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Estimation of Fucokinase and Serum Biochemical Markers in Menopause Women

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Abstract

Fucokinase is involved in the fucosylation of carbohydrates, which are involved in various biological and pathological processes in eukaryotic organisms, such as tissue development, angiogenesis, and fertilization. In our study, FUK in addition to Some enzymes, Hormones, Lipid profiles, oxidants and antioxidants, and other biochemical parameters were measured in serum for (175) women of ages ranging from (18 – 40) years Also, 80 serum samples were collected from women suffering from menopause in the same ages from Mosul city. The results showed that there is a decrease in the FUK, vitamin D, Triglyceride (TG), Very low-density lipoprotein (VLDL), glutathione (GSH) and high levels of alkaline phosphatase (ALP), total bilirubin (TB) and calcium (Ca), Progesterone, Testosterone, low-density lipoprotein (LDL), Atherogenic index and malondialdehyde (MDA) in MP women compared to healthy women. The hormonal changes associated with MP lead to increased liver enzyme levels, indicating a potential risk for liver dysfunction and increased bone turnover, while Ca levels may decline due to decreased estrogen. Total bilirubin and phosphorus levels appear to be less affected. The lipid profile of MP shows significant adverse changes compared to normal premenopausal women. Menopausal women tend to have lower levels of GSH and higher levels of MDA and ONOO-, indicating increased oxidative stress. The comparison of FUK values between MP and healthy women highlights the potential impact of hormonal changes on metabolic pathways. Further research is needed to elucidate the specific mechanisms by which FUK activity is altered in early menopause and to explore the clinical implications of these changes.

Keywords*: Antioxidants, Enzyme, Fucokinase, Hormones, Lipids, Menopause.*

Introduction

Menopause is a progressive ageing process that involves a series of hormonal changes that occur over time and end in the cessation of ovarian follicular activity and menstrual cycles. An early follicular phase during the late reproductive years with an increase in FSH and a decrease in inhibin B are the consequences of the changes that occur, FSH is suppressed by a glycoprotein that occurs when ovarian follicles are fewer [1, 2]. FSH levels are still high as the menopausal transition progresses. The fluctuation and eventual decline of estrogen levels are caused by the permanent cessation of menstruation that defines menopause. Premenopausal women have a preference for 17β- estradiol as their dominant and most potent form of estrogen [3]. Menopause can be classified into several types based on the underlying causes and timing of its onset: Natural menopause, Premature menopause, Induced menopause, Early menopause and Surgical menopause.

Natural menopause occurs as a part of the ageing process, typically between the ages of 45 and 55. It is understood to be the discontinuation of menstruation for 12 consecutive months without any other physiological or pathological reason [4, 5].

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Menopause occurring before the age of 40 is known as premature menopause. This can happen due to genetic factors, autoimmune disorders, or other unknown causes, Induced menopause occurs as a result of medical interventions, such as surgical removal of the ovaries (oophorectomy) or medical treatments like chemotherapy and radiation therapy [6]. Early menopause is defined as menopause between the ages of 40 and 45. Like premature menopause, it can be caused by various factors, including genetics and health conditions, but it is less common than natural menopause. Surgical menopause specifically refers to menopause that results from the surgical removal of the uterus (hysterectomy) along with the ovaries [7].

The enzyme is dependent on ATP and L-fucose, and it produces ADP and beta-L-fucose 1-phosphate [8], Only FUK can convert L-fucose to fucose-1-phosphate, and it can then be used to produce GDP-fucose, Fucosyltransferase is dependent on this substrate as the donor substrate. L-FUK activity can be detected in different tissues. For example, rats and mice possess FUK widely distributed throughout their tissues, particularly in the brain. The levels of FUK in the brain vary significantly from species to species [9].

In eukaryotic organisms, many biological and pathological processes involve fucosylated carbohydrate structures, Examples include the development of tissues, angiogenesis, fertilization, cell adhesion, inflammation, and tumor metastasis. The enzyme FUK is involved in the process of fucosylation, which is the addition of fucose sugar units to a molecule [10]. It has a role in cellular adhesion and immune regulation. The exploration of fucosylation inhibition applications is being done for a variety of clinical applications, which include some that are related to sickle cell disease, rheumatoid arthritis, tumour inhibition, and chemotherapy improvements When a foreign pathogen enters the body, fucosylation can assist with immune response. Increased levels of fucosylation have been reported in several pathological conditions, including inflammation and other diseases [11-14]. Therefore, the focus of our study was on estimating the level of FUK and several Hormones, enzymes, lipid profiles and oxidative stress markers to evaluate the state of menopause with different causes.

Materials and Methods

This research involved 175 serum samples collected from women of different ages, ranging from 18-40 years, and were considered a normal group. Also, 80 serum samples were collected from women suffering from menopause at the same age.

Each lady had her whole medical history collected, and ten mL of venous blood was extracted from each participant in this study. To complete blood serum separation, the blood samples were immediately transferred into plain tubes and put in a water bath at 37^{o}C for 10 minutes before centrifugation at 3000 g for 15 min.

