



## Case Report: Effect of Ajwa Dates on Neutrophil Lymphocyte Ratio of Perimenopausal Women

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### Abstract

Perimenopause, certain hormone levels begin to decrease, especially hormones related to female reproduction, namely the hormones estrogen and progesterone. Estrogen deficiency can cause complaints such as urinary tract infections. The neutrophil lymphocyte ratio is a laboratory parameter that has the potential to be a predictor of bloodstream infection or bacteremia in patients with suspected infection. then bacterial infection can cause systemic inflammation characterized by fever. The high content of polyphenols, flavonoids and flavones contained in Ajwa dates. One of the high levels of flavonoids in dates is a good anti-inflammatory agent. Ajwa extract which contains ethyl acetate, methanolic and water can inhibit the lipid peroxidase enzyme cyclooxygenase (COX-1 and COX-2).

## Introduction

Perimenopause is a new term that covers the years before the final menstrual period in which the menstrual cycle progresses from regular ovulation and a predictable pattern to irregular and increasingly anovulatory cycles until it finally stops menstruating. The length of the menstrual cycle is determined by the speed and quality of follicular growth and development, and the cycle usually varies from woman to woman (Giyartika & Keman, 2020; Government of Indonesia, 2010; Taylor et al., 2019)..

The female genital organs and urinary tract are strongly influenced by estrogen. estrogen deficiency can cause various types of complaints, ranging from mild to severe. genital complaints can include: irritation, burning, itching, vaginal discharge, urinary tract infections, reduced vaginal fluid, and wrinkled vaginal walls. complaints in the urinary tract in the form of frequent micturition, unable to hold urine, painful micturition, frequent night micturition, and incontinence (Darmawan et al., 2014; Saputra et al., 2019; Wiargitha, 2017).

The neutrophil lymphocyte ratio is a laboratory parameter that has the potential to be a predictor of bloodstream infection or bacteremia in patients with suspected infection. the incidence of bacteremia defined as the presence of live bacteria growth in the bloodstream reaches about 1% of total admissions to the hospital. then bacterial infections can cause systemic inflammation characterized by fever. white blood cell populations in immunocompetent patients (monocytes, lymphocytes, and neutrophils) play an important role in the systemic inflammatory response to severe infections (Anisa, 2015; Hamad et al., 2015).

Among the factors that play a role in the high content of polyphenols, flavonoids, and flavones contained in Ajwa dates. one of the high content is flavonoid substances in dates which are good anti-inflammatory agents. Ajwa extracts containing ethyl acetate, methanolic, and water can inhibit the enzymes cyclooxygenase lipid peroxidase (COX-1 and COX-2). Pollen from dates can also be used as an anti-inflammatory agent because it has a role in modulating cytokine expression. Methanol in date fruit extract can reduce plasma fibrinogen. From all these mechanisms, it can be concluded that dates have benefits as anti-inflammatory agents (Nelson, 2008; Royani et al., 2019; Sasmita et al., 2019).

Phoenix dactylifera L. date fruit is one of the fruits that has abundant health benefits, including as an antioxidant, antihyperlipidemia, and hepatoprotective agent, as well as preventing cardiovascular diseases. Metabolic analysis was conducted on 12 types of dates originating from Saudi Arabia to determine the nutritional composition of each type of date. It was revealed that the highest phenoline levels were found in Ajwa dates, while the highest flavonoids were found in Ajwa dates and then in Saffawi dates (Irmayanti et al., 2018; Indonesian Ministry of Health, 2011; Lee et al., 2018).

## Methods

The method used in influencing the results of the effect of ajwa dates on neutrophil lymphocyte ratio levels in perimenopausal women is experimental research using a pre - post test control design, where variables are measured before and after intervention. The research will be conducted in March-May 2022. Screening and sampling stages of the study. The research will be conducted at RSIA Sitti Khadijah I Muhammadiyah Makassar Branch. Sample examination will be carried out at the Research Laboratory of Sitti Khadijah I Muhammadiyah Makassar Branch Jl. R.A Kartini N0. 15-17, Baru, Kec.Ujung Pandang, Makassar City South Sulawesi.

