
THE EFFECT OF FOLIC ACID SUPPLEMENTATION DURING EARLY PREGNANCY ON OROFACIAL CLEFT AMONG CHILDREN 6-24 MONTHS IN KUPANG CITY

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ABSTRACT

Background: Orofacial cleft (OFC) is one of the most common congenital malformations in the world and Indonesia. The causes of OFC are complex, including both intrinsic (genetic) and extrinsic (environmental and behavioral) risk factors. Some studies found that there was an association between folic acid supplementation and the risk of OFC. However, studies on the effect of folic acid supplementation for OFC in Indonesia are lacking. **Purpose:** This study aims to analyze the association of folic acid supplementation during early pregnancy with an orofacial cleft in children in Kupang City. **Methods:** The study was a retrospective case-control study was carried out, with a multistage sampling method including 57 participants. We examined the risk of OFC with folic acid supplementation during early pregnancy. Chi-square analysis was used in the study. **Results:** The results showed that there was a significant association between folic acid use during early pregnancy and the incidence of OFC with a p-value = 0.000 (OR=20,0). **Conclusion:** Folic acid supplementation during early pregnancy can reduce the risk of OFC in children.

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INTRODUCTION

Orofacial cleft (OFC) is a congenital facial abnormality in the form of a cleft lip, cleft palate, or both, causing a direct connection between the nose and mouth (Tobing, 2017). Orofacial cleft is one of the most common congenital abnormalities in children. This condition is found in 1 in 700 births globally (Group, 2011). Based on 2018 Basic Health Research (Riskesmas) data in Indonesia, cleft lip accounts for 0.12% of childhood disabilities in-group aged 24-59 months (BPPS Kementerian Kesehatan RI, 2018). In East Nusa Tenggara Province, the percentage of cleft lip in children 0-59 months of age is 0.16% (RI, 2018).

The formation of the lips and palate in the womb occurs in the 4th to 8th week. OFC occurs if there is a disturbance during that period. However, the cause of OFC is uncertain. Several studies have shown the incidence of OFC is associated with the consumption of folic acid supplements during pregnancy. Folic acid supplementation during the early period of pregnancy is associated with a 33% reduction in the risk of cleft lip with or without cleft palate (Wilcox et al., 2007). Consumption of a single folic acid supplement at a dose of 400 g per day starting before the mother's last menstrual period is known to reduce the risk of cleft lip with or without cleft palate in infants (Hao et al., 2015; Li et al., 2012). Based on Sato's research, 15.1% of cases of cleft lip and palate could be prevented if all pregnant women took folic acid supplements (Sato et al., 2020).

Although it is not the main cause of child mortality, cleft lip and cleft palate can cause problems in physiological functions, such as eating and speaking disorders, as well as children's psychology. Handling OFC doesn't only require cooperation from several scientific approaches but also requires a lifelong treatment from birth to adulthood (Jahanbin, Shadkam, Miri, Shirazi, & Abtahi, 2018; Wehby & Moreno, 2014). The impact will affect both children and their families.

There is only a few research on the effect of taking folic acid supplements on the incidence of OFC in Indonesia, especially in Kupang City. Based on this background, this study was conducted to analyze the effect of folic acid supplement intake during early pregnancy on the incidence of OFC in children in Kupang City.

METHODS

This study uses a case-control design that was conducted in the period of February 2022 to April 2022 at the Wirasakti Army Hospital, Kupang, East Nusa Tenggara. The sampling technique used is multistage sampling, which is a gradual sampling method that begins with the determination of the Wirasakti Army Hospital as a sample hospital due to the availability of access to obtain data, then proceed with taking all respondents who meet the inclusion and exclusion criteria.

The inclusion criteria for the case group were children aged 6-24 months with non-syndromic OFC disorders who participated in social service activities for cleft lip surgery at Wirasakti Army Hospital. All of them were the first children of the family. The control group included children aged 6-24 months without OFC disorders or other congenital disorders who were treated as outpatients at the Pediatric Clinic, Wirasakti Army Hospital. The sample size in the case and control groups used a ratio of 1:2, so the sample size in this study amounted to 57 people. The independent variable in this study was the consumption of folic acid supplements, which was defined as the mother's habit of taking folic acid tablets since one month before pregnancy or during early pregnancy (gestational age 8 weeks). The dependent variable in this study was the incidence of OFC, defined as a cleft lip or cleft palate, or a combination of both, and is diagnosed by a physician.

The data collection process begins with secondary data collection through children's medical records in cleft lip surgery social service activities at Wirasakti Army Hospital in 2020-2022. Samples that meet the inclusion criteria will then be interviewed by telephone or directly to the mother as a respondent, using a questionnaire sheet as a tool. After the required data is collected, the data is processed and analyzed.

The processed data was then analyzed through univariate and bivariate analysis using the Chi-Square test with a 95% confidence interval and calculating the odds ratio (OR). Data were processed using the IBM SPSS 25 application. The research was carried out after obtaining a recommendation from the Health Research Ethics Commission (KEPK) of the Faculty of Medicine and Veterinary Medicine, Universitas Nusa Cendana on February 18, 2022, with UN02220107 as a register number.

