

Evaluation of Fucokinase in groups of postmenopausal patients due to hormonal, surgical, and genetic disorders

Duaa H. Omar¹, Luay A. Al-Helaly^{2*}

^{1,2}Department of Chemistry, College of Science, University of Mosul, Mosul, Iraq; luayhelaly@uomosul.edu.iq (L.A.A.H.).

Abstract: Fucokinase (FUK) is involved in the process of fucosylation of carbohydrates, which are involved in various biological and pathological processes. FUK, in addition to some hormones, lipid profiles, oxidants and antioxidants, and vitamin D, were measured in serum for 175 women aged 18–40 years. The 80 serum samples were collected from women suffering from menopause within the same age range from Mosul city. The appearance of a decrease in FUK activity in all types of postmenopausal patients is due to hormonal, surgical, and genetic disorders, especially the surgical type, compared to healthy women. There is a state of high oxidative stress in all types of menopause, particularly in genetic disorder cases, characterized by decreased glutathione and increased malondialdehyde and peroxyxynitrate. Lipid profile levels showed disorder only in hormonal disorder cases. An increase in progesterone and testosterone levels was observed in hormonal and surgical disorder types, while a decrease was noted in genetic disorder cases. Additionally, vitamin D levels decreased in this group. The findings emphasize the importance of monitoring oxidative stress markers in this population.

Keywords: Antioxidants, Fucokinase, Menopause, Hormones, Genetic, Surgical, Disorders.

1. Introduction

Menopause marks a significant transition in a woman's life, characterized by the cessation of menstrual cycles and a decline in ovarian function. Biochemically, menopause involves complex hormonal changes, primarily a decrease in estrogen and progesterone levels, which can lead to various physiological and metabolic alterations. Understanding the biochemistry of menopause is crucial for addressing the health implications associated with this transition, particularly when it occurs prematurely [1]. The primary biochemical change during menopause is the reduction in the production of estrogen (especially estradiol) and progesterone due to the depletion of ovarian follicles. This decline affects numerous bodily systems, including the reproductive, skeletal, and cardiovascular systems [2]. The hormonal changes during menopause can lead to dyslipidemia, characterized by increased levels of total cholesterol (TC) and low-density lipoprotein cholesterol (LDL). This shift is partly due to the decreased conversion of LDL into estrogen [3]. Menopause is associated with an increased risk of insulin resistance, contributing to metabolic syndrome, which includes obesity and dyslipidemia [4].

Reasons for the early occurrence of menopause include genetic causes, hormonal imbalances, and surgical procedures. Genetic factors can significantly influence the timing of menopause. Conditions such as Turner syndrome and other chromosomal abnormalities can lead to premature ovarian failure, resulting in early menopause [5, 6]. Hormonal imbalances, particularly involving the hypothalamic-pituitary-ovarian axis, can cause premature menopause. Conditions such as polycystic ovary syndrome (PCOS) or autoimmune disorders may disrupt normal hormonal regulation [7]. Surgical procedures, such as bilateral oophorectomy (removal of both ovaries), can induce premature menopause. This procedure is often performed to reduce the risk of ovarian cancer or due to other medical conditions [8]. Fucokinase is an enzyme involved in the metabolism of fucose, a sugar that plays a role in various biological processes, including glycoprotein synthesis. Increased levels of fucosylation have been reported in several pathological conditions, including inflammation and other diseases [9].

While direct research linking FUK to early menopause is limited, the enzyme's activity can be influenced by hormonal changes and nutritional status, both of which are altered during menopause. Women experiencing early menopause may have nutritional deficiencies that affect enzyme levels, including FUK. A lack of essential nutrients

can lead to reduced enzyme activity, potentially impacting metabolic processes [10]. The hormonal changes associated with early menopause can lead to metabolic disorders, which may further influence enzyme activity, including that of FUK. Conditions such as insulin resistance and obesity, often seen in menopausal women [11], or medication [12], can alter the metabolism of sugars and enzymes involved in these pathways [13]. 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 in groups of postmenopausal patients due to hormonal, surgical, and genetic disorders.

