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Study of Possible Changes in Lipid Profiles between Premenopausal and Postmenopausal Women with Hyperthyroidism and Others with Hypothyroidism

Zainab Khidhair Hussain
Department of Biology, College of Science, University of Baghdad, Baghdad, Iraq

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Abstract

Menopause is the lack of menstrual cycle for at least six months. Due to hormonal changes, the alternation of lipid profile as a risk factor related to heart disease increases during menopause . One hundred twenty Iraqi women, aged between 40-65 years, were selected for this study. They were divided into two groups: 60 premenopausal and 60 postmenopausal women, and then each group was further divided into two subgroups: 20 women with hyperthyroidism and 20 with hypothyroidism, as well as 20 healthy women as control group. Blood samples were collected to estimate hormonal parameter by enzyme linked immunosorbent assay (ELISA) and lipid profile using enzymatic technique. The results showed that alterations in lipid profile included decrease in the cholesterol levels, triglyceride, LDL and VLDL. Whereas HDL increased in hyperthyroidism as compared to hypothyroidism and control groups in premenopausal women. In women with postmenopause, alterations of lipid profiles included a decrease in the cholesterol level, triglyceride, high density lipoprotein (HDL), very low density lipoprotein (VLDL) except an increase in low density lipoprotein (LDL) in hyperthyroidism as compared to hypothyroidism and control groups. Also, the level of lipid profiles increased in hypothyroidism rather than hyperthyroidism both in pre and postmenopause. According to this study, the conclusion was reached that there was an increase in the lipid profile level in postmenopausal women than premenopausal women with hypothyroidism when compared to hyperthyroidism.

Keywords: Hyperthyroidism, Lipid profile, Hypothyroidism, Hormones, Menopause

دراسة التغيرات المحتملة في ملف الدهون قبل وبعد سن الياس عند النساء المصابات بفرط افراز الغده الدرقية واخريات مصابات بخمول الغده الدرقية

زينب خضيرحسين
قسم علوم الحياه، كلية العلوم، جامعة بغداد، العراق

الخلاصة

سن الياس هو توقف الدورة الشهرية لمده حوالي سته اشهر .يعتبرالتغير في ملف الدهون عامل خطر لإمراض القلب خلال سن الياس بسبب التغير الهرموني. انتخبت مئه وعشرون عينه من نساء عراقيات بعمر من اربعين – خمسه وستين سنه. قسمت الى مجموعتين ضمت الاولى 60 عينه ما قبل سن الياس ، في حين

*Email: zainab.khidhair@sc.uobaghdad.edu.iq

شملت المجموعة الثانية60 عينه بعد سن الياس، كل مجموعه قسمت الى ثلاث مجموعات ثانويه كل منها يتضمن 20 عينه وهي

مجموعه نساء مصابات بفرط افراز الغده الدرقيه ،مجموعه مصابه بضمور افراز الغده الدرقية ومجموعه نساء سليمات كمجموعه سيطرة .جمعت عينات الدم لإجراء الاختبارات الهرمونية بواسطه تقنيه الامتزاز المناعي المرتبط بالانظيم (الاليزا) وقياس الدهون بواسطه تقنيه انزيميه .اظهرت النتائج تغيرات في ملف الدهون شملت انخفاض في مستوى الكوليستيرول والدهون الثلاثية وكذلك البروتينات الدهنية واطئة الكثافة(LDL) و البروتينات الدهنية واطئة الكثافة جدا (VLDL) بينما ازدادت البروتينات الدهنية عالية الكثافة (HDL) في حاله فرط افراز الغده الدرقية مقارنه بخمول افراز الغده الدرقية ومجموعه السيطرة . شملت التغيرات في ملف الدهون انخفاض في مستوى الكوليستيرول ،الدهون الثلاثية ، HDL و VLDL في حاله فرط افراز الغده الدرقية مقارنه بخمول افراز الغده الدرقية ومجموعه السيطرة. اضافه الى ان مستوى الدهون يزداد في حاله خمول الغده الدرقية اكثر من حاله فرط افراز الغده الدرقية قبل وبعد سن الياس. نستنتج ان مستوى الدهون يزداد في النساء بعد سن الياس اكثر من قبل سن الياس وكذلك في حالة خمول الغده الدرقية اكثر من فرط افراز الغده الدرقية.

