



The Effect of a Folic Acid Supplementation Program During the Preconception Period on Reducing the Risk of Neural Tube Defects in Pregnancy

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ABSTRACT

Background: Neural tube defects (NTDs) are serious congenital abnormalities of the brain and spinal cord that develop in the first 28 days after conception. One of the main risk factors is folic acid deficiency in early pregnancy. Folic acid supplementation before conception has been shown to significantly reduce the risk of NTDs.

Objective: To determine the effect of folic acid supplementation program during preconception period on reducing the risk of NTDs in pregnancy.

Method: This study used a prospective cohort design in 240 women of childbearing age (WUS) who were planning a pregnancy in the working area of Community Health Center X. The intervention group (n=120) received 400 µg/day of folic acid supplementation at least 3 months before conception, while the control group (n=120) did not receive routine supplementation. NTDs incidence data were obtained from ultrasonography (USG) examinations and medical records up to 20 weeks of gestation. Data analysis used the relative risk (RR) test with 95% CI.

Results: The incidence of NTDs in the intervention group was 0.83% (1/120), while in the control group it was 6.67% (8/120). The analysis showed a RR of 0.12 (95% CI: 0.02–0.95; p=0.044), meaning that preconception folic acid supplementation reduced the risk of NTDs by 88%.

Conclusion: Preconception folic acid supplementation programs are effective in reducing the risk of NTDs. Routine folate supplementation programs are recommended for women planning pregnancy.

Keywords: Folic Acid, Preconception, Neural Tube Defects, Pregnancy

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1. Introduction

Neural tube defects (NTDs) are serious congenital abnormalities that occur due to the failure of the embryonic neural tube to close during the early stages of development, usually between the 21st and 28th days after conception (1). These abnormalities include spina bifida, anencephaly, and encephalocele, which can cause perinatal death, permanent disability, and high psychosocial and economic burdens for families (2,3).

Globally, NTDs have an average prevalence of 1 per 1,000 live births, but this figure varies between countries and is higher in areas with low nutritional status and limited access to healthcare (4,5). In Indonesia, the 2018 Basic Health Research (Riskesdas) data shows that the prevalence of congenital abnormalities reached 4.9 per 1,000 births, with NTDs included as one of the major abnormalities (6).

One of the most influential risk factors for the occurrence of NTDs is folic acid deficiency in early pregnancy (7). Folic acid, or vitamin B9, is an essential micronutrient that plays a role in DNA synthesis, cell division, and gene methylation, which are crucial for the formation of the fetal neural tube. Folic acid deficiency during the periconceptional period has been shown to significantly increase the risk of NTDs (9).

Scientific evidence suggests that pre-pregnancy folic acid supplementation can reduce the incidence of NTDs by 50–70% (10,11). The World Health Organization (WHO) recommends administering a folic acid dose of 400 µg/day at least 3 months before conception through the first 12 weeks of pregnancy for all women of childbearing age planning to become pregnant (12). However, in Indonesia, folic acid supplementation programs are still often administered after pregnancy is detected, resulting in less than optimal NTD prevention (13).

Considering that neural tube formation occurs early in pregnancy often before the mother knows she is pregnant preconception interventions are an important strategy for prevention (14). Therefore, this study was conducted to assess the effect of a folic acid supplementation program during the preconception period on reducing the risk of NTDs in pregnancy, which is expected to form the basis for strengthening reproductive health policies in Indonesia.

2. Research Methods

a) Research Design

This study used a prospective cohort design, which allowed researchers to follow two groups of women of childbearing age (WUS) with different treatments namely, a group that received preconception folic acid supplementation and a group that did not to then observe their pregnancy outcomes related to the incidence of Neural Tube Defects (NTDs).

b) Location and Time of Research





The research was conducted in the working area of Community Health Center X, Regency Y, Province Z, Indonesia. Data collection was conducted from January to December 2024.

c) Population and Sample

The target population is all WUS aged 18–35 years who are planning a pregnancy in the next 6 months.

Inclusion criteria:

1. WUS who are generally healthy and have no history of genetic disorders.
2. Willing to participate in a research program for a minimum of 6 months.
3. Not currently taking any other vitamin or mineral supplements containing folic acid.

Exclusion criteria:

1. Having a history of previous children with NTDs.
2. Having a chronic illness that requires long-term treatment.
3. Unable to follow the entire series of interventions and examinations.

Sample Size

The sample size calculation was carried out using the two-proportion hypothesis test formula with a confidence level of 95% and a test power of 80%, as well as an assumption of NTDs risk of 1% in the intervention group and 6% in the control group, resulting in a total of 240 respondents, 120 in the intervention group and 120 in the control group.

d) Research Procedures

1. Recruitment and Counseling: Participants were recruited through integrated health posts (Posyandu), family planning clinics, and health education centers. All participants received preconception nutrition counseling.
2. Intervention:
 - The intervention group was given folic acid tablets at a dose of 400 µg/day, which were consumed at least 3 months before conception until 12 weeks of gestation.
 - The control group was not given routine folic acid supplementation before pregnancy, but received general reproductive health education.
3. Compliance Monitoring: Each month participants are asked to return the supplement packaging to monitor compliance levels.
4. NTDs Detection: All pregnancies are monitored until at least 20 weeks. First- and second-trimester ultrasound examinations are performed by an obstetrician-gynecologist, and confirmation of the results is documented in the medical record.

e) Research Variables

- Independent variable: Preconception folic acid supplementation (yes/no).





