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Research Article

Effectiveness of High Dosage of Calcium, Folic Acid and Vitamin D on Reducing the Risk of Preeclampsion Among Pregnant Women

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Abstract

Aims: to determine the effectiveness of giving high doses of calcium, folic acid and vitamin D to reducing the risk of preeclampsia in the Karawang Health Center in 2023.

Methods: the type of research used in this research is quantitative with a cross sectional research design. The population in this study were 68 pregnant women who were at the Karawang Health Center, Karawang Regency. a sample of 45 pregnant women who were at the Karawang Community Health Center in Karawang Regency and bivariate analysis using the chi-square test.

Results: Most of the use of high-dose calcium were adherent by 26 people (67.8%), most of the use of folic acid were adherent by as many as 30 people (66.7%), most of the use of vitamin D were not adherent by 27 people (60.0%). Most of the risk of preeclampsia blood pressure in normal pregnant women as many as 25 people (55.6%). Giving high doses of calcium, folic acid and vitamin D is effective in reducing the risk of preeclampsia in the Karawang Health Center in 2023 with (P-Value ≤ 0.05).

Conclusion: It can be concluded that giving high doses of calcium, folic acid and vitamin D is effective in reducing the risk of preeclampsia in the Karawang Health Center in 2023.

Keywords :

Calcium, Folic Acid, Preeclampsia, Pregnant Women, Vitamin D

INTRODUCTION

Hypertension in pregnancy is one of the health problems that contributes to high mortality and morbidity in pregnant women. The prevalence of hypertension in pregnancy ranges from 5–15% and is one of three causes of mortality and morbidity in childbirth in addition to infection and bleeding. If chronic hypertension is not treated properly, pregnant women can experience preeclampsia (1)

Preeclampsia is a distinct syndrome that occurs during pregnancy and is characterised by clinical symptoms which include reduced blood flow to organs caused by vasospasm and activation of the endothelium. Despite its uncertain etiology, preeclampsia remains a significant

complication of pregnancy, characterized by elevated blood pressure, proteinuria, and edema.

The incidence of preeclampsia, as reported by the World Health Organisation, varies between 0.51% and 38.4%. Estimates suggest that preeclampsia and eclampsia contribute to around 14% (50,000-75,000) of maternal mortality annually globally. Approximately 5% of all pregnancies in the United States are affected by preeclampsia, with an annual incidence of 23 occurrences per 1,000 pregnancies. Furthermore, the prevalence of preeclampsia differs throughout countries, however typically it is documented to occur in 3-10% of all pregnancies within a country. Preeclampsia

incidence in Indonesia is 123,273 cases per year, which accounts for roughly 5.3%. Maternal mortality caused by preeclampsia is more prevalent in developing nations, with rates ranging from 10% to 25%, maybe attributed to delayed management of cases. Preeclampsia occurs in around 3% to 14% of all pregnancies globally. In underdeveloped regions, preeclampsia is a significant contributor to maternal morbidity and mortality, and result in a perinatal mortality rate that is up to five times higher.

Based on data from West Java, the province has the highest Maternal Mortality Ratio (MMR) at 79.68 per 100,000 KH in 2021 and 78.29 per 100,000 KH in 2022. The primary causes of maternal mortality in Indonesia in 2022 remain bleeding at 32.32%, preeclampsia at 25.25%, and infection at 4.9%. In West Java, the leading causes of maternal death are bleeding at 33%, preeclampsia at 31.8%, and circulatory system disorders at 9.5%. Based on the available statistics, it can be inferred that preeclampsia remains one of the top three causes of maternal mortality (5). According to the 2022 report from the Karawang Regency Health Service, the incidence of Acute Kidney Injury (AKI) was 45 instances per 100,000 live births. This included 14 cases of HDK/Severe Preeclampsia, 15 cases of hemorrhage, 2 cases of infection, and 8 cases of circulatory system diseases. Analysis of data from Karawang Regency reveals that preeclampsia and hemorrhage are the primary factors contributing to maternal mortality (6). Using data from mothers who gave birth at the Karawang Regency Hospital during the 2021 era, the medical records revealed the greatest incidence rate of severe preeclampsia at 5.83%. This rate climbed by 5.93% in 2021. The findings of a pilot study conducted at the Karawang Health Center in 2021 revealed that out of 743 pregnant women, 27 developed preeclampsia. In January-April 2022, a total of 309 pregnant women diagnosed with high-risk pregnancies underwent screening at the Health Center. Out of them, 211 women (68.3% of the total)

were identified as at risk of preeclampsia. Of the total number of moms screened for preeclampsia, 41 (13.3%) were identified. Preeclampsia is categorised into early-onset preeclampsia (PEAD) and late-onset preeclampsia (PEAL) according to the gestational age at which clinical symptoms of preeclampsia are detected. PEAD and PEAL have distinct causal mechanisms. Partial uterine adenocarcinoma (PEAD) is commonly linked to reduced uteroplacental perfusion resulting from poor trophoblast invasion, whereas preterm epithelial adenocarcinoma (PEAL) is generally linked to both external and maternal.