Introduction

Menopause is the date of lack the menstrual cycle through six months or a permanent pause of menstruation. It is a natural physiological change that happen in all women, commonly between the age of 45-50 years. The period represents an alteration from the fertility into infertility age. In this stage women often stop producing ovarian eggs or the ovarian follicles become exhausted. The estrogen production from the ovaries also stops [1]. There are two stages of menopause: the first stage is called premenopausal which characterizes the reproductive stage before the lack of menstrual cycle [2] and the second stage is called postmenopause where the ovaries of a woman stop functioning, either due to natural or pathological reasons [3]. Thyroid diseases mainly affect women and are approximately 5-20 times higher than men. Furthermore, the incidence of furthermost thyroid diseases rises through age. Postmenopausal in elderly women makes them vulnerable to many diseases such as thyroid gland autoimmunity, cancer, goiter and hypothyroidism [4].

The functions of thyroid hormone regulate a wide range of metabolic pathways and processes. It considerably affects lipoprotein metabolism as being one of the potential risk factors for particular cardiovascular disease (CVD) [5, 6]. Indeed, the typical value range of the thyroid-stimulating hormone (TSH) linearly rises in total cholesterol, LDL, triglycerides while a line reduction in HDL ranks has been detected with increase in TSH [7].

Hyperlipidemia is the main cause of CVD and is the utmost common reason of females' death in menopausal age [8]. During the changes in hormones levels lead to a decrease in estrogen level, while increasing that of luteinizing hormone level. Also, follicular stimulating hormone significantly leads to alternation and has an effect on lipids and lipoproteins functions in post-menopausal women. The alternation of lipid profile as risk factors linked with CDK chance is more during menopause due to hormonal changes [9]. The demand of lipid profile test by healthcare in the clinical practice is important as it reflects the results for diagnostic purposes [10]. Patients with growth hormone deficiency (GHD) showed a tendency of instabilities in lipid profile [11]. Also, another study revealed that the parasitic infections such as *T. gondii*, has a role in changing the lower cholesterol, triglycerides and LDL levels, while increasing HDL level [12]. The aim of this study was to detect the alternation in lipid profile both in pre and postmenopausal groups with hyperthyroidism and hypothyroidism.

Material and Methods

Ethics and Subject Recruitment: This study was directly achieved after gaining ethical approval (6502/3 on 21/10/2021) from Scientific Research Committee in the University of Baghdad in Iraq. It was done in the Department of Biology, College of Science, University of Baghdad.

Experimental Design: Blood for trials was collected from women patients at the clinic and laboratories in Baghdad, which included total one hundred twenty women aged between 40-65 years. They were divided into two groups: the first group had 60 pre-menopausal women. This group was then divided into three subgroups: 20 women with hyperthyroidism, 20 with hypothyroidism and 20 healthy women as control. The second group of 60 post-menopausal women was also divided into three subgroups: 20 women with hyperthyroidism, 20 with hypothyroidism and 20 healthy women as control.

Collection of Blood Trials: Veinous blood was taken from women of experimental groups by syringes into tubes. Blood serum was obtained after allowing the blood to clot in the tube without anticoagulant for 10-20 min at room temperature. To calculate the biochemical (lipid profiles) and hormonal assays for all samples, serum separation was done by centrifugal machine at 3000 rpm for five minutes.

