreover, insulin also reduces sodium permeability; the resultant cellular hyperpolarization of cells produces a passive driving force of potassium accumulation within cells[51]. In hyperthyroidism, increased insulin secretion which in turn may affects $\text{Na}^+ - \text{K}^+$ concentration[52]. Sodium and potassium are also present in considerable amount in matrix of bones, therefore, over production of thyroid hormones on bones by increasing bones resorption may mobilize some amounts of sodium and potassium into circulation[53]. Results of the present study are consistent with other studies which indicated increase in serum sodium and a decrease serum potassium in hyperthyroidism[54,55]. In hyperthyroidism, increased atriopeptin levels which in turn increase sodium excretion in urine of hyperthyroid patients[56]. In kidneys, the reabsorption of sodium ions is mediated by aldosterone hormone. Secretion of aldosterone is controlled by sodium concentration in extracellular fluids and its action involve reabsorption of sodium ions from renal tubules by exchange with potassium and hydrogen ions[57]. It appears that a high levels of sodium ions with low level of potassium in extracellular fluids may inhibit aldosterone secretion which in turn lead to increase sodium excretion in urine[23]. Previous studies indicated increased sodium excretion in urine with low level of potassium in hyperthyroid subjects[58; 59]. As well as, Dolev *et al.*, [40] reported that excess thyroid hormone increase sodium and calcium excretion in urine of hyperthyroid subjects

Regarding levels of cholesterol, the results obtained in the present

study pointed out a significant decrease in the cholesterol levels of hyperthyroid groups (table 6). Present data are consistent with previous studies [60,61]. For explanation these results, thyroid hormones play an essential role in lipid metabolism through energy production[62]. Parle *et al.*, [63] who observed that excess thyroid hormones exert direct metabolic effects on lipid metabolism which in turn lead to decrease cholesterol level. One of important reasons to decrease cholesterol level, that, hepatic low density lipoprotein (LDL) receptors are sensitive to thyroid hormones, and these receptors decrease in number in hypothyroidism and elevated in hyperthyroidism hence, T3 and T4 increase hepatic LDL receptors which in turn elevate cholesterol excretion from body via liver [64]. Other reason which explained a decrease of cholesterol level in hyperthyroidism involved that lysosomal acid lipase, the enzyme which hydrolyzes lipoprotein cholesterol esters under thyroid hormones regulation and becomes significantly higher in hyperthyroidism which leads to decrease cholesterol[65].

Results of triglycerides in table(6) showed a significant decrease in both hyperthyroid groups, males and females. Elevated thyroid hormones are accompanied with hypermetabolic rate which in turn increase consumption of oxygen to oxidize nutrient molecules to produce energy[66]. Triglycerides consider a major source of energy fuel in the body. Our results agree with other studies[67, 8]. Thyroid hormones apparently can promote catabolism of very low density lipoprotein (VLDL) and lead to decrease triglycerides[69]. Thyroid hormones may also influence to increase of lipolysis rate[49].