The levels of total cholesterol, triglycerides (TG) and HDL cholesterol were estimated using kits supplied by Biolabo company (France).

Measurement of cholesterol: Cholesterol (and HDL cholesterol) and free fatty acid are the product of the breaking down of cholesterol esters via cholesterol esterase. Δ4-cholestenone and hydrogen peroxide result from the breakdown of Cholesterol by cholesterol oxidase. Peroxidase converts 4-aminoamylpyridine with hydrogen peroxide to a coloured compound. The coloured substances were quantified spectrophotometrically at an OD 510nm, and cholesterol was calculated after extrapolation of the colour intensity to the standard cholesterol solution calibration curve.

Measurement of triglycerides: Glycerol and free fatty acids result from the breakdown of TG catalyzed by TG. Glycerol kinase converts

Glycerol to glycerol-3-phosphate produced adenosine diphosphate. Glycerol phosphate oxidase generates hydrogen peroxide from Glycerol-3-phosphate. Peroxidase converts 4-aminoamylpyridine with hydrogen peroxide to a coloured compound. The coloured substances were quantified spectrophotometrically at an OD 510nm, and TG was calculated after extrapolation of the colour intensity to the standard TG solution calibration curve.

LDL is calculated using the following equation [16].

LDL-C (mg/dl)=[TC-HDL-C]-TG/5

VLDL is calculated using the following equation [16].

VLDL (mg/dl)=TG/5

To determine FUK activity, the formation of l-Fuc-1-P was monitored in the presence of l-Fuc and ATP. One unit of FUK activity was defined as the amount capable of producing 1 μmol of l-Fuc-1-P from l-Fuc and ATP per minute [12]. The principle protocol for determining Fucokinase activity relies on monitoring the enzymatic formation of l-Fuc-1-P in the presence of its substrates, l-Fucose (l-Fuc) and adenosine triphosphate (ATP). This reaction serves as a fundamental biochemical assay to quantify the enzyme's catalytic capacity. Specifically, one unit of Fucokinase activity is defined as the amount of enzyme required to produce 1 μmol of l-Fuc-1-P per minute under standardized assay conditions. The specificity of this definition provides a clear metric for evaluating Fucokinase efficiency and ensures reproducibility in experimental studies. By tracking the production of l-Fuc-1-P, researchers can not only assess Fucokinase activity but also gain insights into metabolic pathways where this kinase plays a crucial role.

The serum progesterone, testosterone, and vitamin D were determined based on the linked enzyme immunosorbent assay (ELISA) technique using kits from BT LAB of China, which is an immunological quantification method based on the sandwich principle. This assay is based on the addition of samples to the pre-coated plate. Then biotinylated antigen was added. The antigens in the samples compete with the biotinylated antigen to bind to the capture antibody and incubate. The unbound antigen is washed away during a washing step. An avidin-HRP is then added and then incubated. Unbound avidin-HRP is washed away during a washing step. TMB Substrate is then added, and color develops. The reaction is stopped by the addition of an acidic stop solution and the colour changes to yellow, which can be measured at 450 nm. The intensity of the colour developed is inversely proportional to the concentration of progesterone in the sample. The concentration of progesterone in the sample is then determined by comparing the O.D. of the samples to the standard curve.

The activity of alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), phosphorus (P), calcium and TSB (Total Serum Bilirubin) were estimated using kits from the Biolabo company (France) [14].

The method for determining total bilirubin described employs a diazo reaction, utilizing 3,5-chlorophenyl diazonium in the presence of a solubilizing agent and within a strongly acidic medium. This process hinges on the chemical coupling of total bilirubin with the diazonium compound, resulting in the formation of an intense red azo dye. The concentration of this dye directly correlates with the amount of total bilirubin present in the sample, making it quantifiable through photometric analysis at a wavelength of 546 nm. This analytical approach exemplifies precision in biochemical testing by relying on colourimetric assessment, where greater dye intensity signifies higher bilirubin concentrations. Such methodology holds

significant diagnostic utility in assessing liver function and detecting jaundice-related conditions since accurate measurement of total bilirubin levels is critical for identifying hepatobiliary diseases. Furthermore, the use of a strongly acidic environment ensures optimal reactivity between the reagents while maintaining methodological consistency and reliability across varied clinical settings.

The enzyme ALT catalyzes the transfer of an amino group from alanine to 2-oxoglutarate, forming pyruvate and glutamate, which are crucial intermediates in metabolic pathways. This assay exploits the ability of NADH or other chromogens to undergo a measurable change—either a decrease in absorbance at 340 nm if coupled with lactate dehydrogenase reactions or a colour change using diazonium salts—reflecting ALT activity through continuous monitoring. The reaction mixture typically includes substrates such as 2-oxoglutarate, often buffered with Tris-HCl at pH 7.4, ensuring optimal enzyme activity under physiological conditions. A calibration curve generated using known ALT standards enables quantification against unknown samples, allowing for the precise determination of enzyme concentrations present within biological specimens such as serum or plasma.