Biochemical Tests: Hormonal tests involved triiodothyronine (T3), thyroxine (T4) and thyroid stimulating hormone (TSH) by using ELISA technique, according to the manufacturer's instructions of TOSOH kit, China. The lipid profile included levels of serum cholesterol [13], levels of triglyceride [14], LDL [15], VLDL [16] and HDL [17] determined by using methods that depended on enzymatic way (Spin react, Spain)

Statistical Analysis: Results were analyzed by the Statistical Analysis Software (SAS). Variances between the groups were identified by least significant difference LSD via the analysis of variance (ANOVA) test.

Results and Discussion

Results of the study showed that there was no significant variation in age LSD value (3.48) in premenopausal women in the means of hyperthyroidism 40.8 ±1.77 years, while hypothyroidism was 40.6 ±1.35 and normal was 42.8 ±2.05., Significant changes in weight of premenopausal women ($P<0.01$) were found between the means of hypothyroidism 111.4 ±6.22 and control group was 73.2 ±4.97. No significant differences were found between the hyperthyroidism (70.2±3.62) and control groups. Regarding TSH level in premenopausal women, the results revealed that there were significant alterations ($P\leq0.01$) among hypothyroidism (10.66 ±0.64), hyperthyroidism (0.050 ±0.01) and the control group (3.22 ±0.25). As well, the results showed that there were significant changes ($P\leq0.01$) between the mean values of T3 and T4 in hyperthyroidism (4.96 ±0.19), (53.26 ±2.69) and control groups (1.27 ±0.04), (7.46 ±0.47) respectively. While no significant differences were found in T3 and T4 mean values in hypothyroidism (1.88 ±0.07), (2.06 ±0.09) respectively and control groups. Results of this study revealed that there were significant differences ($P\leq0.01$) in the mean values of cholesterol (259.2 ±11.94), triglyceride (250.6 ±9.80), LDL (133.16 ±5.63) and VLDL (33.64 ±1.65) in pre-menopausal women with hypothyroidism in comparison to control groups with mean values (127.0 ±6.83), (72.36 ±4.28), (87.2 ±3.61), and (26 ±1.25) respectively. No significant differences in HDL mean values was found among hyperthyroidism (54.2 ±2.68), hypothyroidism (50.2 ±2.06) and the control group (48.8 ±2.28) as shown in (Table 1) and (Figure1).

Table 1: Levels of lipid profile in premenopausal women of the hyperthyroidism, hypothyroidism and control groups

Parameters	Hyperthyroidism	Hypothyroidism	Control	LSD value
Age(year)	40.8 ±1.77	40.6 ±1.35	42.8 ±2.05	**3.48 NS**
Weight(Kg)	70.2 ±3.62 b	111.4 ±6.22 a	73.2 ±4.97 b	**14.52 ****
TSH(mIu/ml)	0.050 ±0.01 c	10.66 ±0.64 a	3.22± 0.25 b	**2.194 ****
T3(ng/ml)	4.96 ±0.19 a	1.88 ±0.07 b	1.27 ±0.04 b	**1.066 ****
T4(ug/dl)	53.26 ±2.69 a	2.06 ±0.09 b	7.46 ±0.47 b	**5.598 ****
Cholesterol (mg/dl)	110.2 ±7.27 b	259.2 ±11.94 a	127.0 ±6.83 b	**42.74 ****
Triglyceride (mg/dl)	82.6 ±4.61 b	250.6 ±9.80 a	72.36 ±4.28 b	**37.05 ****
LDL(mg/dl)	99.2 ±4.77 b	133.16 ±5.63 a	87.2 ±3.61 b	**14.69****
HDL(mg/dl)	54.2 ±2.68	50.2 ±2.06	48.8 ±2.28	**6.03 NS**
VLDL(mg/dl)	25 ±1.53 b	33.64 ±1.65 a	26 ±1.25 b	**4.52 ****

Means with different letters in the same row differs significantly.
**** (P≤0.01).**