References

- (1):-Dahlen, R.(2002). Managing patients with acute thyrotoxicosis. *Critical Care Nurse*. 22(1):20 -26.
- (2):-Takeda, and Kyokao: (2002). Molecular defects in plasma membrane receptors. *Nippon – Rinsho*.60(2):24-51.
- (3):-Ali, K.A.; Sharif, M.T.M.; and Alwan, A.F. (2002). Determination of antithyroglobulin and antithyroperoxidase antibodies in patients with hyperthyroidism by application of ELISA technique. *Iraqi-J.Comm.Med.*, 15(1):59-63.
- (4):-Intenzo, C.M.; Depap, A.E; Jabbour, S.; Miller, J.K; and Capuzzi, D.M.(2002). Scintigraphic manifestation of thyrotoxicosis. *Radiographics*. 23(4):57–69.
- (5):-Mayne, P.D.(1998). *Clinical Chemistry in Diagnosis and Treatment* 6th. ed., Oxford University Press. Inc., P(158- 168).
- (6):-Mohamimad, A.A. and AL-Dabbagh, T.Q. (1999). Clinical evaluation and diagnosis of hyperthyroidism revisited. *Ann. Coll. Med. Mosul*. 25(1-7):1-6.
- (7):-Cachefo, A.; Boucher, P.; Vidon, C.; Dusserre, E.; and Diriason, F. (2001). Hepatic lipogenesis and cholesterol synthesis in hyperthyroid patients. *J. Clin. Endocrinol. Metab.*, 86(11) :7-53.
- (8):-Greenspan, F.S. and Gardner, D.G. (2001). *Basic and Clinical Endocrinology*.6th.ed.,McGraw-Hill Med. Publishing. Philadelphia:(201-212).
- (9):-Weber, G.; Vigone, M.C.; Stroppa, L.; and Chiumello, C. (2003). Thyroid function and puberty. *J. Pediatr. Endocrinol.*,2:25-7.
- (10):-Nogueira, V.; Walter, L.; Averet, N.; Fontaine, E.; Rigoulet M.; and Leverve, X.M. (2002). Thyroid status is a key regulator of both flux and efficiency of oxidative phosphorylation in rat hepatocytes. *J. Biol. Energ. Biomember.*, 34 (1):55-66.
- (11):-Monden, T.; Nakajima, Y.; Hashida, J.; Ishiis, T.; and Shibuja, N.(2006). Expression of thyroid hormone receptors iso form down regulated by thyroid hormone in human medulla blastomal cell. *Endocrin. J.*, 53(2):181-7.
- (12):-Bishop, M.L.; Dube-Engelkirk, J.L.; and Fody, E.P. (2000). *Clinical Chemistr: Principles, correlation's, procedures..* 4th. ed., J.B. Lippincott Williams and Wilkins. Philadelphia P(405-416).
- (13):-Dacie, V. and Lewis, S.M. (1995). *Practical Hematology*. 2nd.ed. Philadelphia, Tokyo., P(352-354).
- (14):-Pittiglio, D.H. and Sacher, R. H.(1987). *Clinical Hematology and Fundamentals of Homeostasis*. F. A. Davis company .Philadelphia(17 – 126).
- (15):-Markarem, A.(1974). *Clinical Chemistry – Principles and Techniques*. 2nd. ed., Herny, D.C.' Cannon, J.W. and Winkelmen editor. Harper and Raw. Hargeston :1128– 1135.
- (16):-Koller, A.(1984). *Clinical Chemistry : total serum protein*. The C.V. Mosby Co. St Louis. Toronto. Princeton. 1316- 1324.
- (17):-Daniel W.W. (1999). *Biostatistics :a Foundation for Analysis in the Health Sciences*. 7th ed. John Wiley. Philadelphia .P(83).
- (18):-Bjoro, J.; Kruger, O.; and Midthjell, K.(2000).Prevalence of thyroid disease, thyroid dysfunction and thyroid peroxidase antibodies in large unselected population. *Eur. J. Endocrinal*. 143(5):39-74.
- (19):-Ahmed, K.H.; Taha, T.H ; and Naji, H.T. (2004). Analysis of thyroid surgery for 100 patients in AL-Kadhimia teaching hospital. *Iraqi– J. Med. Scie.*, 3(1):68-72.
- (20):-Woeber, K.A. and Ingber, S. H. (1974). Interaction of thyroid