The assay relies on the enzymatic reaction whereby AST catalyzes the transfer of an amino group from aspartate to 2-oxoglutarate, resulting in the production of oxaloacetate and glutamate. This reaction subsequently requires the presence of a coupled indicator reaction to facilitate colourimetric detection, commonly involving malate dehydrogenase (MDH) and NADH. When oxaloacetate forms through transamination, it is reduced to malate by MDH while concurrently oxidizing NADH to NAD+, leading to a decrease in absorbance at 340 nm due to NADH consumption—a measurable proxy for AST activity. To ensure precision, samples must be incubated at optimal conditions such as pH and temperature aligning with physiological parameters, typically around pH 7.4 and 37°C, respectively. Furthermore, meticulous calibration using known concentrations of AST helps establish a standard curve against which experimental data can be compared for quantitative results.

The protocol for a colourimetric assay to measure alkaline phosphatase (ALP) activity typically involves the use of chromogenic substrates, which yield a coloured product upon enzyme catalysis, thus enabling quantification based on absorbance readings. ALP is an important biomarker often used in clinical diagnostics for detecting bone and liver diseases, among other conditions. The assay begins with preparing the reaction mixture that consists of an appropriate buffer solution—commonly diethanolamine or carbonate-bicarbonate buffers—which maintains the optimal pH range around 9-10 for ALP activity. A substrate such as para-nitrophenyl phosphate (pNPP) is frequently employed due to its effectiveness in producing a yellow-coloured para-nitrophenol product when dephosphorylated by ALP. After mixing the enzyme sample with this substrate at a specific concentration, usually under controlled temperature conditions like 37°C, the reaction proceeds for a designated period to reach linear phase kinetics. The reaction is then stopped using an alkaline reagent such as sodium hydroxide, stabilizing the chromogenic product and maximizing its spectral properties for detection. Absorbance measurements are subsequently taken at 405 nm using a spectrophotometer to determine the intensity of the colour change, which is directly proportional to enzyme activity levels present in the sample.

Serum UA can be estimated using the Biolabo kit (France) [13]. The protocol involves enzymatic methods, utilizing uricase to oxidize uric acid into allantoin and hydrogen peroxide. This reaction releases measurable byproducts that can be quantified

spectrophotometrically or through colourimetric assays to determine precise uric acid levels. Consistency in sample preparation, reagent accuracy, and environmental control factors like pH and temperature ensure reliability within this procedure.

Calcium was estimated based on the interaction of the compound o-Cresolphthalein with calcium ions to form a red-coloured complex [15]. The principle protocol for calcium estimation utilizes the interaction between the compound o-Cresolphthalein and calcium ions to produce a red-coloured complex, enabling quantitative analysis of calcium concentration. This method is predicated on a colourimetric approach, wherein the reaction of o-Cresolphthalein with free calcium ions results in a chromogenic shift, producing an intensely coloured complex whose absorbance can be measured spectrophotometrically.

The principle protocol for serum phosphorus measurement is a critical component in the diagnostic process for assessing phosphorus levels, which play an essential role in numerous physiological processes, including energy production, bone mineralization, and cellular function. Serum phosphorus testing typically involves a colourimetric assay method, in which inorganic phosphate reacts with molybdate to form phosphomolybdate complexes. These complexes are subsequently reduced to produce a measurable colour change that corresponds to the concentration of phosphorus present in the sample. The accuracy of this procedure depends on strict adherence to pre-analytical protocols, such as proper sample collection—usually requiring fasting blood samples—and avoidance of hemolysis or contamination during handling, as these factors could result in falsely elevated readings.

A modified method was used by researchers to estimate the concentration of MDA in the serum [17]. The interaction of malondialdehyde with thiobarbituric acid (TBA) is crucial for the method. In 1998, [18]. The principle protocol involving the catabolic byproduct of lipid peroxidation highlights a critical biochemical process in oxidative stress research, where malondialdehyde (MDA), a reactive aldehyde formed during lipid peroxidation, serves as a significant biomarker. MDA reacts with thiobarbituric acid (TBA) under acidic and high-temperature conditions to produce a coloured compound known as the thiobarbituric acid reactive substance (TBARS). This coloured product absorbs light at 532 nm, allowing for its quantification via spectrophotometry. The intensity of the colour correlates directly with the concentration of MDA in the sample.

We used the dithiobisnitro benzoic acid (DTNB) to measure the GSH levels [19]. The use of dithiobisnitrobenzoic acid (DTNB), commonly referred to as Ellman's reagent, is a standard protocol for measuring reduced glutathione (GSH) levels due to its specificity and efficiency in detecting thiol groups. This protocol capitalizes on the reaction between DTNB and GSH, which generates 5-thio-2-nitrobenzoic acid (TNB), a yellow-coloured compound measurable through spectrophotometry at 412 nm. The sensitivity of this method ensures accurate quantification even in complex biological samples, providing insights into oxidative stress and redox balance. The absorbance measured corresponds directly to the concentration of free thiol groups present, primarily from GSH molecules. By using DTNB as an efficient reactant, researchers can assess the cellular antioxidant capacity, allowing further investigation into pathophysiological states linked to oxidative damage or therapeutic interventions targeting redox homeostasis. Employing this principle protocol ensures reproducibility and consistency in results while facilitating comparative studies across diverse experimental conditions.

