RESEARCH PAPER

Ajwa Date Consumption Improves Serum Calcium and Hemoglobin Levels in Perimenopausal Women Without Affecting Blood Glucose

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Received: 19th Aug, 2025; Revised: 23th Oct 2025; Accepted: 26th Nov, 2025; Available Online: 1st December, 2025

ABSTRACT

This study aims to determine the effect of giving Ajwa dates (Phoenix Dactilyfera L) on calcium levels, hemoglobin (Hb), and fasting blood glucose (FBG) in perimenopausal women.

The study utilized an experimental design consisting of a pre- and post-test control group. It involved 44 perimenopausal women aged between 42 and 48. The participants were randomly assigned to either the intervention group (n=28) or the control group (n=16). The serum calcium levels in the group receiving the intervention decreased to a lesser degree than the control group (3.58 ± 42.35 % vs 29.85 ± 26.93 %; $p<0.05$). Hb levels in the intervention group increased by 2.33 ± 6.17% compared to the control group Hb levels which decreased by 5.93 ± 4.77% ($p<0.05$). FBG levels in the intervention and control groups were not statistically significantly different ((5.88 ± 11.83 %% vs 11.64 ± 16.28 %; p=0.184). The consumption of Ajwa date fruit has significantly impacted serum calcium and Hb levels in perimenopausal women. However, no significant effect has been observed on this population's FBG levels. These findings suggest Ajwa date fruit may be a useful dietary supplement for managing calcium and Hb levels in perimenopausal women without impairing glucose tolerance.

Keywords: Calcium, Fasting Blood Glucose, Hemoglobins, Perimenopause, Phoenix dactylifera, Date Fruit

How to cite this article: Mappaware NA, Mulyadi FE, Royani I, Syahril E, Akib MN, Harahap W, Rahma M, Yacca SS., Ajwa Date Consumption Improves Serum Calcium and Hemoglobin Levels in Perimenopausal Women without Affecting Blood Glucose. Int J Drug Deliv Technol. 2026;16(1): 160-167. DOI: 10.25258/ijddt.16.1.17

Source of support: Nil.

Conflict of interest: None

INTRODUCTION

Perimenopause is a crucial phase during which bone mineralization is affected due to several physiological factors and hormonal changes. The decline in estrogen levels and age-related processes alter the rate of serum calcium balance in older women [1]. Study on perimenopausal women has revealed that calcium serum in perimenopausal women were lower than in pre-menopause [2]. Maintaining calcium balance is crucial for proper physiological functioning, and it is achieved through a complex interplay of intestinal calcium absorption, renal reabsorption, and bone exchange. This tightly regulated dynamic process maintains normal serum calcium levels. The primary source of calcium for the body is food intake, which allows for the replenishment of bone calcium stores [3][4]. A disruption in any of these mechanisms can lead to pathological conditions such as osteoporosis, renal failure, and hypercalcemia. A decrease in calcium absorption in food follows a decline in estrogen levels, leading to a reduction of serum calcium levels [5]. In addition, estrogen deficiency results in increased bone remodeling, damage to bone microarchitecture, and bone fragility [6]. Some study have revealed that the mean serum calcium levels were lower in the postmenopausal subjects compared with the premenopausal and perimenopausal women

Iron deficiency anemia is a prevalent medical concern amongst perimenopausal women. According to various scientific literature studies, anemia in perimenopausal women aged between 40 and 49 years occurs in approximately 47.9% to 54.5% of cases [7][8]. The menopausal transition can cause changes in menstrual patterns, such as bleeding outside the menstrual cycle, which is one of the leading causes of anemia among perimenopausal women [9]. This highlights the significance of prompt detection and treatment of iron deficiency anemia in perimenopausal women to manage its harmful effects effectively.

Several research studies have indicated a substantial rise in the incidence of glucose metabolism abnormalities in women around and after the age of 50 years [10][11].