2. Materials and Methods

This research involved 175 serum samples collected from women of different ages, ranging from 18 to 40 years, considered a normal group. Additionally, 80 serum samples were collected from women suffering from menopause within the same age range. Each lady had her entire 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 placed in a water bath at 37 °C for 10 minutes before centrifugation at 3000 g for 15 minutes.

The FUK activity was determined by monitoring the formation of l-Fuc-1-P 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. The serum progesterone(P4), testosterone (TST), 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.

The levels of total TC, triglycerides (TG), and HDL cholesterol were estimated using kits from Biolabo, France, and enzymatic methods. The concentration of LDL in serum was calculated using the Friedewald equation.

$$\text{LDL-C (mmol/L)} = \text{TC} - \text{HDL} - (\text{TG}/2.2)$$

The concentration of MDA in serum was estimated using the modified method by researchers [14]. The method depends on the interaction of malondialdehyde with thiobarbituric acid (TBA). In 1998, Nelson [15] created a modified method for determining ONOO. We used dithiobisnitrobenzoic acid (DTNB) to measure GSH levels.

Statistical Analysis: The data were statistically examined using the t-test. The data is presented as means with standard deviations (SD). A significant variation was considered when *P*-values were ≤ 0.05.

3. Results

Patients with menopause due to hormonal disorders: In Table 1, the normal group, represented by women who do not suffer from menopause, and the pathological group, represented by women who suffer from early menopause due to hormonal disorders, show a significant reduction in the mean of FUK and VLDL when compared. There are no significant differences when comparing TC and HDL, while a significant elevation in levels of TG and LDL. The table displays some oxidant and antioxidant markers; a significant reduction in antioxidant markers such as GSH is observed, along with a significant elevation in oxidant markers like MDA and ONOO. Additionally, there is a significant elevation in P4, with no significant differences in Test and Vitamin D.

Table 1.
FUK and biochemical compounds in the group of patients with menopause due to hormonal disorders

Parameters	Control group	Hormonal disorders group	P value
FUK (μmol/L)	1077.49±3.56	964.28±20.04	0.025*
TC (mg/dL)	198.26±1.59	220.71±10	0.046
TG (mg/dL)	129.59±1.91	166.23±5.92	0.01*
HDL (mg/dL)	48.67±0.52	48±1.74	0.967
LDL (mg/dL)	123.39±1.5	139.21±8.30	0.049*
VLDL (mg/dL)	25.92±0.38	21.37±1.18	0.011*
GSH (μmol/L)	7.95±0.1	4.76±0.46	0.001*
MDA (μmol/L)	8.91±0.16	11.8±0.34	0.0001*
ONOO (μmol/L)	119±2.11	135.28±10.42	0.0001*
P4 (ng/mL)	0.49±0.32	1.32±0.47	0.002*
TST (ng/mL)	0.30±0.02	0.33±0.01	0.851
Vitamin D (ng/mL)	25.12±1.89	18.67±3.17	0.035

*Significant at (*P*≤0.05).

Patients with menopause due to surgical disorders: There are significant reductions in FUK, TG, and VLDL, and no significant differences when comparing TC, HDL, and LDL. Additionally, there is a significant reduction in GSH, an elevation in MDA, and no significant differences in ONOO-. The table also shows the levels of some hormones, with a significant elevation in P4 and TST, and no significant differences in Vitamin D.

Table 2.

FUK and biochemical compounds in the group of patients with menopause due to surgical disorders.

Parameters	Control group	Surgery disorder group	P value
FUK (µmol/L)	1077.49±3.56	902.1±18.48	0.016*
TC (mg/dL)	198.26±1.59	200.7±4.85	0.249
TG (mg/dL)	129.59±1.91	108.2±4.97	0.025*
HDL (mg/dL)	48.67±0.52	45.2±1.33	0.657
LDL (mg/dL)	123.39±1.5	133.87±4.33	0.098
VLDL (mg/dL)	25.92±0.38	21.63±0.99	0.025*
GSH (µmol/L)	7.95±0.1	5.88±0.3	0.038*
MDA (µmol/L)	8.91±0.16	13.87±0.41	0.0001*
ONOO (µmol/L)	119±2.11	119.48±8.87	0.597
P4 (ng/mL)	0.49±0.32	0.88±0.42	0.0001*
TST (ng/mL)	0.3±0.02	0.35±0.02	0.012*
Vitamin D (ng/mL)	25.12±1.89	21.37±3.44	0.043

*Significant at ($P \leq 0.05$).

