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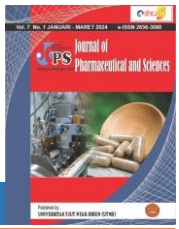

Correlation Between Vitamin C, Cholecalciferol, and Malondialdehyde Levels in Abortus and Normal Pregnancy: An Observational Study

Korelasi Kadar Vitamin C, Cholecalciferol dan Kadar Malondialdehid Antara Kejadian Abortus Dengan Kehamilan Normal : Studi Observasional

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Abstrac

Introduction: Abortion is a pregnancy complication that contributes significantly to maternal morbidity and mortality. Approximately 73 million abortions occur annually worldwide, with the estimated abortion rate in Padang city in 2024 reaching 58.7%. Abortion remains a challenge in obstetrics. The relationship between vitamin C deficiency, cholecalciferol, and elevated MDA levels and abortion remains debated, given the complex pathophysiological mechanisms. **Objective**: to determine the correlation between vitamin C, cholecalciferol, and malondialdehyde levels between abortion and normal pregnancy. **Method**: This study is a comparative study of two unpaired groups with a cross-sectional approach to analyze the average levels of Vitamin C, cholecalciferol, and MDA. The population in this study was pregnant women diagnosed with abortion and all women with normal pregnancies with a gestational age of ≤ 20 weeks who were treated in the delivery room of RSUD dr. M. Zein, RS. dr. Reksodiwiryo Padang, RSUP M. Djamil Padang, RS. Rasidin Padang with a sample size of 30. Data analysis was carried out using an Independent Samples T-test. **Results**: The results of this study showed that Vitamin C levels were lower in the abortion group than in the control group, a significant difference ($p = 0.001$). Cholecalciferol deficiency was more pronounced in the abortion group, a significant difference compared to normal pregnancies ($p = 0.002$). MDA levels were very high in the abortion group, a significant difference ($p = 0.001$). **Conclusion**: There is a significant correlation of Vitamin C and cholecalciferol levels between the occurrence of abortion and normal pregnancy, and there is a significant correlation of malondialdehyde levels between normal pregnancy and the occurrence of abortion.

Keywords: Vitamin C levels, Malondialdehyde, Cholecalciferol.

Abstrak

Pendahuluan: Abortus merupakan komplikasi kehamilan yang berkontribusi paling tinggi terhadap angka morbiditas dan mortalitas maternal. Sekitar 73 juta abortus terjadi setiap tahunnya diseluruh dunia, angka kejadian abortus di kota Padang pada tahun 2024 yaitu 58,7%. Abortus hingga saat ini masih menjadi tantangan dalam dunia kebidanan. Hubungan antara defisiensi Vitamin C, cholecalciferol dan serta peningkatan kadar MDA. **Tujuan**: untuk mengetahui korelasi kadar vitamin C, Cholecalciferol dan Kadar Malondialdehid antara kejadian abortus dengan kehamilan normal. **Metode**: Penelitian ini merupakan penelitian Komparatif dua kelompok tidak berpasangan dengan pendekatan cross sectional untuk menganalisis rerata kadar Vitamin C, cholecalciferol dan MDA pada ibu abortus dan kehamilan normal. Populasi pada penelitian ini adalah ibu hamil dengan diagnosa abortus dan seluruh wanita dengan kehamilan normal dengan usia kehamilan ≤ 20 minggu yang dirawat di dikamar bersalin RSUD dr. M. Zein, RS. dr. Reksodiwiryo Padang, RSUP M. Djamil Padang, RS. Rasidin Padang dengan jumlah sampel 30 sampel. Analisis data dengan uji Independent Sampel T Test. **Hasil**: Hasil penelitian ini menunjukan rerata kadar

Tingkat vitamin C lebih rendah pada aborsi dibandingkan dengan kelompok kontrol, perbedaan yang signifikan (p = 0.001). Defisiensi cholecalciferol lebih menonjol pada aborsi, perbedaan yang signifikan dibandingkan dengan kehamilan normal (p = 0.002). Tingkat MDA sangat tinggi pada kelompok aborsi, perbedaan yang signifikan (p = 0.001). **Kesimpulan**: Terdapat korelasi yang signifikan kadar Vitamin C dan cholecalciferol antara kejadian abortus dan hamil normal dan terdapat korelasi kadar malondialdehid antara hamil normal dan kejadian abortus.

Kata Kunci : Kadar Vitamin C, Malondialdehid, Cholecalciferol.