- hormones with binding protein. Hand Book of Physiology. section 7, Vol. 3, AM. Physiol. Socic., Washington, D.C.,P(187– 196).
- (21):-Lahita, R.G.; Bradlow, H.L.; Fishman, J.; and Kunkel, H.G.(1982).Abnormal estrogen and androgen metabolism in human with systemic androgen metabolism in human with systemic lupus erythrematosis. A.J. Kidney disease. 2:206–211.
- (22):-Smyth, P.P.A.(1994).Pregnancy and thyroid function. J. Endocrinol., 140:S32-S47.
- (23):-Ganong, W. F.(1997).Review of Medical Physiology.18th. ed., Appleton and Lange. Philadelphia ,P (496).
- (24):-Gregerman, R.I. and Davis, P.T. (1978).Effects of intrinsic and extrinsic on thyroid hormones economy in: S.C. Werner and S.H. Ingber (Eds).4th.ed.,Harper and Raw, P(223 – 246)
- (25):-Justo–Firvida, E.; Maceda, S.; Lado –Lado, F.; and Devesa, J.(1995). Hyperthyroidism. As a cause of chronic anemia. An. Med. Interna., 12(9): 44-88.
- (26):-Ma, Y.; Freitage, P.; Zhau, J.; Brune, B. ;Fred, S.; and Fandrey, J. (2004).Thyroid hormone induces erythropoietin gene expression through augmented accumulation of hypoxia inducible factor-1. AM. J. Physiol., 287: R 600- R607.
- (27):-Dainiak, N.; Hoffman, R.; Maffei, L.A.; and Forget, B.G. (1976). Potentiation of human erythropoiesis *in vitro* by thyroid hormones. Nature, 272:260-262.
- (28):-Kubota, K., Tamura, J.; Kurabayashi, H.; Shirakura, T.; and Kobayashi, I.(1993). Evaluation of increased serum ferritin levels in patients with hyperthyroidism. Clin. Investig., 72 (1) : 26-9.
- (29):-Demiroglu,H.(1995).Microcytic anemia and depression in hyperthyroidism. N. Z. Med. J., 108 (1011): 465-6.
- (30):-Fernandez, V.; Simszu, K.; Barros, S.B. M.; Azzalis, L. Pimentel, R.; and Videl, L.A. (1991). Effect of hyperthyroidism on rate liver glutathione metabolism: related enzymes activities, efflux, and turnover. Endocrinol., 29(1): 85-91.
- (31):-Nehal M. and Baquer, N.Z. (1989). Changes in hexokinase and glucose 6 - phosphate dehydrogenase in red blood cells during hypo and hyperthyroidism. Biochem. Intern., 19(1): 193-199.
- (32):-Ford, H. and Carter, J. M. (1988). The haematology of hyperthyroidism: abnormalities of erythrocytes, leukocytes, thrombocytosis, and haemostasis. Postgraduate Med. J., 64:735-742.
- (33):-Motomura, K. and Brent, G.A.(1998). Mechanism of thyroid hormone action. Endocrinol. Metab. Clin. North.AM., 27 :1-23.
- (34):-Saito, H.; Sato, T.; Yamammoto, M.;Kokubun, M.;Inoue;and Saito, K(1982).Hemoglobin A levels in hyperthyroidism. Endocrinol. Jpn.,29(2):137-40.
- (35):-Skare, S. and Frey. H.M.(1980).Iodine induced thyrotoxicosis inapparently normal thyroid glands. Acta. Endocrinol., 94(3):33-6.
- (36):-Marc, A.M. ; Van, W.; and Vander, J. (1999). Analysis of the practice Guideline of the dutch college of general practitioners with respect to the use of blood test. J. AM. Inform. Issoc., 6(4) :322-331.
- (37):-Parmar, M.S. and Sturge, C. (2003). Recurrent hamburger thyrotoxicosis. CMA.J., 2 (5): 169-190.
- (38):-Hrycek, A. (1995). Functional characterization of peripheral blood neutrophils in patients with hyperthyroidism. Folia. Biol.,41 (2):79-87.

- (39):-Tsidale, J.F.; and Kemp, W.E. (1994). Agranulocytosis in hyperthyroidism. *J. Tenn. Med. Asso.*, 87 (10): 33-4.
- (40):-Dolev, E.; Deuster, P.A. ; Solomen B.; Trostamun, U.H.; and Wartofsky, L. (1988). Alteration in magnesium and zinc metabolism in thyroid disease. *metabolism*. 37(1):7-61.
- (41):-Gold, J.G. and Nejad, S. (2002). Thyroid hormone excess on basal metabolic rate. *M.J.*, 3(10):2 – 12.
- (42):-Griffin, J.E. (2000). The thyroid by Griffin, J.E. and Ojeda, S.R. (eds.). *Text Book of Endocrine-Physiology*. 4th.ed., Oxford University Press. P (303-327).
- (43):-AL-Tae, A.H.H. (2002). A new relationship between cytidine deaminase activity and cancer via oxidative hypothesis. *MSC-Thesis*. College of Science. Babylon University.
- (44):-Bishop, M.L.; Fody, E.P.; and Schoeff, L. (2005). *Clinical Chemistry, Principles and correlations, procedures*. 5th .ed., J.B. Lipincott Williams and Wilkins. Philadelphia P(180-220).
- (45):-Graninger, W.; Pirich, K. R.; Speiser, W.; Deutsh, E.; and Waldhausi, W.K. (1986). Effect of thyroid hormones on plasma protein concentrations in man. *J. Clin. Endocrinol. Metab.*, 63:40-88.
- (46):-De-Riva, C.; Virgili, F; and Frigato, F. (1995). Na(+)-K(+) ATPase activity in red cells predicts the recurrence of hyper-thyroidism in patients with Grave's disease. *J. Endocrinol. Invest.*, 18 (9) : 9-83 .
- (47):-Chan, A. Y.; Shinde, R.; Chow, C.C.; Cockram, C.S.; and Swaminathan, R. (2001). Platelets Na, K-ATPase as a tissue marker of hyperthyroidism. *Metabolism*. 50:13-66.
- (48):-Awais, D.; Shao, Y.; and Ismail, B.F. (2000). Thyroid hormone regulation of myocardial Na / KATPase gene expression. *J. Mol. Cell. Cardiol.*, 33:69-80.
- (49):-Haluzik, M.; Nedvidkova, J., Bartak, V.; Dostalova, I.; and Vlcek, P. (2003). The effect of hypo and hyperthyroidism on noradrenergic activity and glycerol concentration in human subcutaneous abdominal adipose tissue associated with microdialysis. *J. Clin. Metab.*, 88(12):50-56.
- (50):-Claud Bennet, J. and Plum, F. (1996). *Cecil Text Book of Medicine*. 20th.ed., W. B. Saunder Comp., Philadelphia Vol.1.P (539).
- (51):-Harry, E.D. (2005). Hyperkalemia and thyroid gland. *J. AM. Metab.*, 8 (1) :270- 561.
- (52):-Cachefo, A.; Boucher, P.; Vidon, C.; Dusserre, E.; and Diriason, F. (2001). Hepatic lipogenesis and cholesterol synthesis in hyperthyroid patients. *J. Clin. Endocrinol. Metab.*, 86(11) :7-53.
- (53):-Shilbayeh, S. (2003). Prevalence of osteoporosis and its reproductive risk factors among Jordanian women: a cross sectional study. *Osteoporos. Int.*, 14(11):29-40.
- (54):-Nellen, H.; Mercado, M.; Mendoza, V.; Villanueva, S.; and Perez, M. (1999). Thyrotoxic periodic paralysis in Mexican Mestizo patients :a clinical, biochemical, and HbA-serological study. *Arch. Med. Res.*, 30 (1):74-6.
- (55):- Jourdian, P.; Pousset, F.; Giard, S.; Komaida, M.; and Thomas, D. (2000). Paralysis hypokalemic thyrotoxicosis. *Arch. Mal. Coeur. Vaiss.*, 93(3) :28 -97.
- (56):-Yamaji, T.; Ishibashi, M.; Takaku, F.; Sato F.; and Kamoi, K. (1988). Plasma atrial natriuretic peptide in state of altered thyroid gland function. *Endocrinol. Jen.*, 35(2):43-8.
- (57):-Kurtzman, N.A. ; Gonzales, J. ; and Defronze, R. (1990). A patient with hyperkalemia and metabolic

