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Article

Effect of fsh on lipid profile in postmenopausal women

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ABSTRACT
The World Health Organization (WHO) and Stages of Reproductive Aging Workshop (STRAW) define menopause as a permanent endpoint of the menstrual cycle for one year that occurs naturally or by induction of surgical procedure, chemotherapy or radiation .The etiology of menopause is classified into physiological and non-physiological. Pathophysiology of menopause includes the decline of ovary function in menopause, response to a loss of ovarian feedback mechanism, and the decline of the hypothalamus and pituitary function. Endocrine changes in menopause lead to alteration of gonadotropin secretion cycle patterns, changes in steroid and peptide hormones through monophasic patterns to increase gonadotropin, and decreased estrogen .Aim: This study aims to investigate the effect of FSH on lipid profile in postmenopausal women. Study design: A cross-section observational study. Method: The study is a cross-sectional study done on 90 women. These women aged more than 50 years had cessation of menstrual cycle for over a year. The blood samples were taken from 90 postmenopausal women, and interviews were conducted using a questionnaire. FSH measure, by ElectroChemiLuminescence (ECL) technology for immunoassay analysis done by Cobas e411 device. Lipid profile measure, by manual techniques done by use of spectrophotometer device. Result: We observed increase in Follicle-stimulating hormone (FSH) during postmenopause has a positive significant correlation with body mass index (BMI) (r 0.350, p 0.001), total cholesterol (TC) (r 0.397, p 0.001) and *Low-density lipoprotein* (LDL) (r 0.421, p 0.001) FSH also correlated positively but insignificant correlation with triglyceride (TG) (r 0.175, p 0.098) and *very low-density lipoproteins* (VLDL) (r 0.055, p 0.604). FHS has a negative significant correlation with Estradiol (r -0.509, p 0.001) and Vit.D(r-0.220, p 0.037) as well as FSH correlated negative but insignificant with age (r -0.142, p 0.183) and High-density lipoprotein (HDL) (r -0.048, p 0.656). Conclusion: The current study showed a significant positive correlation of FSH with TC and LDL, an insignificant positive correlation with TG, and an insignificant negative correlation with HDL.

Keywords: Postmenopause, FSH, Lituenizing Hormone, HDL.

INTRODUCTION

Menopause is the end of a woman's menstrual cycle, which usually occurs between the ages of 45 and 55. Women who smoke and those who have chronic illnesses may have an early menopause [1]. This is not an illness but rather a normal biological process. Menopause and perimenopause—the transitional phase that begins 2 to 8 years before and lasts up to a year after a woman's last menstrual cycle—occur when the ovaries begin to shut down as women age .As women become older, their ovary function decreases. Total follicle depletion, sclerosing blood vessels, and reduced sex steroid production (estrogen) are all symptoms of this condition [2,3]. The reduced ovarian function would impair ovary response to gonadotropin stimulation, altering the hypothalamus-hypophysis-ovary connectio[4,5].

The levels of Follicle Stimulating Hormone (FSH) and Lituenizing Hormone (LH) rise throughout menopause. Furthermore, decreased estrogen levels would cause the endometrium to atrophiate [6]. Menopause symptoms include vasomotor problems, somatic complaints including dyspareunia, hair loss, dry vagina, arthralgia, palpitation, and psychological issues like sleep difficulty and insomnia, mood swings, and cognitive issues [7]. The lipid profile in menopause is characterized by increased cholesterol, triglycerides, low-density lipoprotein (LDL), and apolipoprotein B levels, as well as reduced HDL and apolipoprotein A levels [5]. Menopause results in a reduction in high-density lipoprotein (HDL) concentration as well as structural alterations in HDL. Total cholesterol (TC) and low-density lipoprotein cholesterol (LDL-C) levels are generally greater in postmenopausal women than in premenopausal women [8]. Menopause-related lipid alterations, particularly an increase in LDL-C, have been identified as independent variables contributing to an increased risk of cardiovascular disease in the postmenopausal years [9]. Although massive endocrine hormone changes associated with menopause may have a role in worsening cholesterol levels, the specific underlying mechanism is unknown [10]. Obesity in postmenopausal women is caused by inherited and environmental factors, with poor lifestyle choices contributing significantly to the rise in BMI and waist circumference [11].

This study aims to evaluate the levels of FSH, lipid profile and BMI in postmenopausal women and to show the influence of FSH on lipid profile in postmenopausal women.