Many theories have been adopted about the causes of preeclampsia, including: placental vascularization disorder theory, placental ischemia theory, free radicals, endothelial dysfunction theory, immunological theory, genetic theory, nutritional deficiency theory, and inflammation theory (Cunningham, 2014). However, the basis for the pathogenesis of preeclampsia is damage related to the placenta. Almost all experts agree that vasospasm is the beginning of preeclampsia (8)

Maternal diet during pregnancy is one of the factors related to the etiology of preeclampsia; inadequate diet, especially in terms of calcium, magnesium, selenium, vitamins A and C, is a contributing factor to preeclampsia. Recent epidemiological studies have emphasized the role of vitamin D deficiency in the development of preeclampsia (9)

Calcium needs increase during pregnancy. In addition to being important for maternal and fetal bone health, adequate calcium intake can reduce the incidence of hypertension during pregnancy, reduce the risk of preeclampsia and prevent premature birth (10)

The most common challenge encountered in pregnant women's compliance in consuming calcium supplements is 'forgetting', so a strategy is needed that can help pregnant women remember to consume supplements regularly. Several studies have reported that

the frequency of ANC is significantly related to maternal compliance in consuming calcium supplements (11).

Mineral and nutritional factors play a role as one of the etiologies of predicting hypertension in pregnancy. Several studies have conducted research on calcium intake in normal pregnancies and pregnancies with complications. There is a significant effect of giving calcium and vitamin D tablets to pregnant women on blood pressure, calcium levels and outcomes in babies born (12) Another study found that blood pressure in pregnant women with hypertension after consuming calcium tablets decreased with an average systolic of 4.66 mmHg and an average diastolic of 6.66 mmHg followed by calcium levels in hypertensive women higher with an average of 0.217 mg/dl compared to normotensive women with an average of 0.117 mg/dl (13) Based on the background above, the researcher is interested in raising the title "Effectiveness of giving high-dose calcium, folic acid and vitamin D to reduce the risk of preeclampsia in the Karawang

Health Center Area in 2023".

METHODS

This study employs a quantitative research approach using a cross-sectional research methodology. The study sample consisted of 68 pregnant women who were receiving care at the Karawang Health Center in Karawang Regency. The study included a cohort of 45 pregnant women who sought medical care at the Karawang Health Center located in Karawang Regency. The objective of the bivariate analysis was to determine if there was a relationship between the independent factors and the dependent variables proposed in the conceptual framework. The purpose of the bivariate analysis was to determine the presence of a relationship between two variables, namely the dependent variable and the independent factor. In order to assess the impact of the two variables in this study, the researcher employed a statistical diagnostic known as the T chi-square test.

RESULTS

Table 1. Effectiveness of high-dose calcium administration in reducing the risk of preeclampsia in the Karawang Health Center Area in 2023

High dose calcium	Decreased risk of preeclampsia				Total		P Value
	Normal		TD Tall		n	%	
	n	%	n	%			
Obedient	23	88,5	3	11,5	26	100	0,000
Not obey	2	10,5	17	89,5	19	100	
Total	25	55,6	20	44,4	45	100	

From table 1. shows that respondents who are not compliant in consuming high doses of calcium experience high blood pressure (89.5%). The results of the Chi-Square test show that giving high doses of calcium is effective in reducing the risk of preeclampsia in the Karawang Health Center Area in 2023 (P-Value $0.000 \leq 0.05$).

Table 2. Effectiveness of folic acid administration in reducing the risk of preeclampsia in the Karawang Health Center Area in 2023

Folic acid	Decreased risk of preeclampsia				Total		P Value
	Normal		TD Tall		n	%	
	n	%	n	%			
Obedient	22	73,3	8	26,7	30	100	0,001
Not obey	3	20,0	12	80,0	15	100	
Total	25	55,6	20	44,4	45	100	



From table 2. shows that respondents who are not compliant in consuming folic acid experience high blood pressure (80.0%). The results of the Chi-Square test show that the administration of folic acid is effective in reducing the risk of preeclampsia in the Karawang Health Center Area in 2023 (P-Value $0.001 \leq 0.05$).