acidosis AM.J. kidney – Dis., 15:333-335.

(58):-McCaffrey, C. and Quamme, G.A. (1984). Effects of thyroid status on renal calcium and magnesium handling. *Can. J. Comp. Med.*, 48(1):51-7.

(59):-Disashi, T.; Iwaoka, T.; Inoue, J.; and Naomi, S. (1996). Magnesium metabolism in hyperthyroidism. *Endocrinol. J.*, 43 (4):397- 402.

(60):-Dimitraidis, G.D. and Raptis, S.A. (2001). Thyroid hormone excess and glucose intolerance. *Exp. Clin. Endocrinol. Diabetes.* 109(2):39-S 225.

(61):-

Berghout,A.;Vandewetering,J.;and Klootwi,P.(2003).Cardiacand metabolic effects in patients with multinodular goiter. *Neth. J. Med.*, 61(10):318-376.

(62):-Erem,C.; Deger, O.; Bostan, M.; Orem, A.; and Sonmez, M. (1999).Plasma lipoprotein(a)concentrations in hypothyroid, euthyroid, and hyperthyroid subjects. *Acta. cardiol.*, 54(2):77- 81.

(63):-Parle, J.V.; Franklyn, J.A. ; Cross, K.W.; Jones, S.R., and Sheppard, M.C. (1992).Circulatory lipids and minor abnormalities of thyroid function. *Clin. Endocrinol.*, 37(5):41-4.

(64):-Hayashi, H.; Mizushima, N.; Yoshinaga, H.; and Kawamitsu, H.(1996).The relationship between lipoprotein (a) and low density lipoprotein receptors during treatment of hyperthyroidism. *Horm. Metab. Res.*,28 (8):7-384.

(65):-Coates, P.M.; Hoffman, G.M.; and Fine gold, D.N. (1982). Effect of thyroid hormones on human mononuclear leukocyte lysosomal lipase activity. *J. Clin. Endocrinol. Metab.*, 54(3):55-99.

(66):-Guyton, W.D. (2004). Antioxidants in patients with hyperthyroidism. *Clin. Lab. Med.*, 42(2) :154-158.

(67):-Scottolini, A.G, Bhagavan, N.V.; and Oshiro, T.H. (1980). Serum high-density lipoprotein cholesterol concentration in hypo and hyperthyroidism. *Clin. Chem.*, 26 (5) : 58-7.

(68):-Tsimihodimos, V.; BairaKtari, E; Tzallas, C.; and Miltiadus, G.(1999). The incidence of thyroid function abnormalities in patients attending an out patient lipid clinic. *Thyroid.* 9(4):36-8.

(69):-Abrams, J.J.; Grundy, S.M.; and Ginsber, H.(1980). Metabolism of plasma triglycerides in hypo and hyperthyroidism in man.*J. Lipid.Res.*,22(2):17- 22.