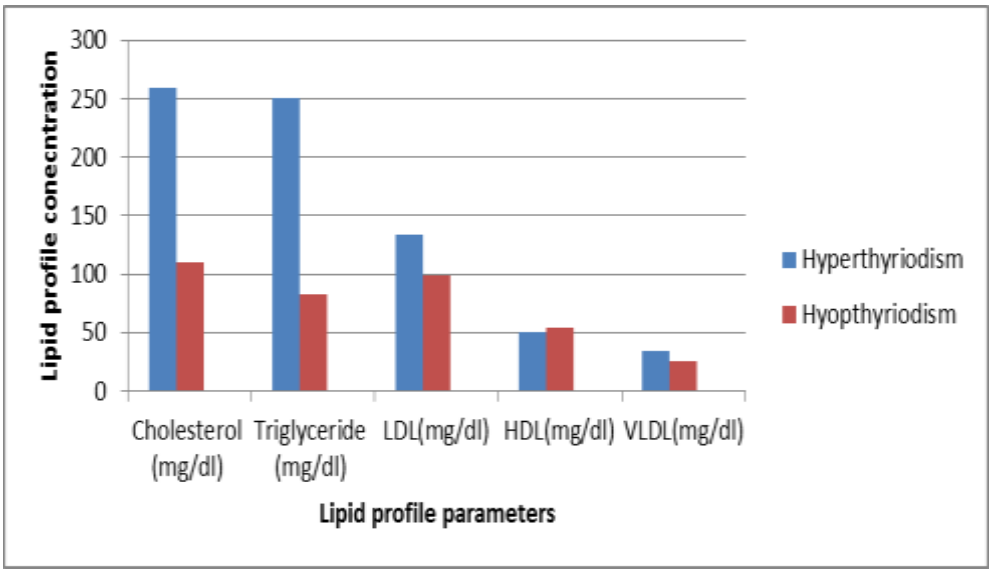

Figure 1: Levels of lipid profile in premenopausal women of the hyperthyroidism and hypothyroidism groups

Also, the results revealed no significant variation in LSD value (4.73) in post-menopausal women among age means of hyperthyroidism (58.6 ±2.92), hypothyroidism (59.4 ±3.05) and normal (59.2 ±2.38). Whereas there were highly significant changes among the means of weight in postmenopausal women (P≤0.01) (9.41), the weight of women with hypothyroidism which was high (110.8 ±6.21), and more than the women with hyperthyroidism (61.6 ±2.67) and control (75.4 ±3.37). Regarding the TSH level in post-menopausal women was high significant alterations (P≤0.01) (2.76) which was higher in hypothyroidism (46.8 ±2.76) rather than hyperthyroidism (0.013 ±0.006) and control (3.25 ±0.12). There were highly significant differences in T3 levels among postmenopausal women (P≤0.01) (1.292), whereas it was (6.1 ±0.54) in hyperthyroidism which was higher than hypothyroidism (1.41 ±0.07) and control (1.32 ±0.07). Also T4 level in postmenopausal women showed highly significant difference (P≤0.01) (5.448), whereas in hyperthyroidism was (91.88 ±4.02) which was more

than hypothyroidism (1.54 ±0.06) and control (7.80 ±0.42). The cholesterol concentration in postmenopausal women recorded a highly significant difference (P≤0.01) (52.73), in hypothyroidism (374 ±13.52) which was more than hyperthyroidism (86.4 ±3.48) and control (147 ±7.19). As well, the concentration of triglyceride in post-menopausal women was highly significant different (P≤0.01) (45.86), in hypothyroidism it was (260.4 ±10.75) which was more than hyperthyroidism (108.6 ±7.05) and control (52.18 ±2.67). Regarding the LDL level in postmenopausal women, a highly significant difference was recorded (P≤0.01) (5.102), in hyperthyroidism it was (47.4 ±2.16), hypothyroidism (42.2 ±2.09) and in control in was (49.6 ±1.95). While The HDL level in postmenopausal women was highly different (P≤0.01) (7.824), in hyperthyroidism it was (21.4 ±1.08), hypothyroidism (59.38 ±2.38) and in control (25.2 ±1.40). the VLDL level in post-menopausal women was high important differences (P≤0.01)(12.50), it was in hyperthyroidism (61.6 ±3.44) more than hypothyroidism (110 ±8.03) and in control (75.4 ± 3.72) as shown in (Table 1) and (Figure 1).