METHOD AND MATERIALS

Study design

A prospective cross-sectional observational study was carried out in Kirkuk Public Hospital from the last of December 2021 to the end of March 2022. The study included 90 postmenopausal women. These women were aged more than 50 years and had had more than one year after postmenstrual cycle cessation. The information about postmenopausal women in this study was retrieved from the women themselves.

The information collected from postmenopausal women was carried out using a questionnaire designed by the investigator. The questionnaire includes demographic characteristics such as age, weight, length, etc.

Inclusion criteria

Women are more than 50 years and cessation from menstrual cycle is more than one year.

Exclusion criteria

Women less than 50 years and women more than 50 years old but have liver or kidney disease or are taking one of these drugs-

1. Hormonal therapy.
2. Antihyperlipidemic drugs.
3. VitD therapy.

Ethical approval

Each patient was educated about the research's specifics, filled out a questionnaire, and signed a consent form to participate in the study, according to the Tikrit University College of Medicine's scientific committee. Kirkuk's directorate of health has also granted permission to visit Kirkuk General Hospital and collect patient samples.

Sample Collection and Preparation:

About five milliliters of blood were collected from the antecubital vein of fasting postmenopausal women at (8.0-10.0 Am), put in gel tubes without any anticoagulant at room temperature for 10-15 minutes, and allowed to clot. The tube was then centrifuged (3000 rpm) for 15 minutes. The clear serum was pipetted into three clear dry Eppendorf and stored at -20°C until used for the various investigations. The levels of FSH and Lipid Profile were measured.

Method

FSH was measured by ElectroChemiLuminescence (ECL) technology for immunoassay analysis done by Cobas e411 device. Lipid profile measured by manual techniques done by use of spectrophotometer device.

Statistical Analysis.

All patients signed an informed consent to participate in the study, and the ethical committee of Tikrit University, College of Medicine approved the study. All data were presented as mean and standard deviation (SD). Statistical analysis was implemented with correlation Analysis. A P value of less than 0.05 was regarded as significant. Analysis was performed by IBM SPSS Statistics for Windows version 23.0.

	N	Mean	Std. Deviation
Age (year)	90	58.056	4.9477
MD.	90	8.733	2.00
BMI	90	32.140	6.4419
CHO. (mg/dl)	90	200.469	49.8266
TG. (mg/dl)	90	181.948	45.4592
VLDL (mg/dl)	90	35.2293	8.00
HDL (mg/ dl)	90	38.993	9.4027
LDL (mg/ dl)	90	124.602	30.2774
FSH (IU/L)	90	62.4774	15.56938
Vit.D(ng/Ml)	90	17.8804	4.00780

Table 1. Descriptive Statistics

RESULTS

The study is a cross-sectional study which is conducted on 90 women. This study evaluated the levels of parameters such as FSH, lipid profile and BMI. These parameters levels are presented in Table (1); the (mean±SD) were: age was (58.07±4.95) years, menstrual duration was (8.73±2.00) years, BMI was (32.14±6.44) kg/m^2, TC. Was (200.47±48.83) mg/dl, TG was (181.95±45.46)mg/dl,VLDL was (35.23±8.00)mg/dl, HDL was (38.99±9.41) , LDL was (124.60±30.28) and mean FSH was (62.48±15.57) .We observed FSH during menopause correlated positively significantly with BMI(r 0.350,p 0.001), TC (r 0.397, p 0.001) and LDL(r 0.421, p 0.001). FSH also correlated positively but insignificantly with TG (r 0.175, p 0.098) and VLDL (r 0.055, p 0.604). FSH correlated negatively but insignificantly with age (r -0.142, p 0.183) and HDL (r -0.048, p 0.656).

Correlation between FSH and Age

The study showed a Negative correlation between FSH and Age in postmenopausal women (r: 0.055); the result was insignificant (P:>0.05), as shown in Figure 1.

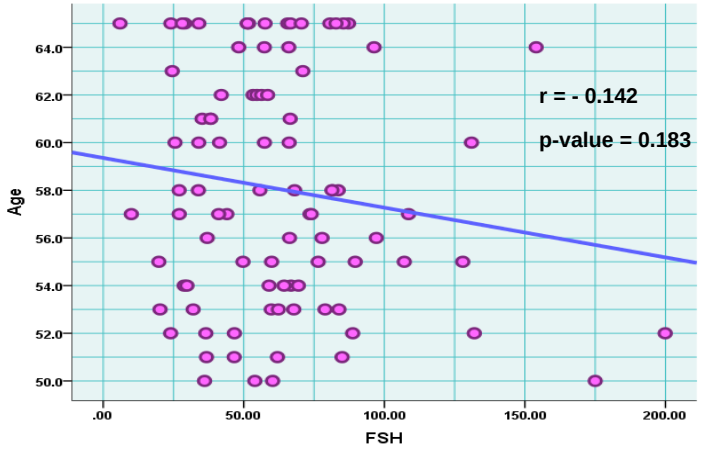

Figure 1. The correlation of FSH in (lU/L) with age (years) in postmenopausal women.