Statistical Analysis: The data was analyzed using the t-test to determine statistical significance. The mean and standard deviations (SDs) are included when presenting the data. A significant variation was considered when the *P*-values were ≤ 0.05.

Results

FUK and Some enzymes: When measuring FUK and comparing them between the groups, we notice a significant reduction When measuring an AST, ALT and ALP activity and comparing it between the normal and pathological conditions, we notice that there is a significant increase but and when measuring TSB we also notice significant rises, Inorganic phosphorus (P) was also measured and compared, but we did not find a significant difference when comparing calcium, we notice a significant rise (Table 1).

Table 1. Fuk and some Enzymes with Other Parameters Levels in Menopause Patients

Parameters	Control	Patients	p-value
FUK (µmol/L)	1077±3.56	926±10.38	0.0001*
ALT (U/L)	8±0.22	145±0.64	0.039*
AST (U/L)	11±0.23	13±0.49	0.036*
ALP (U/L)	93±1.91	98±2.38	0.051*
TSB (mg/dL)	0.42±0.01	0.47±0.03	0.016*
P (mg/dL)	3±0.04	3±0.07	0.392
Ca (mg/dL)	6±0.09	6.5±0.18	0.002*
*Significant at (P≤0.05).			

Some hormones and lipid profiles: Table 2 shows when measuring progesterone, there was a significant rise between the normal and pathological conditions. When measuring testosterone, we notice a significant rise, but there is a significant decrease in Vit D. When measuring and comparing the lipid profile, we notice that there is a significant rise in Chole and low-density lipoprotein (LDL) and atherogenic index (Athero), however, there was a significant decrease in both triglycerides (TG) and very low-density lipoprotein (VLDL), but we did not find a significant difference when comparing high-density lipoprotein (HDL).

Table 2. Some Hormones and Lipid Profile Levels in Menopause Patients

Parameters	Control	Patients	p-value
Progesterone (ng/mL)	0.49±0.32	0.83±0.27	0.002*
Testosterone (ng/mL)	0.3±0.02	0.38±0.001	0.004*
Vitamin D (ng/mL)	25±1.89	18±1.7	0.002*
Cholesterol (mg/dL)	175±1.59	211±5	0.029*
TG (mg/dL)	130±1.91	109±3	0.0001*
HDL (mg/dL)	49±0.52	47±1	0.227
LDL (mg/dL)	123±1.50	141±4.03	0.049*
VLDL (mg/dL)	26±0.38	22±0.6	0.0001*
Atherogenic index	3.8±0.04	4.5±0.07	0.024*
*Significant at (P≤0.05)			

Some oxidants and antioxidants: A significant decrease was observed in GSH and a significant increase in MDA, ONOO- and UA (Table 3).

Table 3. Oxidants And Antioxidant Levels in Menopause Patients

Parameters	Control	Patients	p-value
GSH (µmol/L)	8±0.1	4.65±0.17	0.0001*
MDA (µmol/L)	9±0.16	15±0.18	0.0001*
$ONOO^-$ (µmol/L)	119±2.11	141±5.35	0.044*
UA (mg/dL)	3±0.05	5±0.11	0.028*
*Significant at (P≤0.05)			

Correlation between FUK with biochemical parameters: The present study showed a significant positive correlation between FUK with HDL in patient groups. While significant negative correlation between FUK with ALT and atherogenic index. Whereas there was no correlation between FUK with AST, ALP, TSB, P, Ca, Cholesterol, TG, LDL, VLDL, Progesterone, Testosterone, Vitamin D, GSH, UA, MDA and ONOO (Table 4).

Table 4. Correlation Between Fuk with Biochemical Parameters in Menopause Patients

Parameters	Menopause patient	
	R-value	**P value**
ALT	-0.676	0.016*
AST	0.052	0.872
ALP	-0.187	0.561
TSB	0.369	0.238
P	-0.182	0.570
Ca	-0.256	0.421
Chole	-0.235	0.462
TG	-0.011	0.973
HDL	0.731	0.007*
LDL	-0.545	0.067
VLDL	-0.012	0.971
Atherogenic index	-0.841	0.001*
Progesterone	0.102	0.752
Testosterone	-0.453	0.139
Vitamin D	0.144	0.656
GSH	-0.013	0.969
UA	0.429	0.164
MDA	-0.496	0.101
ONOO	0.434	0.159

Discussion

The significant decrease in FUK enzyme values observed in women experiencing early menopause compared to those in a normal premenopausal state can be attributed to several interrelated factors, including hormonal changes and their impact on metabolic pathways. [20]. During menopause, the decline in estrogen and progesterone significantly alters metabolic processes. Estrogen is essential for the regulation of various metabolic pathways, and its decrease can lead to the dysregulation of enzymes involved in glucose and lipid metabolism. [21] This hormonal shift may directly affect FUK activity, as FUK is involved in fucose metabolism, which is critical for glycoprotein synthesis and cellular signalling.