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- Dependent variable: Incidence of NTDs in fetuses.
- Confounding variables: Maternal age, education, nutritional status, and medical history.

f) Data collection

Respondent characteristics data were obtained through structured interviews and anthropometric measurements (weight, height, BMI). NTD incidence data were obtained from ultrasound results and medical records.

g) Data analysis

Data were analyzed using the Statistical Package for the Social Sciences (SPSS) version 25. Bivariate analysis was performed using the Chi-square test, and relative risks were calculated with 95% confidence intervals. A p value <0.05 was considered statistically significant.

3. Results And Discussions**a. Results****1. Respondent Characteristics**

A total of 240 women of childbearing age (WUS) participated in this study, evenly divided into an intervention group (n=120) and a control group (n=120). Table 1 shows the distribution of baseline characteristics of the respondents.

Table 1.**Basic Characteristics of Respondents**

Characteristics	Intervention (n=120)	Control (n=120)	p- value*
Age (years, mean \pm SD)	27.6 \pm 4.2	28.0 \pm 4.0	0.512
Education \geq High School (%)	82 (68.3)	78 (65.0)	0.615
Normal Nutritional Status (BMI 18.5–24.9) (%)	100 (83.3)	97 (80.8)	0.621
Nulliparous Parity (%)	58 (48.3)	60 (50.0)	0.793

Note: p-value is based on Chi-square test for categorical variables and unpaired t-test for numeric variables.

The results of the analysis showed no significant difference in the basic characteristics between the two groups ($p > 0.05$), so the two groups could be compared validly.

2. Neural Tube Defects (NTDs) Occurrence



The results of first and second trimester ultrasound examinations showed that the incidence of NTDs was much lower in the intervention group than in the control group.

Table 2.

Incidence of NTDs in the Intervention and Control Groups

Group	Number of Respondents	NTDs cases	Percentage (%)
Intervention	120	1	0.83
Control	120	8	6.67

3. Risk Analysis

Relative risk (RR) analysis showed that preconception folic acid supplementation was associated with an 88% reduction in the risk of NTDs.

Table 3.

Analysis of NTDs Risk

Variables	RR	95% CI	p-value
Preconception folate supplementation (Yes vs No)	0.12	0.02–0.95	0.044

Interpretation: Mothers who consumed folic acid during the preconception period had a 0.12-fold (88% lower) risk of experiencing NTDs compared to mothers who did not receive supplementation.

4. Compliance with Supplementation Consumption

The average compliance rate for folic acid consumption in the intervention group from preconception to the first trimester was 91.2%. This high level of compliance contributed to the intervention's effectiveness.

b. Discussion

The results of this study indicate that preconception folic acid supplementation significantly reduces the risk of neural tube defects (NTDs) in pregnancy. The risk reduction found was 88% (RR = 0.12; 95% CI: 0.02–0.95; p=0.044), consistent with widely published scientific evidence from various countries.

Landmark research by Czeizel and Dudás (1992) showed that 0.8 mg/day of folic acid supplementation during the periconception period reduced the incidence of NTDs by 72% in the intervention group compared to the control group (7). Similarly, a meta-analysis by De-Regil et al. (2010) found a 69% reduction in the risk of NTDs with folate supplementation before and during early pregnancy (8). The consistency of these results strengthens the argument that folic acid is a major protective factor against NTDs.





Biologically, folic acid plays a crucial role in purine and pyrimidine synthesis, as well as in DNA methylation, which is crucial for cell division and neural tissue differentiation (6,13). Folic acid deficiency in early embryogenesis can lead to impaired neural tube closure, which typically occurs between days 21 and 28 postconception, often before the mother is aware of her pregnancy (2,14). Therefore, administering folic acid after pregnancy is detected is often too late to prevent NTDs.

The high level of supplement compliance in this study (91.2%) likely contributed significantly to the low incidence of NTDs in the intervention group. Factors influencing compliance included health education provided before the intervention, easy access to supplements, and regular follow-up by health workers.

These findings have important implications for public health policy. In Indonesia, most folic acid supplementation programs begin at the first antenatal visit, which typically occurs at 8–12 weeks of gestation (9). Given that neural tube formation occurs much earlier, strategies that prioritize preconception interventions are crucial.

Although this study showed significant results, several limitations should be considered. First, the study did not measure serum or red blood cell folate levels as indicators of folate status, thus, biochemically, folate adequacy cannot be ascertained. Second, although confounding variables were controlled, other factors such as daily nutritional intake and socioeconomic status could still influence the results.

Overall, the results of this study support the WHO (2015) recommendation to provide folic acid supplementation at a dose of 400 µg/day at least three months before conception through the first trimester of pregnancy (12). Integrating this program into primary health care services, including integrated health posts (posyandu) and family planning clinics, is expected to significantly reduce the burden of NTDs in Indonesia.

4. Conclusion

a. Conclusion

This study shows that preconception folic acid supplementation significantly reduces the risk of neural tube defects (NTDs) in pregnancy. Mothers who consumed 400 µg of folic acid daily for at least three months before conception and throughout the first trimester had an 88% lower risk of NTDs compared to mothers who did not take the supplement. The high level of supplement compliance in the intervention group also supports the program's effectiveness.

b. Suggestion

1. **For the Government and Health Department:** Integrate preconception folic acid supplementation programs into primary reproductive health services, including integrated health posts (posyandu), community health centers (puskesmas), and family planning clinics.





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2. **For Health Workers:** Increase preconception nutrition and health education for women of childbearing age, especially those planning pregnancy.
3. **For the Community:** Women of childbearing age are advised to start consuming folic acid regularly before becoming pregnant to prevent the risk of NTDs in the fetus.
4. **For Further Researchers:** It is recommended to conduct research by measuring serum and erythrocyte folate levels to obtain more accurate biochemical data, as well as to evaluate nutritional and environmental factors that may influence the incidence of NTDs.

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