With the independent variable being ajwa dates and the dependent variable being perimenopausal neutrophil lymphocytes. The number of respondents in this case study was 1 perimenopausal woman. Ajwa dates are consumed as many as 7 ajwa dates in the morning before meals for 8 weeks, of which 7 ajwa dates have 60-80gr.

## Result and Discussion

The research was conducted in March-May 2022 at RSIA Sitti Khadijah I Muhammadiyah Makassar Branch. With the number of respondents 1 perimenopausal woman who was given ajwa dates. Data collection was carried out by interview, checking neutrophil lymphocytes and giving ajwa dates, how to consume ajwa dates and conducting direct and online monitoring to ensure clients eat ajwa dates and evaluate. Evaluation will be carried out by rechecking calcium levels after the research is carried out, then the data that has been obtained and the results of interviews and observations are presented in tabular form.

Table 1. Characteristics of Respondents at RSIA Sitti Khadijah I Muhammadiyah Makassar Branch

<b>RESPONDENT 1</b>	
Name	Mrs. R
Age	46 Years
Jobs	Laundry Staff
Status	Marry
Address	Perm Kodam Lorong 2 no 8
No HP	0829828XXXX

These maternal characteristics were screened for anti-inflammation by selecting age at perimenopause, baseline neutrophil lymphocytes and number of parities. Mothers did not take supplements during the study to better monitor the effects of ajwa date fruit consumption.

Table 2. Checklist for Consuming Ajwa Date Fruit

No.	Week 1							
	1	2	3	4	5	6	7	8
1. RESPONDENT 1	√	√	√	√	√	√	√	√

Based on Table 2, the respondents were very obedient in consuming ajwa dates in the morning before breakfast.

Table 3. Neutrophil Lymphocyte Picture of Mrs.R Before and After Given Ajwa Date Fruit

Name	Neutrophils before ajwa date palm fruit administration	Neutrophils after ajwa date fruit administration	Lymphocytes before ajwa date fruit administration	Lymphocytes after being given ajwa date fruit	Ket
RESPONDENT 1	5.4/74.2%	5.3/73.7%	0.8/10.9%	0.7/10.0%	Declining

Based on Table 3 obtained data on respondents before and after giving ajwa dates. Neutrophil Lymphocytes in respondents before giving ajwa dates and after routine administration of ajwa dates, decreased by an average of 0.1/99% in 8 weeks.

Perimenopause is a phase in the aging process, when a woman transitions from the reproductive to the non-reproductive period 11. Aging of the female reproductive system is evident when entering perimenopause, where there is a decrease in the number and function of oocytes and marked endocrine changes. Inflammation and accumulation of reactive oxygen species (ROS) are most influential in the decline of ovarian reserve (Ni, 2016; Zahorec, 2001).

Neutrophils are the main component of leukocytes that actively migrate towards the immune system or organ. Where neutrophils release large amounts of ROS (Reactive Oxygen Species) that induce damage to cell DNA (31), so it can be said that when the neutrophil lymphocyte ratio value increases, it means that the amount of ROS in the body is also in a larger amount. Then ADCC (Antibody-Dependent Cell-Mediated Cell) can directly kill the virus and trigger humoral immunity. Neutrophils can be triggered by virus-related inflammatory factors, such as interleukin-6, interleukin-8, tumor necrosis factor, granulocyte colony stimulating factor, and interferon-gamma factors, which are produced by lymphocytes and endothelial cells (Baratawidjaja, 2000; Wulandari, 2019; Yang et al., 2020).