Research indicates that menopausal women often experience increased insulin resistance

[22]. This condition could lead to changes in enzyme activity, including FUK, as the body's metabolic state shifts. Insulin resistance is associated with altered glucose metabolism, which may reflect decreased FUK levels.

Lower FUK levels in early menopausal women may have important health implications. Fucose metabolism is linked to immune function and inflammation. A decrease in FUK could contribute to increased susceptibility to metabolic disorders and inflammation [23]. Studies indicate that women undergoing early menopause may exhibit higher levels of ALT and AST compared to those who experience menopause at the typical age. This increase may be attributed to the earlier loss of estrogen's protective effects on the liver [24].

Studies have shown that women experiencing early menopause often have higher ALP levels compared to their premenopausal counterparts. This increase is attributed to accelerated bone resorption due to decreased estrogen levels, which normally help maintain bone density [25, 26]. Research indicates that TSB levels do not significantly differ between normal and early menopausal women. However, hormonal changes during menopause can indirectly affect liver function, which may influence other liver enzymes more than bilirubin levels.

Postmenopausal women, particularly those who experience early menopause, often exhibit lower serum calcium levels. This decline is due to increased bone resorption and decreased intestinal absorption of calcium, exacerbated by lower estrogen levels [27]. Studies have reported that early menopausal women may have calcium levels that fall below the normal reference range, indicating a higher risk for osteoporosis and fractures [28].

Phosphorus levels tend to remain stable; however, some studies suggest that they may be slightly altered in conjunction with calcium levels. In early menopausal women, phosphorus levels may not show significant differences compared to normal menopausal women, but individual dietary and metabolic factors can influence these values.

In normal premenopausal women, During the luteal phase, progesterone levels peak and experience fluctuations throughout the menstrual cycle. In early menopausal women, progesterone levels significantly decline due to reduced ovarian function. This decline can lead to symptoms such as irregular menstrual cycles and an increased risk of endometrial hyperplasia [29]. Testosterone levels in premenopausal women are generally stable but can vary with the menstrual cycle.

In early menopausal women, testosterone levels may not decline as sharply as estrogen and progesterone, but the ratio of androgens to estrogens changes, which can lead to symptoms such as decreased libido and changes in body composition [30]. Some studies suggest that early menopausal women may experience an increase in free testosterone levels relative to estrogen, potentially leading to symptoms of hyperandrogenism [31].

Normal premenopausal women typically have adequate levels of vitamin D, which can be influenced by sun exposure and dietary intake. Early menopausal women often exhibit lower levels of vitamin D, which may be linked to changes in body composition and lifestyle factors. Vitamin D deficiency is associated with an increased risk of osteoporosis and cardiovascular diseases in this population. Studies indicate that maintaining adequate vitamin D levels is essential for mitigating some of the adverse health effects associated with menopause [30].

Typically, premenopausal women have lower total cholesterol levels due to the protective effects of estrogen. Studies indicate that total cholesterol levels significantly increase in early menopausal women compared to their premenopausal counterparts. This increase is attributed to the decline in

estrogen, which normally helps maintain a favourable lipid profile [32].

Triglyceride levels are generally lower in premenopausal women, Research shows that triglyceride levels rise significantly in early menopausal women, contributing to an unfavourable lipid profile and increasing cardiovascular risk [33]. LDL levels are typically lower in premenopausal women due to estrogen's role in lipid metabolism. There is a marked increase in LDL cholesterol levels in early menopausal women, which is a significant risk factor for cardiovascular disease [32, 33]. HDL levels are generally higher in premenopausal women, providing a protective effect against heart disease. HDL levels tend to decrease in early menopausal women, further exacerbating cardiovascular risk. The reduction in HDL is particularly concerning as it is associated with increased atherogenic risk [32, 33].

The atherogenic index, calculated as the ratio of total cholesterol to HDL cholesterol, is significantly higher in early menopausal women compared to normal women. This indicates a greater risk for atherosclerosis and cardiovascular events [34]. The higher atherogenic index in early menopausal women compared to their premenopausal counterparts is primarily due to hormonal changes, altered lipid metabolism, and lifestyle factors. These changes significantly increase the risk of atherosclerosis and cardiovascular events. [35].

In normal premenopausal women, GSH levels are typically higher, reflecting a robust antioxidant defence system. Early menopausal women often exhibit significantly lower GSH levels. This decline is associated with increased oxidative stress due to hormonal changes, particularly the reduction of estrogen, which plays a role in maintaining antioxidant levels [36, 37].

Normal premenopausal women generally have lower MDA levels, indicating less oxidative stress. In contrast, early menopausal women show significantly elevated MDA levels. This increase is attributed to heightened oxidative stress resulting from decreased estrogen levels, which normally help mitigate oxidative damage [37, 38]. Research indicates that ONOO levels may be elevated in early menopausal women compared to normal women. This increase is linked to the overall rise in oxidative stress during menopause, contributing to various menopausal symptoms and health risks [39].