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Introduction

Abortion is a major complication of pregnancy and a leading cause of maternal and fetal morbidity and mortality. The maternal mortality rate due to abortion remains high. The causes of abortion can be divided into fetal and maternal factors: maternal age, anatomical abnormalities, immunological factors, infections, chronic diseases, endocrine disorders, and decreased vitamin C levels in the body. Cholecalciferol can also increase malondialdehyde (MDA) levels in abortion cases. Vitamin C directly stimulates collagen synthesis. Vitamin C and cholecalciferol (D3) also function as reducing agent by transferring hydrogen atoms with their single electrons to reactive oxygen species (ROS). Increased oxidative stress corresponds to increased MDA formation. Oxidative stress will cause damage and destruction of trophoblast cells, which will progress to abortion [1].

According to the *World Health Organization* (WHO), maternal deaths due to abortion are between 15 and 50%. Based on data, the National Health Service (NHS) in 2021 estimated that 23 million spontaneous abortions occur annually worldwide. Furthermore, the number of abortions occurring before 12 weeks of gestation ranges from 60-75% [2]. In Indonesia, the number of maternal deaths has increased, with 4,221 deaths in 2019, 4,627 deaths in 2020, and 7,389 deaths in 2021. The report stated that of the 7,389 maternal deaths, the majority were caused by bleeding (1,320 cases), hypertension in pregnancy (1,077 cases), abortion (207 cases), circulatory disorders (65 cases), and heart disease (335 cases). Furthermore, data and information from the Indonesian Health Profile in 2021 showed that the number of abortions in Indonesia reached 1,280 [3].

Based on previous data, the percentage of miscarriage in Indonesia is 4% in the group of ever-married women aged 10–59 years. The percentage of spontaneous abortion incidents in Indonesia based on age groups is 3.8% in the 15–19 age group, 5.8% in the 20–24 age group, 5.8% in the 25–29 age group, and 5.7% in the 30–34 age group. The likelihood of miscarriage occurring in women of childbearing age is 10%–25%. Abortion is a contributor to maternal mortality. In West Sumatra Province in 2018, the MMR was recorded at 111 people; this number of incidents increased in 2019 to 116 people [4].

First-trimester spontaneous abortion is one of the most common pregnancy complications, with an estimated incidence in the general population of approximately 10–20% of all clinical pregnancies. This figure may be higher when including biochemical *pregnancy loss*. In addition to the psychological burden on the family, abortion is also associated with increased healthcare costs, the need for medical follow-up, and the risk of morbidity in subsequent pregnancies. Understanding the biological factors underlying abortion is important for improving prevention and management strategies [5].

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In the last two decades, evidence suggests that oxidative stress plays a central role in the pathogenesis of abortion. An imbalance between free radical (reactive oxygen species/ROS) production and maternal-placental antioxidant capacity can trigger damage to trophoblast lipids, proteins, and DNA, disrupting implantation, spiral artery remodeling, and placental development. The most widely used markers of lipid peroxidation are malondialdehyde (MDA). Elevated MDA levels are consistently associated with poor pregnancy outcomes (abortion, preeclampsia, fetal growth restriction) [6].

On the other hand, maternal antioxidant micronutrient status is especially vitamin C (ascorbic acid) and vitamin D (cholecalciferol; measured as 25-hydroxyvitamin D/25(OH)D), potentially modulating the risk of abortion. Vitamin C is the main water-soluble antioxidant in plasma that neutralizes ROS, regenerates vitamin E, and supports decidual tissue collagenization and immune function [7]. Vitamin D has immunomodulatory effects (suppressing the immune response). *Th1proinflammatory (increasing Treg*), supports trophoblast differentiation, angiogenesis, and feto-maternal tolerance. Vitamin D deficiency in pregnancy remains prevalent globally, especially in tropical regions with sun protection practices, diets low in vitamin D sources, and genetic variations in vitamin D metabolism [8].

The identification of biomarkers such as vitamin C, cholecalciferol, and malondialdehyde has great potential in early detection and prevention of pregnancy complications, particularly abortion. Spontaneous abortion remains a reproductive health problem that causes physical and psychological impacts, so understanding biochemical factors such as vitamin C, vitamin D, and MDA levels is very important for the development of promotional and preventive efforts. Therefore, this study aims to reduce the incidence of abortion through promotion and prevention by simultaneously analyzing the correlation between vitamin C, cholecalciferol, and MDA levels in cases of abortion and normal pregnancy [8].