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During perimenopause, hormonal fluctuations can affect blood glucose levels, which may lead to metabolic dysregulation. Insulin resistance can be intensified due to the decline in hormones such as estradiol [12]. Women in their perimenopausal phase also tend to experience a rise in fasting blood glucose levels, even if they are not diabetic. This indicates that menopause can have a direct impact on glucose metabolism [13][14]. However, it's important to note that genetic and environmental factors can also contribute to an increase in fasting blood glucose levels during menopause. Therefore, a comprehensive understanding of all these factors is essential for the effective management of blood glucose levels in non-diabetic women [12].

Ajwa dates are an extensively studied fruit due to their potential health benefits. Numerous studies have shown that Ajwa dates possess anti-inflammatory and antioxidant properties [15][16]. Antihyperlipidemic effects [17], hepatoprotective properties [18], nephroprotective effects [19], anticancer properties [20][21]. Furthermore, Ajwa dates are considered superfoods due to their complete macro and micronutrient composition. A recent study aimed to evaluate the effects of Ajwa dates on serum calcium levels, hemoglobin (Hb), and fasting plasma glucose (FPG) levels in perimenopausal women, giving potential health benefits. This study was conducted scientifically rigorously, and the results may interest medical professionals interested in the potential health benefits of Ajwa dates.

METHODS

Study design

This experimental study was conducted at Sitti Khadijah 1 Muhammadiyah Makassar Hospital in South Sulawesi, Indonesia, between May and October 2021. The study employed a pre-post control design and received ethical approval for research involving human subjects from the Hasanuddin University Health Research Ethics Commission (letter number 330/UN4.6.4.5.31/PP36/2021). The study design aimed to minimize potential biases and confounding factors, and the ethical approval ensures that the study adhered to the principles of research ethics, including informed consent, confidentiality, and protection of participants' rights.

Inclusion and exclusion criteria

The study's inclusion criteria comprise the following: (1) female aged between 42 and 48 years, (2) married status, (3) pre-menopausal status, (4) parity number ≥ 1, and (5) willingness to participate the study and provide informed consent. However, the study has specific exclusion criteria that must be met. These are as follows: (1) FBG level must be less than 126 mg/dl, (2) Not consuming any drugs that can cause changes in calcium serum levels or FPG like lithium, steroid, thiazide diuretic, teriparatide, or tamoxifen, (3) individuals with a history of ovarian disorders such as polycystic ovary syndrome (PCOS) or previous ovarian surgery, (3) history of smoking, (4) women who are currently using hormonal contraception, (5) individuals with chronic infectious diseases such as tuberculosis or malaria, and (6) non-communicable degenerative diseases such as cancer, chronic kidney failure, and diabetes mellitus.

Intervention

All participants in the study were first explained the research procedures, goals, and potential benefits before being asked for written consent. Afterwards, a screening process was conducted to determine which individuals met the inclusion and exclusion criteria. This screening process involved an assessment of medical history, a physical examination, a body mass index (BMI) and fasting blood glucose (FBG) levels measurement, and a transvaginal ultrasound. Those who met the criteria were then randomly assigned to either the intervention group (n=28) or the control group (n=16).

The study was designed as a randomized controlled trial, aimed at evaluating the effect of a dietary intervention on a specific health outcome. The intervention group was instructed to consume 7 Ajwa dates each morning before breakfast for a duration of 8 weeks, with each date weighing between 60-80 grams. The Ajwa dates were packaged into seven labeled plastic packaging containing 49 dates, and each participant in the intervention group received one weekly package. To ensure uniformity in the study, the participants were given a diary sheet to record their daily intake of Ajwa dates. At the same time, the control group was instructed not to consume these dates. To gather precise information about the dietary habits of both groups, a 24-hour food recall was conducted for all participants.

Outcome measurement

Blood samples were collected from all participants in both the control and intervention groups twice, following an overnight fast of 8 hours. The first blood sample was taken on the third day of the menstrual cycle, while the second sample was taken eight weeks after the initial one. For each sample, three millilitres of venous blood were drawn. The serum calcium levels were determined using the ELISA method, which involved a kit from Lab Science (catalogue number E-BC-K103-M) with a sensitivity of 0.07 mmol/L. Additionally, the fasting blood glucose and haemoglobin levels were evaluated using standard laboratory analysis.