Normal premenopausal women typically have balanced UA levels, which contribute to their antioxidant capacity. UA levels may be altered, with some studies suggesting an increase. This change can be a compensatory response to increased oxidative stress, although excessively high UA levels can also pose health risks [36, 37].

The positive correlation between FUK and HDL suggests that as FUK levels increase, HDL levels also tend to rise. HDL is frequently termed as 'good cholesterol' because it facilitates the removal of other forms of cholesterol from the bloodstream, thus playing a protective role against cardiovascular diseases. This relationship may indicate that higher FUK levels are associated with better lipid profiles and cardiovascular health [40]. The negative correlation between FUK and ALT suggests that higher FUK levels are associated with lower ALT levels. Elevated levels of ALT can indicate liver damage or dysfunction, as it is a marker of liver function. This finding may imply that higher FUK levels are linked to better liver health or less liver injury in the patient groups studied [41]. The negative correlation with Athero (likely referring to atherogenic indices or markers) indicates that higher FUK levels are associated with lower atherogenic risk. This could suggest that higher FUK levels may be protective against the development of atherosclerosis, which is characterized by the buildup of fats, cholesterol, and other substances in and on the artery walls [40].

The absence of correlation between FUK and parameters such as AST, ALP, TSB, P, Ca, cholesterol, TG, LDL, VLDL, progesterone, testosterone, Vitamin D, GSH, UA, MDA and ONOO- may indicate that FUK does not significantly influence or is not influenced by these biochemical parameters in the studied population. This could be due to biochemical pathways reasons: FUK may be involved in specific metabolic pathways that do not directly interact with the pathways influencing these other parameters.

Conclusion

Changes in FUK values in early menopausal women suggest hormonal influences on metabolism, warranting further investigation. Significant differences in ALT and AST levels indicate potential liver dysfunction risks associated with hormonal changes in early menopause. Elevated ALP levels indicate increased bone turnover, while calcium levels may decline. These changes highlight the need for monitoring women's health in early menopause. Early menopausal women experience decreased progesterone and altered testosterone levels, impacting overall health and necessitating monitoring. Adverse changes in lipid profiles (Increased cholesterol and triglycerides; decreased HDL) elevate cardiovascular risk, emphasizing the need for monitoring and interventions. Early menopausal women show increased oxidative stress markers, indicating potential health risks that require attention. FUK displays selective influences on lipid metabolism and liver function, with specific correlations to HDL and liver enzymes. Overall, these findings underscore the importance of monitoring various health parameters in early menopausal women to mitigate risks and improve health outcomes.

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Conflict of Interest

The authors declare no conflict of interest.

Ethical Approval

The study was approved by the College of Science at the University of Mosul.

References

[1]. Djahanbakhch, O., Ezzati, M., Zosmer, A., 2007, Reproductive ageing in women. The Journal of Pathology: *A Journal of the Pathological Society of Great Britain and Ireland*, 211(2), 219-231. doi:10.1002/path.2108.

[2]. Welt, C. K., McNicholl, D. J., Taylor, A. E., Hall, J. E., 1999, Female reproductive ageing is marked by decreased secretion of dimeric inhibin. *The Journal of Clinical Endocrinology & Metabolism*, 84(1), 105-111. doi:10.1210/jcem.84.1.5381.

[3]. Doshi, S.B., Agarwal, A., 2013, The role of oxidative stress in menopause. *Journal of mid-life health*, 4(3), 140-146. doi:10.4103/0976-7800.118990.

[4]. Lumsden, M. A., Davies, M., Sarri, G., 2016, Diagnosis and management of menopause: the National Institute of Health and Care Excellence (NICE) guideline. JAMA Internal Medicine, 176(8), 1205-1206. doi:10.1001/jamainternmed.2016.2761.

[5]. Santoro, N., Roeca, C., Peters, B. A., Neal-Perry, G., 2021, The menopause transition: signs, symptoms, and management options. *The Journal of Clinical Endocrinology & Metabolism*, 106(1), 1-15. doi:10.1210/clinem/dgaa764.

[6]. Vogt, E. C., Real, F. G., Husebye, E. S., Björnsdottir, S., Benediktsdottir, B., Bertelsen, R. J., Øksnes, M., 2022, Premature menopause and autoimmune primary ovarian insufficiency in two international multi-centre cohorts. Endocrine Connections, 11(5). doi:10.1530/EC-22-0024.

[7]. Faubion, S. S., Kuhle, C. L., Shuster, L. T., Rocca, W. A., 2015, Long-term health consequences of premature or early menopause and considerations for management. Climacteric, 18(4), 483-491. doi:10.3109/13697137.2015.1020484.

[8]. Park, S. H., Pastuszak, I., Drake, R., Elbein, A. D., 1998, Purification to Apparent Homogeneity and Properties of Pig Kidneyl-Fucose Kinase. *Journal of Biological Chemistry*, 273(10), 5685-5691. doi:10.1074/jbc.273.10.5685.

[9]. Wang, Y., Lee, G. F., Kelley, R. F., Spellman, M. W., 1996, Identification of a GDP-L-fucose: polypeptide fucosyltransferase and enzymatic addition of O-linked fucose to EGF domains. Glycobiology, 6(8), 837-842. doi:10.1093/glycob/6.8.837.