The neutrophil-lymphocyte ratio is one of the indicators of an inflammatory response. One of the physiological reactions of the immune system to systemic inflammation is an increase in neutrophil counts and a decrease in lymphocyte counts. Neutrophilia or increased neutrophil levels are often associated with an inflammatory response to infection and tissue damage. Meanwhile, lymphocytopenia or decreased lymphocyte levels are associated with a poor prognosis related to a decreased inflammatory response to infection. RNL levels can be influenced by age factors, especially in women, where elderly women get lower NLR levels due to decreased estrogen levels due to menopause in healthy populations. In a study conducted by Liu et al, patients were grouped by age (age < 50 years; age ≥ 50 years) and neutrophil-lymphocyte ratio (low risk: < 3.13; high risk ≥ 3.13), the analysis was done with Kaplan-Meier showing there was a significant difference in the two groups (p = 0.00028 and p = 0.0005). Higher neutrophil counts and lower lymphocyte counts result in high neutrophil-lymphocyte ratio values, which can be interpreted that areas with extensive damage with more repair effects result in poor clinical outcomes (Cuevas et al., 2013; Schauss, 2013; Yasin et al., 2015).

Where ajwa dates contain phytochemical compounds with antioxidant and anti-inflammatory activity. Date fruits contain phytochemical compounds, including flavonoids and polyphenols.

Natural polyphenols have many biological activities, especially as antioxidants and anti-inflammation (Agustina et al., 2019).

The use of date fruit in vitro is closely related to anti-inflammatory, anti-angiogenic and antimicrobial activities. The review proved that both in vivo and in vitro, date fruits have anti-inflammatory activity, strongly associated with secondary metabolites and antioxidant activity. The anti-inflammatory effect of dates can be attributed to polyphenolic compounds that act as antioxidants, which scavenge free radicals generated during the inflammatory process and prevent unwanted biochemical reactions. This is inferred from the observation that date fruits can inhibit the production of nitric oxide and TNF- $\alpha$ . Date fruits increase the activity of superoxide dismutase and catalase enzymes, indicating a potential mechanism by which date fruits modulate enzymatic behavior, thereby triggering the signal cascade of the antioxidant defense system in inflammatory situations (Agustina et al., 2019; Wulandari, 2019).

The antioxidant, anti-inflammatory, and antitumor effects of aqueous ethanol extracts of *Phoenix dactylifera* L. dates were found to show significant inhibitory activity against phospholipase A2 (PLA2) activity depending on the extract dose. At a concentration of 130 g dry extract/mL, *P. dactylifera* extract reduced 50% of the enzyme activity in a highly significant manner ( $p < 0.001$ ). Inhibition of phospholipase A2 (PLA2) serves as a key regulation in the development of inflammatory disorders and can deplete the source of arachidonic acid which is a mediator of inflammation (Baliga et al., 2011; Julfitriyani et al., 2016; Rahmani et al., 2014).

The neutrophil-lymphocyte ratio in perimenopausal women was found to have a higher number of neutrophils and a lower number of lymphocytes resulting in a high neutrophil-lymphocyte ratio value, which can be interpreted that areas with extensive damage with more repair effects result in poor clinical outcomes<sup>30</sup>. Neutrophils are a major component of leukocytes that actively migrate towards immune systems or organs. Where neutrophils release large amounts of ROS (Reactive Oxygen Species) that induce damage to cell DNA, so it can be said that when the neutrophil lymphocyte ratio value increases, it means that the amount of ROS in the body is also in a larger amount. Dates are a good source of antioxidants. Based on several studies, Ajwa date extract has a function as a tissue protective effect because it is rich in antioxidant content, where in Ajwa dates there is a high polyphenol content of 455.88 mg/100 g when compared to other types of dates such as Sukkari 377.66 mg/100 g and Khalas 238.54mg/100g. Antioxidants are compounds that can counteract free radicals by giving one electron to free radical compounds, so that the activity of free radicals can be inhibited. Antioxidants function to prevent oxidative stress (de Jager et al., 2015; de Jager et al., 2012; McCarthy & Raval, 2020; Nugroho et al., 2013).

## Conclusion

After examining the neutrophil lymphocyte ratio, the results showed that the respondents experienced a decrease of 0.1% within 8 weeks. It is proven that giving ajwa dates to respondents is effective in reducing the neutrophil lymphocyte ratio in perimenopausal women consuming ajwa dates in accordance with the recommendations that have been given to respondents.

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