RESULTS

Respondent Characteristics	OFC Incident			
	Case (n=19)		Control (n=38)	
	Frequency (n)	Percentage (%)	Frequency (n)	Percentage (%)
Mother's Age (Year)				
- < 20	0	0	4	10.5
- 20-24	4	21.1	8	21.1
- 25-29	7	36.8	7	18.4
- 30-34	2	10.5	12	31.6
- ≥ 35	6	31.6	7	18.4
Mother's Education				
- Elementary/Equivalent	2	10.5	0	0
- Junior High School/Equivalent	4	21.1	8	21.1
- Senior High School/Equivalent	4	21.1	8	21.1
- University	2	10.5	11	28.9
Mother's Profession				
- Working	11	57,9	22	57,9
- Not Working	8	42,1	16	42,1
Family Income				
- Low	15	78,9	25	65,8
- High	4	21,1	13	34,2
Child Gender				
- Male	7	36,8	25	65,8
- Female	12	63,2	13	34,2
Child Birth Status				
- Preterm	8	42,1	0	0
- Aterm	11	57,9	38	100

The characteristics of the participants in the case and control groups are shown in Table 1. In both the case and control groups, the majority of participants were of a non-risk gestational age, highly educated, working mothers, and had low

incomes. The case group was dominated by females, while the control group was dominated by males. All preterm children were in the case group, while all children in the control group were born at term.

Table 2

Effect of Folic Acid Supplements Consumption During Early Pregnancy on OFC Incidence

Folic Acid Consumption	OFC Incident				Total	p-value	OR	95% CI	
	Case		Control						
	n	(%)	n	(%)					n
- Not Consuming Folic Acid	15	78,9	6	15,8	21	36,8	0,000	20,0	4,903-81,590
- Consuming Folic Acid	4	21,1	32	84,2	36	63,2			
Total	19	100	38	100	57	100			

Table 2 shows the distribution of folic acid consumption during early pregnancy in the case and control groups. It is known that the majority of respondents in the case group did not take folic acid during early pregnancy, while most of the respondents in the control group took folic acid during early pregnancy. Based on Table 2, it is known that there is a significant effect between the consumption of folic acid supplements in early pregnancy on the incidence of Orofacial Cleft (OFC) in Kupang City with a p-value = 0.00. The OR value of 20.0 indicates pregnant women who do not take folic acid supplements in early pregnancy have a risk of giving birth to children with orofacial clefts (OFC) 20.0 times higher than those who take folic acid supplements in early pregnancy in Kupang City.

DISCUSSION

Table 2 shows a significant effect between the consumption of folic acid supplements during pregnancy on the incidence of OFC. These results are in line with the meta-analysis study by Jahanbin et al in 2018 which showed that taking folic acid supplements during the early period of pregnancy can reduce the risk of OFC. This study involved 6 cohort studies and 31 case-control studies with the conclusion that folic acid supplementation in the period from 3 months before conception to the first trimester of pregnancy can reduce the risk of OFC by 28%.8 These results are consistent with a previous meta-analysis study in 2008 by Johnson, who also concluded that folic acid supplementation was protective against OFC (Johnson & Little, 2008).

Folic acid is an important component in the process of DNA biosynthesis and amino acid metabolism. During pregnancy, the need for folic acid increases to support the growth of the fetus and the blood supply of the fetus from the mother. Taking folic acid supplements as early as possible, especially if started before pregnancy, can reduce the incidence of cleft lip/palate and cleft palate only by 40% and 35% (Jahanbin et al., 2018). The recommended dose of folic acid supplement for women who planning a pregnancy is 400 micrograms, that consumption of 400 micrograms of folic acid daily without other vitamins starts before the mother's last menstrual period was associated with a reduced risk of OFC in China (Li et al., 2012). Research conducted by Wehby et al (2012) stated that high doses of folic acid supplementation, which is 4 milligrams, can also

be used to prevent the recurrence of OFC in subsequent children (Wehby & Moreno, 2014).

This study has several limitations. The first is the difficulty in reaching respondents due to the distance factor and the limitations of meeting face to face during the pandemic. This limitation was overcome by reaching respondents by telephone. The second limitation is the difficulty in terms of communication, where not all respondents can speak Indonesian fluently so some questions are not answered properly. To overcome this, the researchers involved other health workers who could communicate in the respondent's daily language. The third limitation is the limitation of remembering different past information in the case and control groups (recall bias). This is minimized by determining the research sample at a young age so that the time between pregnancy and the interview is relatively shorter. In addition, this study also did not include in-depth information on the duration and dose of folic acid supplement consumption by respondents.

CONCLUSION

Folic acid supplementation during early pregnancy can reduce the risk of OFC in children. These results emphasize the need for an educational campaign about the importance of folic acid use in women of childbearing age, especially those who decide to have a baby, as well as folic acid use in early pregnancy to protect against OFC.

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