Relationship between FSH and BMI

The study showed a positive relationship between FSH and BMI in postmenopausal women (r: 0.350); the result was significant (P:<0.05), as shown in Figure 2.

Correlation between FSH and TC

The study showed a positive correlation between FSH and total cholesterol in postmenopausal women (r: 0.397); the result was significant (P:<0.05), as shown in Figure 3.

Relationship between FSH and LDL

The study showed a positive relationship between FSH and LDL in postmenopausal women (r: 0.421); the result was significant (P:<0.05), as shown in Figure 4 .

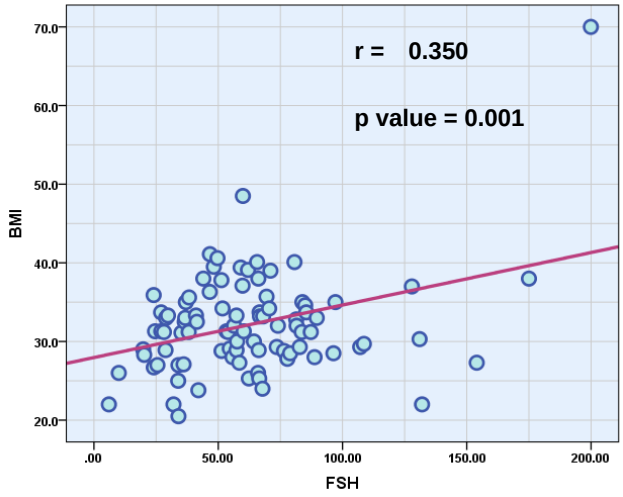

Figure 2. The relationship between FSH in (IU/L) and BMI in (kg/m²) in postmenopausal women.

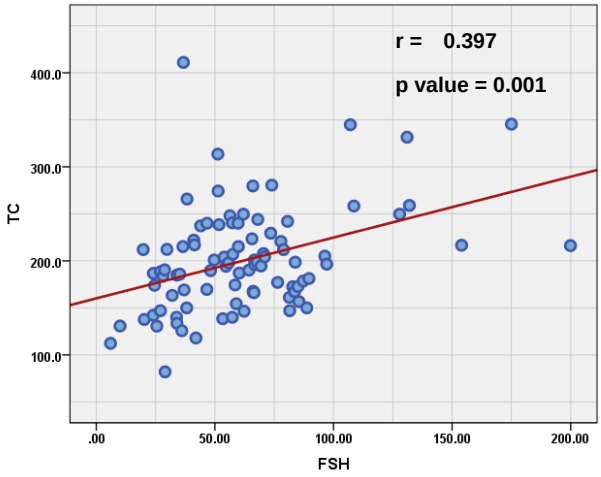

Figure 3. The correlation of FSH in (IU/L) with Total cholesterol in (mg/dl) in postmenopausal women.

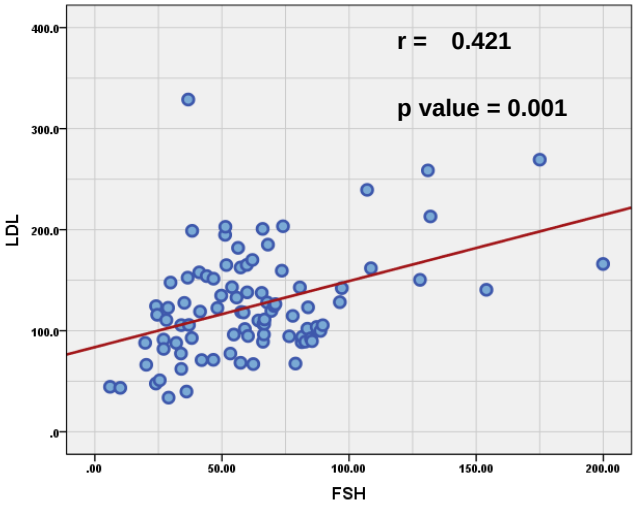

Figure 4 . The relationship between FSH in (IU/L) and LDL in (mg/dl) in postmenopausal women.