Table 2: Levels of lipid profile in Post-menopausal women of the hyperthyroidism, hypothyroidism and control groups

Parameters	Hyperthyroidism	Hypothyroidism	Control	LSD value
Age (year)	58.6 ±2.92	59.4 ±3.05	59.2 ±2.38	**4.73 NS**
Weight (Kg)	61.6 ±2.67 c	110.8 ±6.21 a	75.4 ±3.37 b	**9.41 ****
TSH(mIu/ml)	0.013 ±0.006 c	46.8 ±2.76 a	3.25 ±0.12 b	**2.76 ****
T3(ng/ml)	6.1 ±0.54 a	1.41 ±0.07 b	1.32 ±0.07 b	**1.292 ****
T4(ug/dl)	91.88 ±4.02 a	1.54 ±0.06 c	7.80 ±0.42 b	**5.448 ****
Cholesterol(mg/dl)	86.4 ±3.48 c	374 ±13.52 a	147 ±7.19 b	**52.73 ****
Triglyceride(mg/dl)	108.6 ±7.05 b	260.4 ±10.75 a	52.18 ±2.67 c	**45.86 ****
LDL(mg/dl)	47.4 ±2.16 a	42.2 ±2.09 b	49.6 ±1.95 a	**5.102 ****
HDL(mg/dl)	21.4 ±1.08 b	59.38 ±2.38 a	25.2 ±1.40 b	**7.824 ****
VLDL(mg/dl)	61.6 ±3.44 c	110 ±8.03 a	75.4 ±3.72 b	**12.50 ****

Means with different letters in the same row differs significantly.
**** (P≤0.01).**

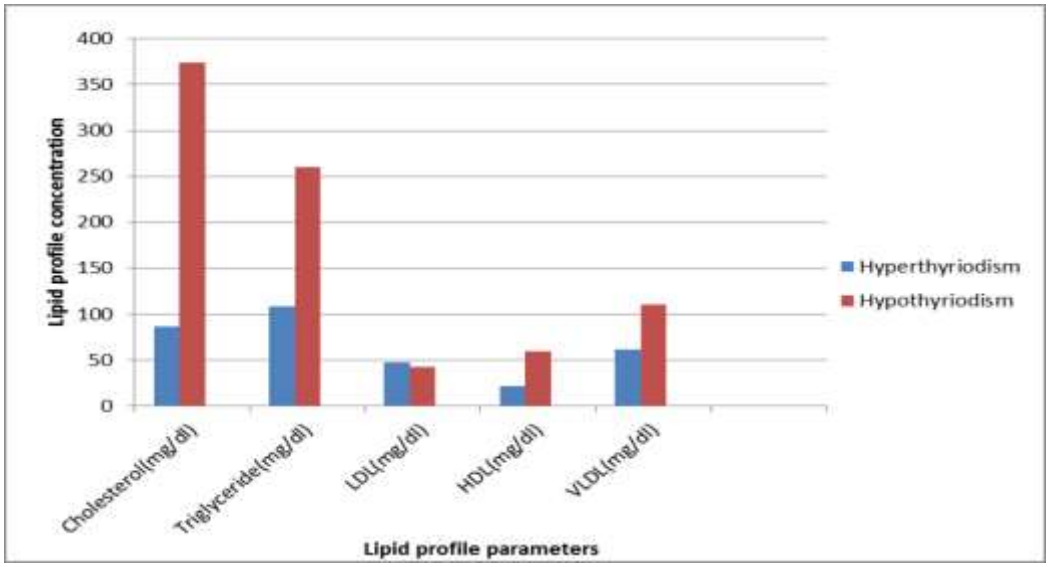

Figure 2: Levels of lipid profile in Post-menopausal women of the hyperthyroidism and hypothyroidism groups