Data analysis

The study findings were reported using mean values and standard deviations. An independent t-test was used to compare the percentage changes observed in serum calcium and fasting blood glucose (FBG) levels between control and intervention groups. Furthermore, the Mann-Whitney test was used to compare the percentage change in haemoglobin levels between control and intervention groups.

RESULTS

Flow of participants

59 perimenopausal women aged 42-48 years and meeting the study inclusion criteria were screened and then eligible to be included as subjects for this study. 9 people were not included in the study because 2 people had fasting blood sugar levels ≥ 126 mg/dl and 7 other people were using hormonal contraception. 50 perimenopausal women were then randomly divided into the intervention group (30 subjects) and the control group (20 subjects). Of the 30

subjects in the intervention group, 1 subject was unwilling to continue participating in the research, and 1 other subject changed residence, making follow-up impossible. In the control group, 4 subjects were unwilling to have their post-intervention blood drawn. At the end of the research, there were 44 participants, with 28 in the intervention group and 16 in the control group (Fig. 1).

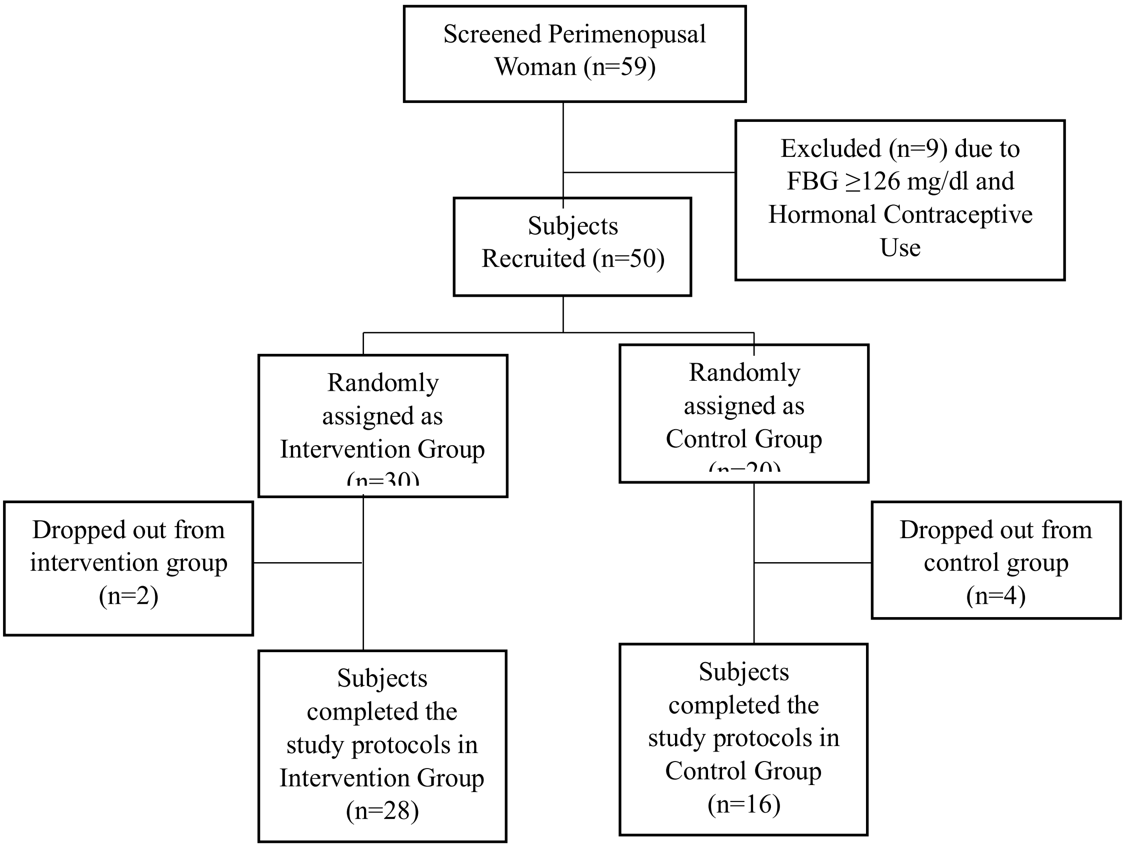

Figure 1. Flowchart of participants

Blinding protocols

Subjects were selected using a simple random sampling technique to be grouped into an intervention group (30 people) and a control group (20 people). Each subject will be given a sealed envelope containing numbers 1-50 written randomly. Each subject who took an envelope containing the numbers 1-30 will be categorized into the intervention group, while subjects who took an envelope containing the numbers 31-50 will be assigned to the control group. There was no specific blinding protocol applied in this study. All subjects in the intervention group intentionally consumed Ajwa dates as a part of the study's dietary intervention.

Table 1. The baseline and nutritional intake characteristics of study participants

Variables	**Intervention group (n=28)**	**Control group (n=16)**	***p-value***
Ages[a] (years)	44.79±2.28	44.69±2.24	0.719[c]
Blood pressure[a] (mmHg)			
Systolic	118.57±10.79	121.25±13.60	0.849[c]
Diastolic	81.07±7.37	80.00±12.65	0.776[c]
Body mass index[b]			[c]
Underweight	2 (7,1 %)	0 (0,0 %)	0.384
Normal	5 (17,9 %)	3 (18,8 %)	
Overweight	4 (14,3 %)	7 (43,8 %)	
Obesity I	13 (46,4 %)	5 (31,2 %)	
Obesity II	4 (14,3 %)	1 (6,2 %)	
Parity[b]			
Primipara	4 (14,3 %)	4 (25 %)	0.310[d]
Multiparous	24 (85,7 %)	12 (75 %)	
Nutritional intake			

Total Kalori[a]	1689.26 ± 337.86	1700.89 ± 397.97	0.918 [f]
Karbohidrat[a] (gram)	303.72 ± 122.64	326.06 ± 142.66	0.587 [f]