Relationship between FSH and TG

The study showed a positive relationship between FSH and triglycerides in postmenopausal women (r: 0.175); the result was insignificant (P:>0.05), as shown in Figure 5.

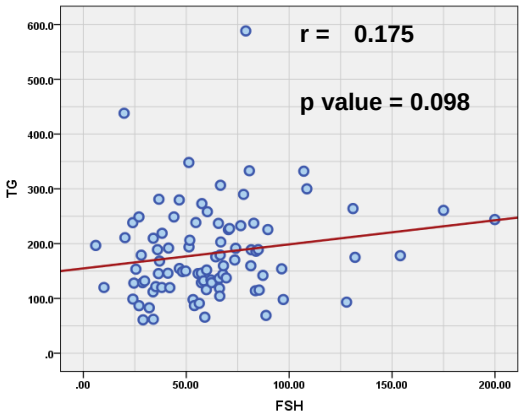

Figure 5. The relationship between FSH in (mIU/L) and triglycerides in (mg/dl) in postmenopausal women.

Correlation between FSH and VLDL

The study showed a weak positive correlation between FSH and VLDL in postmenopausal women (r: 0.055); the result was insignificant (P:>0.05), as shown in Figure 6.

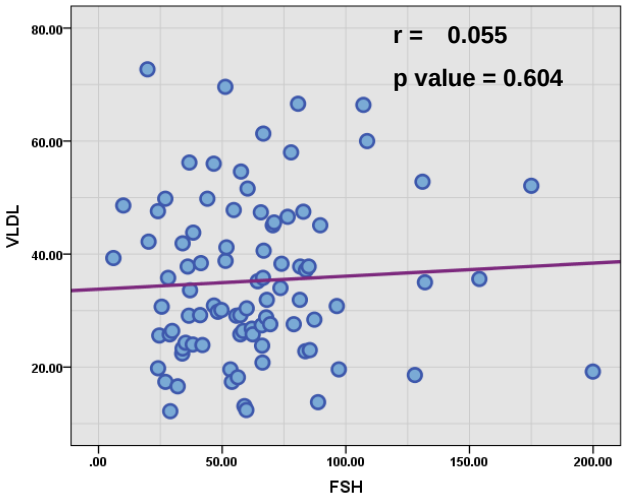

Figure 6. The correlation between FSH in (lU/L) and VLDL in (pg/ml) in postmenopausal women.

Relationships between FSH and HDL

The study showed a weak negative relationship between FSH and HDL in postmenopausal women (r: - 0.048); the result was insignificant (P:>0.05), as shown in Figure 7.

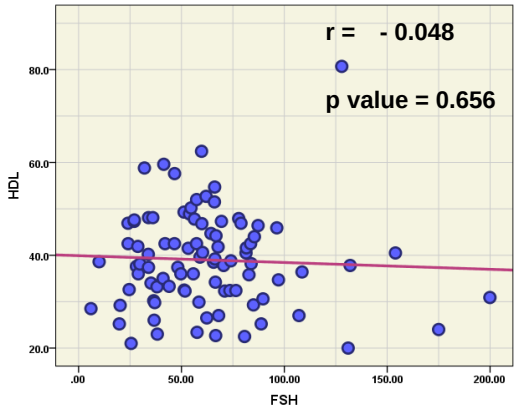

Figure 7. The relationship between FSH in (IU/L) and HDL (mg/dl) in postmenopausal women.

DISCUSSION

FSH correlations

Correlation between FSH and Age

The study showed a weak Negative correlation between FSH and Age in postmenopausal women (r: 0.055); the result was insignificant because the p-value was more than (0.05), as shown in Figure 4 – 1. The ovaries become less sensitive to follicle-stimulating hormone after menopause, which explains the FSH negative correlation with age (FSH). As a result, the ovaries stop generating estrogen and progesterone, decreasing estrogen levels and increasing FSH levels in the body [12,13].

Studies of younger and older postmenopausal women reveal that aging affects the hypothalamus and pituitary independent of steroid feedback loss. Between the ages of 50 and 75, LH and FSH levels drop by 30–40% after menopause. The complicated effects of aging on GnRH secretion explain these gonadotropin alterations, with a 22 percent decrease in GnRH pulse frequency compensated by a 14 percent increase in total GnRH secretion above that attributable to ovarian function loss alone. There are also age-related effects in the pituitary, with older postmenopausal women having 30% lower LH and FSH responses to GnRH than younger postmenopausal women [14].