Table 3. Effectiveness of vitamin D administration in reducing the risk of preeclampsia in the Karawang Health Center Area in 2023

Vitamin D	Decreased risk of preeclampsia				Total		P Value
	Normal		TD Tall		n	%	
	n	%	n	%			
Obedient	17	94,4	1	5,6	18	100	0,000
Not obey	8	29,6	19	70,4	27	100	
Total	25	55,6	20	44,4	45	100	

From table 3. shows that respondents who are not compliant in consuming vitamin D experience high blood pressure (70.4%). The results of the Chi-Square test show that giving vitamin D is effective in reducing the risk of preeclampsia in the Karawang Health Center Area in 2023 (P-Value $0.000 \leq 0.05$).

Table 4. Effectiveness of high-dose calcium, folic acid and vitamin D administration in reducing the risk of preeclampsia in the Karawang Health Center Area in 2023

Intervention	P Value
Giving High Doses of Calcium	0,000
Folic acid	0,001
Vitamin D	0,000

From table 4, it is shown that the most effective intervention starting from the intervention of providing high-dose calcium, folic acid and vitamin D based on the amount of reduction in the risk of normal preeclampsia is greater with a P Value of 0.000 is the intervention of providing high-dose calcium.

DISCUSSION

Overview of the use of high-dose calcium, folic acid and vitamin D in the Karawang Health Center Area in 2023

Based on the results of the study, it shows that the use of high-dose calcium in the Karawang Health Center Area in 2023 was mostly compliant with 26 people (67.8%) and non-compliant with 19 people (42.2%).

Dietary calcium intake refers to the quantity of calcium obtained from food and ingested

during a day. The recommended daily calcium intake for pregnant women aged 30-35 years is 1200 mg, whereas for pregnant women aged 20-29 years it is 1300 mg. Dietary calcium requirements rise throughout pregnancy as it is utilized to replenish the mother's calcium stores for the development of new tissue in the foetus. Adequate calcium intake during pregnancy substantially decreases the likelihood of hypertension in pregnant women by fourfold compared to those who do not consume sufficient calcium. The significance of calcium in gestational hypertension is paramount, as insufficient calcium intake in the diet might precipitate hypertension. Calcium serves to regulate blood concentration under muscular contraction activity. The contraction of blood vessel muscles is crucial since it help to regulate blood pressure.

In pregnant women, the recommended daily intake of magnesium increased from 100-250 mg/day to 350-620 mg/day under typical circumstances, compared to non-pregnant women. Renal calcium excretion rises throughout pregnancy starting from the first trimester and reaches its peak in the third trimester. This phenomenon arises from the physiological process of enhanced calcium absorption by the mother's intestines. Women diagnosed with gestational hypertension have significantly reduced urinary calcium excretion compared to normotensive women, however the reduction is not as pronounced as in pregnant women with pre-eclampsia. In comparison to normotensive women, women with chronic hypertension generally exhibit reduced urine calcium excretion (14). The University of London was the pioneering institution to identify the requirement of calcium for muscle contraction. It is now understood that calcium plays a crucial role in connecting contractile tissue, which stimulates cellular tissue contraction for hormone release, with all tissues that react to different physiological stimuli and contribute to maintaining blood pressure balance. Investigations conducted by McCarron et al and Strazzullo et al have shown that individuals with hypertension may have renal excretion of calcium and sodium (15). Folic acid was predominantly used by 30 individuals (66.7%), while 15 individuals (33.3%) did not adhere to the recommended regimen. Folic acid and Folate are chemical and nutritionally identical compounds to folic acid, often known as water-soluble essential vitamins. These bonds function as coenzymes in the transportation of individual carbon units in the cycle of amino acid metabolism and the production of nucleic acids. The chemical structure of this coenzyme is a tetrahydrate. Folate serves as a carbon donor in the production of serine and glycine, directly in the synthesis of purine and pyrimidine bases, indirectly in synthesis, and as a methyl donor to convert homocysteine to methionine by

remethylating it. Dietary folic acid is a formulation of folate in the form of polyglutamate, which is readily degraded during cooking (16).