Experimental Section

This study is a comparative study of two unpaired groups with a cross-sectional approach to analyze the average levels of Vitamin C, cholecalciferol, and MDA in mothers with abortion and normal pregnancies. The study was conducted in May-June 2025 at M.Zein Painan Hospital, Dr. Reksodiwiryo Padang Hospital, Rasidin Padang Hospital, and M. Djamil Padang General Hospital. The population in this study was pregnant women diagnosed with abortion and all women with normal pregnancies with a gestational age of ≤ 20 weeks who were treated in the delivery room of Dr. M. Zein Hospital, Dr. Reksodiwiryo Padang Hospital, M. Djamil Padang General Hospital, and Rasidin Padang Hospital, totaling 85 people. The sample in this study was part of the population that met the inclusion and exclusion criteria of 30 people.

Every pregnant woman who had an abortion and every normal pregnant woman who came to have her pregnancy checked at the inpatient ward of M. Zein Hospital, M. Djamil Hospital Padang, Dr. Reksodiwiryo Hospital Padang, and Rasidin Hospital Padang met the inclusion and exclusion criteria and were included in the sample. Mothers who met the research criteria were selected as research subjects and explained prior to obtaining informed consent (IC) about the research to be conducted. If they agreed, the mothers were asked to sign the informed consent form. Next, a 3 cc sample of blood was taken from the mother's median cubital vein. The blood was then placed in a centrifuge tube (vacuum tube) without EDTA by allowing the syringe handle to release the blood from the syringe tube by itself. The blood sample was then centrifuged at a speed of 2000-3000 rotations per minute (rpm) for 20 minutes at the Bayangkara Hospital Laboratory in Padang. The serum resulting from centrifugation was stored in a sample cup. The blood is then sent to the Biomedical and Biochemistry Laboratory of the Faculty of Medicine, Andalas University, Padang, and stored at -20°C or 80°C until testing is performed.

Materials and Apparatus

Researchers will collect data related to vitamin C, cholecalciferol, and malondialdehyde levels between abortions and normal pregnancies. This will be done by taking blood samples and analyzing them using ELISA and spectrophotometer methods. After the data is collected, researchers will use statistical methods to analyze the correlation between vitamin C, cholecalciferol, and malondialdehyde levels between abortions and normal pregnancies. This will involve statistical analysis techniques such as person-to-person correlation or regression analysis to evaluate the relationship between these variables. In conducting the analysis, researchers will consider other factors that may influence abortions, such as age, body mass index (BMI),

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history of previous abortions, and comorbidities. Controlling these variables will ensure that the research results reflect the true correlation between vitamin C, cholecalciferol, and malondialdehyde levels between abortions and normal pregnancies. After the analysis is complete, researchers will interpret the results to determine whether there is a relationship between vitamin C, cholecalciferol, and malondialdehyde levels between abortions and normal pregnancies. This will illustrate the extent to which these levels influence the incidence of abortion.

Results

Normality of the data for Vitamin C, MDA, and cholecalciferol levels was assessed using the Shapiro-Wilk test for both the abortion and normal pregnancy groups. The results indicated that all variables in both groups were normally distributed ($p > 0.05$ for all tests, see Table 1.

Table 1. Normality Test (Shapiro-Wilk) for Vitamin C, MDA, and Cholecalciferol Levels

Variable	Abortion Group (n=15) P value	Normal Pregnancy Group (n=15) P value
Vitamin C	0.056	0.052
MDA	0.089	0.076
Cholecalciferol	0.053	0.058

Note: A Shapiro-Wilk test p-value > 0.05 indicates a normal distribution.

Table 2. Correlation of Vitamin C, MDA, and cholecalciferol

Variables(Unit)	Abortion (n=15) Mean ± SD	Normal Pregnancy (n=15) Mean ± SD	P value
Vitamin C (µmol/dL)	0,62±0,12	0,86±0,15	0.001
MDA	4,74±0,82	28,3±6,1	0,002
Cholecalcifero	19,7±5,6	28,3±6,1	0,001

Vitamin C levels were lower in the abortion group than in the control group, a significant difference ($p = 0.001$). Cholecalciferol deficiency was more pronounced in the abortion group, a significant difference compared to normal pregnancies ($p = 0.002$). MDA levels were very high in the abortion group, a significant difference ($p = 0.001$).