Lemak[a] (gram)	41.98 ± 24.08	44.33 ± 15.11	0.727 [f]
Protein[a] (gram)	88.62 ± 34.99	88.81 ± 32.82	0.932 [g]
Vit. A[a] (IU)	5181.43 ± 11148.01	2474.46 ± 7849.43	0.231 [g]
Viit C[a] (miligram)	924.88 ± 2918.68	100.89 ±275.75	0.098 [g]

[a]Mean ± Standard Deviation [b]Frequency (%) [c]Mann-Whitney test [d]Fisher-exact test [e]Chi Square test [f]Independent t-test [g]Mann-Whitney test

Baseline data

Table 1 provides a comprehensive overview of the fundamental attributes of the individuals belonging to both the intervention and control groups. The study compared various demographic and clinical parameters, such as age, blood pressure, BMI, and parity, between the two groups. Based on the findings, the groups were evenly matched at the start of the study, as there were no noticeable variations between them. Additionally, the nutritional intake of the participants was evaluated by measuring their total calorie, carbohydrate, fat, protein, and vitamin A and C consumption. The outcomes of the study indicate that there were no significant variations in the nutritional intake of the participants belonging to the intervention and control groups during the initial phase of the research. These outcomes suggest that the two groups possessed similar baseline characteristics, including demographic and clinical parameters, as well as their dietary habits. These findings are crucial as they establish the foundation for the study and help ensure that the results of the research are not influenced by any significant variations in the two groups at the outset of the study. Such homogeneity at the baseline is essential for ensuring that any observed differences between the groups during the study can be attributed to the intervention rather than baseline differences.

The comparison of serum calcium levels between intervention and control group

The primary aim of the study was to investigate the efficacy of a particular treatment on serum calcium levels in two groups of participants. The study analyzed the calcium levels recorded in both the intervention and control groups before and after the treatment, which is presented in Table 2. Initially, there was no significant difference in the mean serum calcium levels between the two groups. However, after eight weeks of treatment, the mean serum calcium levels in the intervention and control groups were reduced to 1.09 ± 0.32 mmol/L and 0.73 ± 0.26 mmol/L, respectively. It is noteworthy that the decrease in serum calcium levels was found to be significantly less pronounced in the intervention group when compared to the control group (3.58 ± 42.35% vs. 29.85 ± 26.93%) ($p<0.05$). This implies that the treatment was effective in preventing a considerable decrease in serum calcium levels in the intervention group.