Biosynthesis of folate in plants involves the combination of a heterobicyclic pteride ring, para-aminobenzoic acid (PABA), and glutamic acid. Folate is indispensable for the development of the foetus. Upon absorption, folate functions as a cofactor for several crucial cellular processes, such as the transfer of single-carbon units. Furthermore, its function in DNA synthesis makes folate essential for cell division. Additionally, folate serves as a substrate for many processes that impact the metabolism of several amino acids. These processes include, among others, transmethylation and transsulfuration (17). Disruption of DNA synthesis leads to aberrant cell division. Hence, the initial clinical presentation of folate insufficiency is the excessive division of neutrophils, which is subsequently succeeded by the generation of megablastic marrow cells, macrocytic red blood cells, and ultimately macrocytic anemia. Foetal development is characterized by extensive and continuous cell division. Because folate plays a crucial role in the production of nucleic acids, its requirement rises during tissue development. Throughout pregnancy, folate-dependent processes encompass the augmentation of red blood cell count, expansion of the uterus, and development of the placenta and neonate. An elevation in homocysteine levels is the metabolic consequence of folate insufficiency. Genomic abnormalities in the synthesis of the enzyme cystathionine β -synthase, 5,10-methylene tetrafolate reductase, lead to moderate to severe elevations in plasma homocysteine levels.

Thus, during gestation, inadequate folate consumption, either alone or in conjunction with different alleles of the folate gene, can disrupt the development and reproduction of foetal or placental cells. This elevated risk is associated with spontaneous abortion, premature delivery, or intrauterine growth

restriction. Augmented folate consumption for both the mother and fetus can subsequently facilitate growth and gestation, resulting in enhanced birth weight and prolonged gestational period.

A total of 27 individuals (60.0%) did not adhere to the recommended intake of vitamin D, whereas 18 individuals (40.0%) were compliant. Insufficient vitamin D levels in pregnant women not only adversely affect pregnant women, but also pose a risk to the developing fetus. Insufficient levels of vitamin D in pregnant women can lead to reduced bone mineral concentrations, impaired glucose balance, and subsequent softening of the skull bones resulting from inadequate bone formation in the uterus. Insufficient vitamin D levels can also contribute to preterm birth. The observed phenomenon can be attributed to the regulatory function of vitamin D in the human body, exerting anti-inflammatory and immunomodulatory effects by inhibiting the synthesis of inflammatory cytokines.

Description of the risk of preeclampsia in the Karawang Health Center Area in 2023

The research findings indicate that the risk of preeclampsia in the Karawang Health Center Area in 2023 was predominantly within the normal range, with 25 individuals (55.6%) at risk, while 20 individuals (44.4%) had high blood pressure.

Preeclampsia is a typical pregnancy syndrome with signs of hypertension where there is an increase in systolic blood pressure ≥ 140 mmHg or an increase of ≥ 30 mmHg from before pregnancy or an increase in diastolic ≥ 90 mmHg or an increase of ≥ 15 mmHg from before pregnancy. In addition to hypertension, proteinuria is also found with a urine protein level of 300 mg per 24 hours or 30 mg/dk (1+ on the dipstick) in a random urine sample and edema. And often accompanied by disorders in various organ systems, and usually occurs in primigravida. This disease is often detected in the 3rd trimester of pregnancy and is likely to worsen as the gestational age increases. The incidence of preeclampsia is not yet known,

but there are several predisposing factors such as multiple pregnancies, diabetes mellitus, history of maternal hypertension, hydatidiform mole, obesity, low socioeconomic status, primigravida (young: age <20 years and old: age >35 years) (Jayani DD, 2019). Developing countries have a higher incidence of preeclampsia than developed countries. Because developed countries have better prenatal care. The incidence of preeclampsia is influenced by genetic factors, race, parity, and the environment. Other factors that influence the incidence of preeclampsia are age and history of hypertension. According to a study, a history of hypertension is the most risky factor for the incidence of preeclampsia. It is very dangerous if a pregnant woman experiences preeclampsia because it can have a direct impact on the fetus, namely low birth weight (LBW) due to spasm of the spiral arterioles of the deciduas, decreased blood flow to the placenta which results in impaired placental function. Placental damage can result in fetal hypoxia, intrauterine growth restriction (IUGR) and death in the womb. In addition to having a negative impact on the baby, pregnant women can also experience quite serious events such as placental abruption, placental abruption, hypofibrinogenemia, hemolysis, cerebral hemorrhage, capillary damage, blindness, pulmonary edema, liver necrosis, heart damage. And if preeclampsia worsens, eclampsia will occur, and the worst complication is death in the mother (18).