[10]. Ma, B., Simala-Grant, J. L., Taylor, D. E., 2006, Fucosylation in prokaryotes and eukaryotes. Glycobiology, 16(12), 158R-184R. doi:10.1093/glycob/cwl040.

[11]. Zhang, N. Z., Zhao, L. F., Zhang, Q., Fang, H., Song, W. L., Li, W. Z., Gao, P., 2023, Core fucosylation and its roles in gastrointestinal glycoimmunology. *World Journal of Gastrointestinal Oncology*, 15(7), 1119. doi:10.4251/wjgo.v15.i7.1119.

[12]. Kotake, T., Hojo, S., Tajima, N., Matsuoka, K., Koyama, T., Tsumuraya, Y., 2008, A bifunctional enzyme with L-fucokinase and GDP-L-fucose pyrophosphorylase activities salvages free L-fucose in Arabidopsis. *Journal of Biological Chemistry*, 283(13), 8125-8135. doi:10.1074/jbc.M710078200.

[13]. Fossati, P., Prencipe, L., Berti, G., 1980, Use of 3, 5-dichloro-2-hydroxybenzenesulfonic acid/4-aminophenazone chromogenic system in direct enzymic assay of uric acid in serum and urine. Clinical chemistry, 26(2), 227-231. doi:10.1093/clinchem/26.2.227.

[14]. Reitman, S., Frankel, S., 1957, A colourimetric method for the determination of serum glutamic oxalacetic and glutamic pyruvic transaminases. *American Journal of Clinical Pathology*, 28(1), 56-63. doi:10.1093/ajcp/28.1.56.

[15]. Moorehead, W. R., Biggs, H. G., 1974, 2-Amino-2-methyl-1-propanol as the alkalizing agent in an improved continuous-flow cresolphthalein complex one procedure for calcium in serum. Clinical chemistry, 20(11), 1458-1460. doi:10.1093/clinchem/20.11.1458.

[16]. Farukhi, Z., Mora, S., 2018, The future of low-density lipoprotein cholesterol in an era of nonfasting lipid testing and potent low-density lipoprotein lowering. Circulation, 137(1), 20-23. doi:10.1161/CIRCULATIONAHA.117.031857.

[17]. Guidet, B., Shah, S. V., 1989, Enhanced in Vivo H2O2 generation by rat kidney in glycerol-induced renal failure. *American Journal of Physiology-Renal Physiology*, 257(3), F440-F445. doi:10.1152/ajprenal.1989.257.3.F440.

[18]. VanUffelen, E. B., Van der ZEE, J., de Koster, M. B., VanSteveninck, J., Elferink, G. J., 1998, Intracellular but not extracellular conversion of nitroxyl anion into nitric oxide leads to stimulation of human neutrophil migration. *Biochemical Journal*, 330(2), 719-722. doi:10.1042/bj3300719.

[19]. Sedlak, J., Lindsay, R. H., 1968, Estimation of total, protein-bound, and nonprotein sulfhydryl groups in tissue with Ellman's reagent. *Analytical Biochemistry*, 25, 192-205.

[20]. Ko, S. H., Jung, Y., 2021, Energy metabolism changes and dysregulated lipid metabolism in postmenopausal women. Nutrients, 13(12), 4556. doi:10.3390/nu13124556.

[21]. Ko, S. H., Kim, H. S., 2020, Menopause-associated lipid metabolic disorders and foods beneficial for postmenopausal women. Nutrients, 12(1), 202. doi:10.3390/nu12010202.

[22]. Ou, Y. J., Lee, J., Huang, S. P., Chen, S. C., Geng, J. H., Su, C. H., 2023, Association between Menopause, postmenopausal hormone therapy and metabolic syndrome. *Journal of Clinical Medicine*, 12(13), 4435. doi:10.3390/jcm12134435.

[23]. McCarthy, M., Raval, A. P., 2020, The peri-menopause in a woman's life: a systemic inflammatory phase that enables later neurodegenerative disease. *Journal of Neuroinflammation*, 17, 1-14. doi:10.1186/s12974-020-01998-9.

[24]. Ortmann, O., Beckermann, M. J., Inwald, E. C., Strowitzki, T., Windler, E., Tempfer, C.,

Guideline Group., 2020, Peri-and postmenopause—diagnosis and interventions interdisciplinary S3 guideline of the association of the scientific medical societies in Germany (AWMF 015/062): short version. Archives of gynaecology and obstetrics, 302, 763-777. doi:10.1007/s00404-020-05682-4.

[25]. Bhattarai, T., Bhattacharya, K., Chaudhuri, P., Sengupta, P., 2014, Correlation of common biochemical markers for bone turnover, serum calcium, and alkaline phosphatase in post-menopausal women. *The Malaysian Journal of Medical Sciences*: MJMS, 21(1), 58.