Table 2. Comparison of calcium levels between intervention and control group

Group	Calcium levels (mmol/L)[a]		Mean Δ calcium levels[a]	Mean % Δ calcium levels	p-value[b]
	Before	After			
Intervention	1.23 ± 0,34	1.09 ± 0.32	↓ 0.13 ± 0.47	↓ 3.58 ± 42.35	***0.031**
Control	1.07 ± 0,19	0.73 ± 0.26	↓ 0.34 ± 0.33	↓ 29.85 ± 26.93	

[a] Mean ± Standard Deviation [b]Independent t-test

The comparison of Hb levels between intervention and control group

The study findings presented in Table 3 provide descriptive data on the levels of haemoglobin (Hb) that were measured in the intervention and control groups before and after the treatment. The results of the study reveal that the group that consumed 7 Ajwa dates per day for eight weeks experienced a remarkable increase in Hb levels by 2.33 ± 6.17%. In contrast, the control group showed a decrease in Hb levels by 5.93 ± 4.77%. The percentage change in Hb levels between the two groups was statistically significant (p-value <0.05), which suggests that Ajwa date consumption has a positive impact on Hb levels.

Table 3. Comparison of Hb levels between intervention and control group

Group	Hb levels (mg/dl)[a]		Mean Δ Hb Levels[a]	Mean % Δ Hb Levels	p-value[b]
	Before	After			
Intervention	13.12 ± 0.78	13.43 ± 1.07	↑ 0.30 ± 0.78	↑ 2.33 ± 6.17 %	**0,000***
Control	13.61 ± 0.86	12.79 ± 0.96	↓ 0.81 ± 0.67	↓ 5.93 ± 4.77 %	

[a] Mean ± Standard Deviation, [b]Mann-Whitney U test

The comparison of FBG levels between intervention and control group

Table 4 displays the fasting blood glucose (FBG) levels of both the intervention and control groups before and after an eight-week treatment. The study found a significant difference in mean FBG levels between the two groups prior to the treatment. The data showed that the mean FBG levels increased after the treatment to 100.64 ± 8.39 mg/dl and 105.94 ± 9.59 mg/dl in the intervention and control groups, respectively. Interestingly, the mean increase in FBG levels in the intervention group was found to be lower than that of the control group, with the intervention group showing a mean increase of 5.88 ± 11.83% and the control group showing a mean increase of 11.64 ± 16.28%. However, it is worth noting that the difference between the groups was not statistically significant, with a p-value greater than 0.05. Overall, the results of the study suggest that although the treatment did appear to have some impact on FBG levels in both groups, there was no significant difference between the intervention and control groups.

Table 4. Comparison of FBG levels between intervention and control group

Group	FBG levels (mg/dl)[a]		Mean Δ FBG levels[a]	Mean % Δ FBG levels	*p-value*[b]
	Before	After			
Intervention	95.75 ± 9.39	100.64 ± 8.39	↑ 4.89 ± 11.03	↑ 5.88 ± 11.83 %	0.184
Control	96.13 ± 10.94	105.94 ± 9.59	↑ 9.81 ± 15.43	↑ 11.64 ± 16.28 %	