The effectiveness of high dose calcium, folic acid and vitamin D administration in reducing the risk of preeclampsia in the Karawang Health Center Area in 2023

The study findings indicated that 89.5% of respondents who did not adhere to proper calcium intake had elevated blood pressure. Statistical analysis using the Chi-Square test revealed that administering high doses of calcium was successful in decreasing the likelihood of developing preeclampsia in the Karawang Health Center Area in 2023 (P-Value $0.000 < 0.05$). Hence, the study findings indicate a distinction between

pregnant women with inadequate calcium consumption and those with adequate calcium intake. This observation is also supported by the study undertaken by Tanzil in 2018. However, the observed change in systole and diastole values before and after the administration of calcium pills ($p > 0.05$) does not demonstrate the same phenomenon. While there were variations in the mean values of systole and diastole between the two groups, the study undertaken (19) yielded identical results. Inadequate calcium consumption in pregnant women leads to elevated levels of parathyroid hormone (PTH), which stimulates the increase of intracellular calcium by modulating the permeability of the cell membrane to calcium. Consequently, calcium ions present in the mitochondria are liberated into the cytosol. Elevated intracellular calcium levels induce spontaneous contraction of smooth muscle in blood vessels, leading to vasoconstriction and consequently higher blood pressure (20).

The respondents who failed to adhere to folic acid intake reported a prevalence of high blood pressure (70.0%). The Chi-Square test determined that the administration of folic acid effectively decreased the risk of preeclampsia in the Karawang Health Center Area in 2023, with a P-Value of $0.001 < 0.05$.

Analysis indicates that there is a correlation between folic acid insufficiency and the occurrence of preeclampsia. Folic acid has a crucial role in the development of preeclampsia due to its involvement in homocysteine metabolism regulation. Folic acid insufficiency has been demonstrated to result in elevated levels of homocysteine, with evidence indicating that nearly two-thirds of hyperhomocysteinemia cases are attributed to deficiencies in vitamin B12 and B5. Homocysteine is a sulfur-containing amino acid. Experimental data supports the hypothesis that excessive homocysteine promotes endothelium damage by engaging in an auto-oxidation process that generates

reactive oxygen groups, including superperoxide and hydrogen peroxide (16).

A majority of respondents (70.4%) who did not adhere to the recommended intake of vitamin D reported experiencing elevated blood pressure. Statistical analysis using the Chi-Square test revealed that administering vitamin D was successful in decreasing the likelihood of developing preeclampsia in the Karawang Health Center Area in 2023 (P-Value $0.000 < 0.05$). Research undertaken by Dror DK, et al. provided evidence that vitamin D levels throughout the early stages of pregnancy contribute to the regulation of risk factors for problems, as well as promoting foetal growth, bone development, and immunological maturity. The study undertaken by Caroline Lechteemann, et al. revealed a notable disparity in the mean vitamin D levels between pregnant women diagnosed with preeclampsia (18.2 ± 20 ng/ml) and pregnant women without the condition (33.3 ± 27.3 ng/dl). Furthermore, the variation in the mean vitamin D levels was also observed with the transition of seasons, namely during winter. Such mothers are deficient in UV radiation emitted by sunlight. Light of ultraviolet wavelength can transform pre-vitamin D into vitamin D3. The early identification of preeclampsia is accomplished by the analysis of several biological, biophysical, and biochemical indicators prior to the manifestation of clinical symptoms associated with preeclampsia syndrome. This is achieved by identifying pregnancies at high risk and implementing preventive measures to minimize disease complications and mortality by modifying Ante Natal Care (ANC). Contemporary obstetrics faces the primary obstacle of detecting early pregnancies that are at a high risk of developing preeclampsia and implementing the required measures to mend the placenta and decrease the occurrence of this condition.

CONCLUSIONS

Most of the high-dose calcium users were compliant as many as 26 people (67.8%),

most of the folic acid users were compliant as many as 30 people (66.7%), most of the vitamin D users were not compliant as many as 27 people (60.0%). Most of the risk of preeclampsia blood pressure in normal pregnant women as many as 25 people (55.6%). Administration of high-dose calcium, folic acid and vitamin D is effective in reducing the risk of preeclampsia in the Karawang Health Center Area in 2023 with (P-Value \leq 0.05).

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