Estrogen-negative feedback at the hypothalamic level remains unchanged in older compared with younger postmenopausal women; low-dose estrogen administration is associated with a significant decrease in circulating levels of LH and FSH and a parallel decrease in the overall amount of GnRH, with no effect on pulse frequency. The addition of progesterone decreased pulse frequency in postmenopausal women with a concomitant decrease in the overall amount of GnRH, neither of which effects differed with aging [14]. The effect of estrogen-negative feedback on the LH response to GnRH is not affected by aging, although the FSH response to GnRH is attenuated with aging. AS well as Serviente, [15] showed no significant correlation between FSH and Age.

The current study showed a positive correlation between FSH and BMI in postmenopausal women (r: 0.350); the result was significant because the p-value was less than (0.05), as shown in Figure 4 - 2. FSH, particularly during menopause, can influence total body weight and fat mass. FSH and FSHR have not been studied for their potential significance in fat formation and redistribution in people as they age. We hypothesized that FSHR might be expressed in human

adipocytes (fat cells) and that high circulating FSH levels would affect adipocyte activities throughout aging because of the documented association between high circulating FSH levels and increasing female body weight. As well as, the [16] observed similar results positive correlation of FSH with BMI in postmenopausal women. On the other hand, the current study disagreed with a study done by [15].

In this study, FSH showed a significant positive correlation with TC (r: 0.397 p:0.001) and LDL(r: 0.421 p: 0.001) in postmenopausal women, as shown in Figures 3 -4, and 4 – 5, respectively. This study showed a positive correlation of FSH with TG (r: 0.175, p:0.098) and VLDL (r:0.055, p: 0.604) and a negative correlation with HDL (R:-0.048, P: 0.656), but these correlations were insignificant because p-value more than (0.05). In a cohort of 400 postmenopausal Chinese women, there was a similar relationship between serum FSH, TC and LDL-C done by Song et al. [17]. Song et al. found a similar association between serum FSH, TC, and LDL-C in a group of 400 postmenopausal Chinese women [17]; Song et al. also demonstrated that evidence from the animal literature described the molecular processes by which FSH might affect lipid levels directly. Lower LDL receptor expression produced by FSH was linked to reduced LDLR expression, resulting in a rise in TC and LDL levels. Human liver tissue has FSH receptors, and when exposed to FSH, the expression of the low-density lipoprotein receptor (LDLR) is lowered. [17]
FSH has also been shown to stimulate lipid biosynthesis in adipose tissue, [18] and lipid droplet formation in human adipose tissue, [19] again demonstrating that FSH may directly influence lipid metabolism, specifically on TC and LDL-C. The study done by [20] By screening molecules related to cholesterol metabolism based on mRNA and protein expression variations, they found FSH-regulated cholesterogenesis. By measuring the rate of hepatic de novo cholesterol biosynthesis and the expression of its rate-limiting enzyme, 3-hydroxy-3-methyl-glutaryl-coenzyme A reductase (HMGCR), they demonstrated the direct influence of FSH on cholesterol biosynthesis. The work by Song et al. reports that FSH may react with its receptors in hepatocytes and decrease LDLR levels, which subsequently attenuates the endocytosis of LDL-C, increasing circulating LDL-C level [17].

Similarly, Serviette et al. found that participants with greater serum FSH levels had higher levels of both TC and LDL-C in a study of 588 postmenopausal women [15]. In this investigation, FSH had a positive association with TC, LDL, TG, and VLDL and a negative correlation with HDL but no significant link with TG, VLDL, or HDL. Menopause causes a rise in FSH, which can cause dyslipidemia by raising TC, TG, and LDL while lowering HDL. This dyslipidemia is a well-known independent risk factor for CVD and cerebral ischemic stroke in postmenopausal women, and it is also linked to other metabolic disorders, including diabetes, obesity, and fatty liver. A study done by [21] agreed with this study and found that high FSH leads to increased TC, LDL and TG and a decreased HDL in postmenopausal women.

CONCLUSIONS

The study showed an insignificant negative correlation between FSH and age in postmenopausal women. The study demonstrated a significant positive relationship between FSH and BMI in postmenopausal women.
There is a significant positive correlation between FSH and TC and LDL, but an insignificant positive correlation with TG and an insignificant negative correlation with HDL in postmenopausal women.

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