Patients with menopause due to genetic disorders show a significant reduction in FUK, with non-significant differences in TC, TG, HDL, LDL, and VLDL. There is a significant reduction in GSH and a significant elevation in MDA and ONOO-. The table also indicates a significant reduction in P4 and Vitamin D, with non-significant differences in TST (Table 3).

Table 3.

FUK and biochemical compounds in the group of patients with menopause due to genetic disorders.

Parameters	Control group	Genetic group	P value
FUK (µmol/L)	1077.49±3.56	970.05±18.06	0.048*
TC (mg/dL)	198.26±1.59	207.38±11.23	0.986
TG (mg/dL)	129.59±1.91	107.83±5.73	0.960
HDL (mg/dL)	48.67±0.52	46.61±2.43	0.383
LDL (mg/dL)	123.39±1.5	139.22±8.72	0.836
VLDL (mg/dL)	25.92±0.38	21.55±1.14	0.960
GSH (µmol/L)	7.95±0.1	5.67±0.32	0.023*
MDA (µmol/L)	8.91±0.16	12±0.42	0.049*
ONOO- (µmol/L)	119±2.11	135.11±13	0.042*
P4 (ng/mL)	0.49±0.12	0.28±0.13	0.001*
TST (ng/mL)	0.3±0.02	0.32±0.01	0.098
Vitamin D (ng/mL)	25.12±1.89	19.56±5.09	0.025*

*Significant at ($P \leq 0.05$).

4. Discussion

The significant reduction in FUK activity between women who do not suffer from menopause (normal group) and those experiencing early menopause due to hormonal disorders (pathological group) can be attributed to several factors related to hormonal changes and metabolic processes [14]. Here are some key reasons: Women undergoing early menopause experience a significant drop in estrogen levels, which plays a crucial role in various metabolic processes, including enzyme regulation. Estrogen is known to influence the activity of several enzymes, including those involved in metabolic pathways [15]. The reduction in estrogen can lead to decreased activity of enzymes like FUK, which may be involved in carbohydrate metabolism and other physiological functions. This can result in altered metabolic states in women with early menopause [16].

Very Low-Density Lipoprotein (VLDL) is primarily produced in the liver and is influenced by insulin sensitivity and hormonal status. In premature menopause, hormonal imbalance can lead to increased hepatic production of VLDL, but the significant reduction in FUK may impair VLDL metabolism, leading to lower levels in this group compared to controls [17], and the significant differences in TC may indicate that hormonal changes

associated with premature menopause do not uniformly affect all lipid fractions. HDL levels can remain stable due to compensatory mechanisms in lipid metabolism despite other changes [18].

The elevation in TG can be attributed to insulin resistance, which is often exacerbated by hormonal changes in menopause. Insulin resistance leads to increased lipogenesis and decreased lipolysis, resulting in higher TG levels [19]. Similarly, the increase in LDL levels can be linked to hormonal imbalance and changes in lipid metabolism. Estrogen typically has a protective effect on lipid profiles, and its deficiency can lead to increased LDL levels, contributing to cardiovascular risk [17].

Glutathione is a crucial antioxidant that protects cells from oxidative stress. A significant reduction in GSH levels in the pathological group indicates a compromised antioxidant defense system. This reduction can lead to increased susceptibility to oxidative damage, which is particularly concerning in the context of early menopause, where hormonal changes already predispose women to various health issues, including cardiovascular diseases and metabolic disorders [20]. The significant elevation of MDA in the pathological group suggests increased oxidative damage to lipids, which can contribute to cellular dysfunction and inflammation. This is consistent with findings that postmenopausal women exhibit higher levels of oxidative stress markers compared to their premenopausal counterparts, indicating that menopause exacerbates oxidative stress [21].

Peroxynitrite is a reactive nitrogen species that can cause significant cellular damage. Its elevation in the pathological group further supports the notion of heightened oxidative stress. ONOO formation is often associated with inflammation and can lead to nitration of proteins, which disrupts their function and contributes to various pathologies, including cardiovascular diseases and neurodegenerative disorders [22].