[a] *Mean ± Standard Deviation,* [b]*Independent t-test*

DISCUSSION

Multiple research studies have been conducted to investigate the serum calcium levels in women belonging to different age groups, such as premenopausal, perimenopausal, and postmenopausal women. Research has consistently demonstrated that perimenopausal and postmenopausal women experience a decline in serum calcium levels, which is evidenced by lower mean serum calcium levels when compared to premenopausal women.[2],[1]. This decline was also observed in our study, where both the control and intervention groups experienced a reduction in serum calcium levels. These findings are in line with previous studies, highlighting the significance of monitoring serum calcium levels in women during and after the menopausal transition. The primary reason for the decrease in serum calcium levels in perimenopausal women is attributed to the reduction in intestinal calcium absorption caused by the direct impact of estrogen on calcium absorption. Estrogen has been shown to decrease the levels of 1,25(OH)2D and also directly alters the intestinal response to 1,25(OH)2D.[3] Additionally, hormonal deficiencies and age-related factors lead to elevated urinary excretion of calcium, which further contributes to decreased serum calcium levels. The proximal tubule, which is a segment of the nephron in the kidney, is responsible for reabsorbing essential substances such as glucose, amino acids, and electrolytes from the filtrate. However, certain conditions and factors can lead to dysfunction of this vital process, resulting in significant health issues. Fortunately, estrogen replacement therapy has been found to be effective in correcting this issue by restoring normal function and balance to the proximal tubule. This therapy can help improve overall kidney function and prevent further complications.[22]

Depleted calcium levels in the blood will trigger the body to extract calcium from the bones to perform vital functions. This can lead to a reduction in the amount of calcium present in the bones, ultimately causing a condition called osteoporosis. A decrease in calcium intake and absorption results in lower levels of ionized calcium in the blood, which triggers the secretion of parathyroid hormone (PTH), leading to the mobilization of calcium from the bone through osteoclastic activity. This effect is known as secondary hyperparathyroidism. When the parathyroid hormone (PTH) increases, it triggers vitamin D activation by the liver and kidneys. This results in higher levels of serum calcium by enhancing calcium absorption in the intestines. When there is a deficiency of estrogen in the body, the bones respond more extensively to PTH. This leads to the removal of more calcium from the bones, which increases serum calcium levels. Ultimately, it results in a decrease in circulating PTH levels, vitamin D, and intestinal calcium absorption.[23],[3]

Estrogen, a hormone produced mainly in the ovaries of women, is an essential component in maintaining bone health. It plays a crucial role in the regulation of bone metabolism by interacting with several proinflammatory cytokines, such as interleukin-1 (IL-1), interleukin-6 (IL-6), tumour necrosis factor-alpha (TNF-α), granulocyte-macrophage colony-stimulating factor (GM-CSF), macrophage colony-stimulating factor (M-CSF), and prostaglandin-E2 (PGE2). These cytokines lead to an increase in bone resorption by expanding the pool of pre-osteoclasts in the bone marrow. Estrogen has been found to regulate their expression and activity, thereby reducing bone loss. In postmenopausal women, estrogen levels decline, leading to an increased risk of osteoporosis due to the lack of estrogen's protective effect on bone metabolism. Research has shown that the rise in osteoclasts after ovariectomy can be hindered or lessened by obstructing the production or reaction to IL-1, IL-6, TNF-α, or PGE2. Additionally, estrogen has been discovered to increase the production of transforming growth factor-beta (TGF-β), which suppresses bone resorption by directly reducing osteoclast activity and encouraging apoptosis. These findings suggest that estrogen replacement therapy may be a promising approach to prevent or treat bone loss in postmenopausal women. Overall, the role of estrogen in bone metabolism is complex and involves intricate interactions with cytokines and growth factors. Understanding these interactions is critical for developing effective therapeutic strategies for bone-related disorders.[24]

The outcomes of a recent scientific study have indicated that the regular consumption of Ajwa dates can have a positive impact on the serum calcium and haemoglobin (Hb) levels of perimenopausal women. The group that was given Ajwa dates experienced a significantly slighter decrease in serum calcium levels compared to the group that did not receive them. In contrast, Hb levels increased in the former and decreased in the latter. Ajwa dates are known to be a rich source of a variety of essential minerals, such as calcium, iron, manganese, magnesium, sodium, zinc, potassium, and phosphorus[25], which makes them excellent dietary supplements for maintaining adequate mineral intake.[26] Calcium and iron are important elements in the formation of blood in bone marrow. Iron is used to make hemoglobin. Perimenopausal women can suffer iron deficiency caused by iron loss during long-irregular menstruation. Previous study on teenagers shows that consuming ajwa dates elevates Hb levels.[27] Additionally, Ajwa dates contain high levels of phenolic compounds and flavonoids, which have potent antioxidant and anti-inflammatory properties, enabling them to reduce levels of pro-inflammatory mediators. This, in turn, has the potential to inhibit osteoclast activity in the bone resorption process. The minerals present in Ajwa dates, including magnesium, zinc, copper, potassium, and selenium, act as cofactors for various enzymes and enhance their antioxidant activity. These findings suggest that the regular consumption of Ajwa dates may have significant beneficial effects on the bone health and overall well-being of perimenopausal women.[28],[16].