Discussions

Research results show that there is a significant correlation between vitamin C and cholecalciferol levels in cases of abortion and normal pregnancy, and there is no correlation between malondialdehyde levels in normal pregnancy and cases of abortion. The findings of lower vitamin C and D levels in abortuses, as well as higher MDA, are consistent with many reports that place oxidative stress and immune dysregulation as the pathophysiological axis of recurrent abortion or premature abortion [9]. The literature also emphasizes that vitamin D deficiency is common in women of reproductive age and is associated with poor obstetric outcomes. However, evidence for interventions (antioxidant supplementation) remains mixed; effects are likely contextual (influenced by baseline status, dose, and timing) [10].

Vitamin C is a major water-soluble antioxidant that neutralizes ROS (reactive oxygen species) in the extracellular space and cytosol, regenerates oxidized vitamin E, and plays a role in collagen synthesis for the integrity of the chorioamniotic membrane [11]. Vitamin C deficiency reduces ROS scavenging capacity, allowing the formation of lipid peroxidation products (MDA) that can damage trophoblast and endothelial cell membranes, triggering early placental dysfunction and implantation disorders [12].

In pregnancy, Vitamin D modulates immunity, shifting the response from Th1 (pro-inflammatory) to Th2/Treg (tolerogenic) dominance, increasing IL-10, suppressing TNF-α/IL-6, and supporting trophoblast invasion through activation of VDR (vitamin D receptor) in the decidua and placenta [13]. Vitamin D deficiency is associated with excessive inflammation and suboptimal placentation quality, which is synergistic with high oxidative stress [14].

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MDA is the end product of lipid peroxidation. Increased MDA levels reflect oxidative stress, which can induce damage to membrane lipids, proteins, and DNA in the conceptus tissue, trigger trophoblast apoptosis, and early placental instability [15]. The positive relationship between MDA and the incidence of abortion and the negative relationship between MDA and vitamin C/D found in this study are in line with the above mechanism [16].

The results of this study indicate that vitamin C and cholecalciferol levels are lower, while malondialdehyde (MDA) levels are higher in the abortion group compared to normal pregnancies. These findings support the hypothesis that antioxidant micronutrient deficiency and increased oxidative stress play a role in the pathogenesis of spontaneous abortion. These findings are consistent with the classic study by Gupta et al. (2007), which described that oxidative stress, characterized by an increase in lipid peroxidation biomarkers such as MDA, is one of the important mechanisms in pregnancy failure. Gupta emphasized that low antioxidant reserves, including vitamins C and E, make pregnant women more susceptible to oxidative damage [13].

Furthermore, the results of this study also support the report by Jeyabalan & Caritis (2022), which highlights the important role of vitamin D in pregnancy. They conclude that vitamin D3 (cholecalciferol) deficiency is associated with an increased risk of obstetric complications, including miscarriage, through the mechanisms of placental immunity disruption and oxidative stress. The data in this study showing lower vitamin D levels in abortions reinforces these findings. Furthermore, the results of this study are highly consistent with the article "Correlation Between Vitamin C, Cholecalciferol and Malondialdehyde Levels in Abortus and Normal Pregnancy," which directly reports a significant relationship: lower levels of vitamin C and vitamin D, while higher levels of MDA in abortions compared to normal pregnancies. The similarity of these results adds to the strength of the evidence that a combination of vitamin deficiency and increased oxidative stress is a determining factor in abortion. However, there are several nuances that need to be noted. Not all studies show consistent results, due to population heterogeneity (differences in nutritional status, sun exposure, dietary habits), laboratory methods (ELISA, HPLC, spectrophotometry), and confounding variables (such as smoking, infection, obesity). For example, in some populations with high sun exposure, the difference in vitamin D levels between abortion and normal pregnancy is sometimes insignificant, unlike findings in areas with endemic vitamin D deficiency [4].

Thus, the results of this study support the main literature (Gupta, 2007; Jeyabalan & Caritis, 2022; and related correlational studies), while reinforcing the pathogenesis model of abortion involving the interaction of antioxidant deficiency, vitamin D metabolism disorders, and increased oxidative stress. The minor differences that may arise are more likely due to population context and methodology rather than fundamental contradictions. Limitations of this study include the small sample size and cross-sectional design, which cannot establish causality [4] [13].

Conclusion

Rarity of the Kadarvitamin C and cholecalciferol (Vitamin D)tends to be lower in the abortion group than in normal pregnancies. Many MDA Lipid peroxidation markers were higher in the abortion group, and there was a significant association between low vitamin C and vitamin D levels and increased MDA and increased chance of abortion.

Conflict of Interest

All authors declare no conflict of interest in this research.

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