The significant reduction in FUK activity in women with early menopause due to surgical reasons indicates important metabolic alterations. FUK, an enzyme critical for fucose metabolism, plays a role in glycoprotein synthesis and cell signaling. A decrease in its activity may suggest impaired metabolic function, which can disrupt cellular communication, especially in the context of hormonal fluctuations associated with early menopause [23].

This reduction in FUK levels is associated with an increased risk of metabolic disorders, such as insulin resistance and obesity, underscoring the need for monitoring metabolic health in this population. Overall, these findings highlight the necessity for further research into the implications of FUK reduction and potential management strategies [24].

Many women with early menopause have underlying autoimmune conditions that can affect hormonal balance and metabolic processes. These disorders can lead to dysregulation of enzymes, including FUK, contributing to lower enzyme levels [25]. Conditions like insulin resistance and obesity, often associated with hormonal imbalances, can lead to altered enzyme activity [26].

The observed reductions in TG and VLDL suggest alterations in lipid metabolism associated with early menopause. This could indicate a shift in energy utilization or changes in fat distribution due to hormonal changes following surgical menopause. Lower levels of these lipids may also reflect a decreased risk of certain cardiovascular conditions, although the overall health impact requires further investigation [27].

The significant decrease in GSH, a key antioxidant, indicates a compromised antioxidant defense system in women with early menopause. This reduction can lead to increased oxidative stress, which is associated with various health issues, including cardiovascular diseases and metabolic disorders [28]. The increase in MDA, a marker of lipid peroxidation, suggests heightened oxidative damage in the pathological group. This finding aligns with the understanding that oxidative stress is elevated in postmenopausal women, contributing to the risk of chronic diseases [27].

The significant increase in P4 and TST levels in women with early menopause may reflect compensatory hormonal changes following the loss of ovarian function. Elevated TST can have various effects, including potential impacts on mood and energy levels, while increased progesterone may influence metabolic processes [29].

The reduction in FUK suggests a potential impairment in metabolic function or energy production pathways in women with early menopause due to genetic disorders. This could indicate a shift in metabolic homeostasis that warrants further investigation [30].

The lack of significant changes in these lipid parameters suggests that the lipid profile remains relatively stable despite hormonal changes associated with early menopause. This stability may indicate that the underlying genetic disorders do not significantly impact lipid metabolism in this population [31].

The decrease in GSH, a key antioxidant, indicates a compromised antioxidant defense system. This reduction may lead to increased susceptibility to oxidative damage, which is particularly concerning in the context of menopause, where oxidative stress is already elevated [32]. The increase in MDA, a marker of lipid peroxidation, and ONOO, a potent oxidant formed from nitric oxide and superoxide, suggests heightened oxidative stress. This

elevation indicates that the balance between oxidants and antioxidants is skewed, potentially leading to cellular damage and contributing to the pathophysiology of early menopause [33].

The decrease in progesterone levels may reflect the loss of ovarian function and its associated hormonal changes. Progesterone is crucial for various metabolic processes, and its reduction could impact mood and metabolic health. Similarly, the reduction in vitamin D levels is concerning, as vitamin D is vital for bone health and metabolic function, particularly in postmenopausal women [34]. The stability of TST levels suggests that, despite the hormonal changes associated with menopause, TST production may remain unaffected in this group. This could have implications for mood and energy levels, as TST plays a role in these areas [35].

5. Conclusion

The significant reduction in Fucokinase enzyme levels in women with early menopause compared to those who are not menopausal can be attributed to hormonal changes, autoimmune disorders, genetic factors, metabolic syndromes, and nutritional influences. Understanding these factors is crucial for developing targeted interventions to manage the health of women experiencing early menopause. The findings emphasize the importance of monitoring oxidative stress markers in this population. Interventions, such as dietary modifications and antioxidant supplementation, could help mitigate oxidative stress-related health risks. Additionally, early menopause, particularly when surgical, leads to notable alterations in lipid profiles and hormonal levels. The complex relationship between metabolic dysfunction, oxidative stress, and hormonal changes suggests a need for targeted interventions to manage these issues effectively.

Transparency:

The authors confirm that the manuscript is an honest, accurate, and transparent account of the study; that no vital features of the study have been omitted; and that any discrepancies from the study as planned have been explained. This study followed all ethical practices during writing.

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