[26]. Pardhe, B D., Pathak, S., Bhetwal, A., Ghimire, S., Shakya, S., Khanal, P. R., Marahatta, S. B., 2017, Effect of age and estrogen on biochemical markers of bone turnover in postmenopausal women: a population-based study from Nepal. *International Journal of Women's Health*, 781-788. doi:10.2147/IJWH.S145191.

[27]. Bansal, N., Katz, R., de Boer, I. H., Kestenbaum, B., Siscovick, D. S., Hoofnagle, A. N., Ix, J. H., 2013, Influence of estrogen therapy on calcium, phosphorus, and other regulatory hormones in postmenopausal women: the MESA study. *The Journal of Clinical Endocrinology & Metabolism*, 98(12), 4890-4898. doi:10.1210/jc.2013-2286.

[28]. Ohta, H., Sugimoto, I., Masuda, A., Komukai, S., Suda, Y., Makita, K., Nozawa, S., 1996, Decreased bone mineral density associated with early menopause progresses for at least ten years: cross-sectional comparisons between early and normal menopausal women. Bone, 18(3), 227-231. doi:10.1016/8756-3282(95)00480-7.

[29]. Penzias, A., Azziz, R., Bendikson, K., Falcone, T., Hansen, K., Hill, M., Young, S., 2021, Diagnosis and treatment of luteal phase deficiency: a committee opinion. Fertility and Sterility, 115(6), 416-423. doi:10.1016/j.fertnstert.2021.02.010.

[30]. Kolcsár, M., Berecki, B., Gáll, Z., 2023, Relationship between Serum 25-Hydroxyvitamin D Levels and Hormonal Status in Infertile Women: A Retrospective Study. Diagnostics, 13(19), 3024. doi:10.3390/diagnostics13193024.

[31]. JI, T., 2009, Relative androgen excess during the menopausal transition predicts incident metabolic syndrome in midlife women: study of Women's Health Across the Nation. Menopause, 16, 257-264. doi:10.1253/circj.CJ-12-0613.

[32]. Kilim, S. R., Chandala, S. R., 2013, A comparative study of lipid profile and oestradiol in pre-and post-menopausal women. *Journal Of Clinical and Diagnostic Research*: JCDR, 7(8), 1596. doi: 10.7860/JCDR/2013/6162.3234.

[33]. Ambikairajah, A., Walsh, E., Cherbuin, N., 2019, Lipid profile differences during menopause: a review with meta-analysis. Menopause, 26(11), 1327-1333. doi:10.1097/GME.0000000000001403.

[34]. Guo, Q., Zhou, S., Feng, X., Yang, J., Qiao, J., Zhao, Y., Zhou, Y., 2020, The sensibility of the new blood lipid indicator——atherogenic index of plasma (AIP) in menopausal women with coronary artery disease. Lipids in Health and Disease, 19, 1-8. doi:10.1186/s12944-020-01208-8.

[35]. Barua, L., Faruque, M., Banik, P. C., Ali, L., 2019, Atherogenic index of plasma and its association with cardiovascular disease risk factors among postmenopausal rural women of Bangladesh. *Indian Heart Journal*, 71(2), 155-160. doi:10.1016/j.ihj.2019.04.012.

[36]. Ansar, S., Alhefdhi, T., Aleem, A. M., 2015, Status of trace elements and antioxidants in premenopausal and postmenopausal phase of life: a comparative study. *International Journal Of Clinical And Experimental Medicine*, 8(10), 19486.

[37]. Pinchuk, I., Weber, D., Kochlik, B., Stuetz, W., Toussaint, O., Debacq-Chainiaux, F., Lichtenberg, D., 2019, Gender-and age-dependencies of oxidative stress, as detected based on the steady-state concentrations of different biomarkers in the MARK-AGE study. Redox Biology, 24, 101204. doi:10.1016/j.redox.2019.101204.

[38]. Cervellati, C., Bergamini, C. M., 2016, Oxidative damage and the pathogenesis of menopause-related disturbances and diseases. Clinical Chemistry and Laboratory Medicine (CCLM), 54(5), 739-753. doi:10.1515/cclm-2015-0807.

[39]. Malekian, S., Mirghafourvand, M., Najafipour, F., Ostadrahimi, A., Ghassab-Abdollahi, N., Farshbaf-Khalili, A., 2023, The associations between bone mineral density and oxidative stress biomarkers in postmenopausal women. *Korean Journal of Family Medicine*, 44(2), 95. doi:10.4082/kjfm.22.0022.

[40]. Kathak, R. R., Sumon, A. H., Molla, N. H., Hasan, M., Miah, R., Tuba, H. R., Ali, N., 2022, The association between elevated lipid profile and liver enzymes: a study on Bangladeshi adults. Scientific reports, 12(1), 1711. doi:10.1038/s41598-022-05766-y.

[41]. Islam, S., Rahman, S., Haque, T., Sumon, A. H., Ahmed, A. M., Ali, N., 2020, Prevalence of elevated liver enzymes and its association with type 2 diabetes: A cross-sectional study in Bangladeshi adults. Endocrinology, diabetes & metabolism, 3(2), e00116. doi:10.1002/edm2.116.