Ajwa dates are known to contain 50 grams of carbohydrates per 100 grams, with a moderate glycemic index (GI) and low glycemic load (GL).[29],[30] Foods with a low GI or GL are beneficial for maintaining proper insulin sensitivity and glycemic control. They also diminish cardiovascular disease and type 2 diabetes risk by promoting healthy body weight and reducing fat storage.[31] This study has further proven that the intervention group's FBG levels increased less than the control group. Because of that, Ajwa dates, which have been considered very sweet and high in glucose, can still be recommended as a nutritional food supplement without causing impaired glucose tolerance.

Ajwa dates are a rich source of quercetin, a bioactive flavonoid that exhibits a wide range of biological benefits. Studies have revealed that Quercetin exhibits potent antioxidant, anti-inflammatory, antiapoptotic, and mitochondrial biogenesis properties.[32],[33]. It has been found to have a positive impact on ovarian health by preventing the degeneration of follicular cells and reducing haemorrhage, vascular congestion, and oedema in laboratory animals. Quercetin reduces follicular cell apoptosis and aids in healthy ovarian function. Furthermore, animal and human granulosa cells (GCs) treated with Quercetin have shown an increase in GC viability, which has resulted in the maintenance of estrogen production.[32]

This study provides valuable insights into the potential benefits of Ajwa dates on calcium and haemoglobin levels of perimenopausal women. Please note that the researcher solely funded this research and it was not part of any project or funded by any institution. This includes product purchasing, laboratory testing, and logistics. Furthermore, due to a lack of sponsors, we were unable to code RCTs, and the sample size needed to be more prominent due to the reluctance of human subjects to enrol. The study has provided significant information. However, it is imperative to conduct additional research with a more extensive sample size and adequate funding to ensure the accuracy and validity of the findings. The inclusion of a larger sample size would allow for a more representative sample of the population. At the same time, adequate funding would provide researchers with the resources necessary to conduct a more comprehensive study. Therefore, further research is required to adequately validate the results of the study and provide a more in-depth understanding of the topic.

CONCLUSION

The consumption of Ajwa dates has been found to have an impact on serum calcium and haemoglobin levels in perimenopausal women. The study found no notable variation in the levels of fasting blood glucose (FBG) between perimenopausal women who consumed Ajwa dates and those who did not. Further research is required, using hormonal biomarkers, to understand better the metabolic changes that occur in perimenopausal women as a result of consuming Ajwa dates and to establish the potential health benefits associated with their consumption.

Declarations

Ethics approval and consent to participate

Ethics Commission of Health Research of the Faculty of Medicine in Universitas Hasanuddin approved to this study with approval number 64/UN4.6.4.5.31/PP36/2019 with protocol number UH18120943. The authors confirmed that all methods were carried out following the relevant guidelines and regulations (Helsinki Declaration).

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing Interests

We, the authors, declare that we have no competing interests.

Authors' contributions

NAM: Conceptualization, research design, data collection, data analysis, and initial draft writing. IRY, ES: Supervision, data validation, final manuscript editing. FEM: Data processing, data visualization, and contribution to the results and discussion sections. MWH, MNA: Field data collection, activity documentation, and literature review. SSY, MR: Development of research instruments, contribution to discussion writing, and language and structure revision. All author read and approved the manuscript.

Funding

The authors received no financial support for the research, authorship, and/or publication of this article.

Acknowledgments

We extend our highest appreciation and gratitude to all research respondents. We also thank to RSIA Sitti Khadijah I Muhammadiyah Makassar for facilitating this research.

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