In this study, we compared the lipid profile in premenopausal with postmenopausal women between hyperthyroidism and hypothyroidism. The cardiovascular disease incidence increased in both sexes with age, but more risk was observed after menopause in women [18]. Thyroid hormone considerably affects metabolism of lipoprotein leading to hyperlipidemia in hypothyroidism [19]. Many studies have considered the link levels of TSH within the normal range of lipid levels in women. Usually, changes in hormonal concentration in menopause are parallel with the change in lipid profile metabolism. Due to condensed production of estrogen from ovaries leads to an increase in the cholesterol levels [20]. Afterward menopause stage occurrence changes lipid rank, with augmented LDL levels [21]. Level of TSH was considerably related with serum cholesterol, LDL ,triglycerides and VLDL in Premenopausal and Postmenopausal women[22]. However, It is expressed in a wide-ranging of extra thyroidal cells, in addition to its role in the adipogenesis and lipolysis [23,24]. In actual, receptors of TSH are found in hepatocytes [25], the TSH hormone can control up 3-hydroxy-3-methylglutaryl coenzyme A reductase expression and regulate cholesterol level increasing via liver [26], there is a relationship between TSH and lipids metabolism with an important and a variable role of sex hormones between men and women [27].

In visceral obesity (increasing in adipose tissues) and insulin resistance increasing (hyperinsulinemia) were not independent prognosticators of an augmented quantity of LDL after regulating of HDL and TG concentration [28]. On the contrary, estrogen rises HDL level which is considered the good cholesterol by the amplification of apolipoprotein –A-1 (apoA-I) production in liver and lowering hepatic tissue elimination of HDL cholesterol through falling decreasing the lipase enzyme activity. Thus, the decrease in estrogen levels during menopause affects these functions [29]. Asvold *et al*., found an increase in serum (TC), (LDL-C) and (TGs) and decrease in (HDL-C) levels accompanied with TSH hormone increase[30]. Furthermore, present studies showed lower LDL and cholesterol levels in hyperthyroidism [31]; whereas a few data could not show such a correlation [32], Bonithon-Kopp suggested that total serum cholesterol and LDL considerably increased in postmenopausal women [33]. Another study demonstrated that many changes in lipid profile occur in menopause including the increase in VLDL and LDL levels which are accompanied by a decrease in HDL levels, these changes could be considered as a risk factor for cardiovascular disease in Bangladesh population [34]. Inaraja *et al*., [35] reported important alterations in levels of LDL and HDL during the menopausal transition [35]. In addition, menopausal age associates with critical changes in body structure and compositions such as fat tissue increasing. Similarly, Carr [37] found a such alterations tendency in cholesterol, triglyceride and LDL levels during menopause. in Moreover, menopause leads to alternation in metabolic and hormonal levels like various lipoprotein abnormalities (LDL, VLDL and HDL) as well as thyroid diseases [38]

Conclusion

Alterations of lipid profile in premenopause included decreased cholesterol, triglyceride, LDL and VLDL levels, with an increase in HDL in the hyperthyroidism but not the hypothyroidism group. While in postmenopause, lipid profile changes included decreasing in the levels of cholesterol, triglyceride, HDL and VLDL with an increased LDL levels in the hyperthyroidism but not in the hypothyroidism group. In addition to the level of lipid profile that increased in hypothyroidism rather than hyperthyroidism in pre and postmenopause, the risk of cardiovascular disease could higher due to the alteration in lipid profile as well as the loss of estrogen level.

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