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Nausea and Vomiting of Pregnancy: Multiple Contributing Factors

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Abstract
Nausea and vomiting are common conditions in earlier pregnancy. Some studies have suggested that nausea and vomiting during pregnancy (NVP) is caused by multiple factors, however, few studies assessed family support and psychological factors. The present study aimed to assess the prevalence of NVP and its contributing factors. A cross-sectional study was conducted in five Primary Health Centers in Semarang during August 2023. A total of 99 eligible pregnant women were included. A logistic regression was used to determine the significant contributing factors of NVP. The prevalence of moderate to severe and mild NVP was 71.7% and 28.3% respectively. Bivariate analysis indicated that gestational age and anxiety level significantly influence NVP (p-value <0.05). Women with greater gestational age (OR= 2.462; 0.954-6.356) and mild anxiety (OR=3.337; 1.240-8.982) were more likely to experience NVP during their pregnancy. Gestational of 12 weeks and mild anxiety are strongly associated with NVP. These findings highlight the crucial of psychological factors despite other health-related conditions.

Keywords: NVP, Risk Factor, First Trimester.

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1. INTRODUCTION

Nausea and vomiting during pregnancy (NVP) or emesis gravidarum, are common experiences during pregnancy that range from mild to moderate severity, affecting up to 70 of pregnant women worldwide. However, these symptoms may become more aggravated than is typical – hyperemesis gravidarum, which is reported in 0.3–10.8% of pregnant women. In Indonesia, it was reported rates vary widely, with 1-3% in all pregnancies (Oktavia, 2016), in which 543 cases from 2.203 pregnant women (67.9%), of 60-80% among prim gravida, and 40 – 60% on multigravida (Retni et al., 2020).

NVP, often known as morning sickness, is the second most common indication for pregnancy hospitalization due to severe NVP - hyperemesis gravidarum (HG). Almost 90% of pregnant women experienced nausea, while vomiting may be seen in 28-52% of all pregnancies (Jennings & Mahdy, 2023). Although it is a common symptom during pregnancy, the effects on pregnancy, both short and long-term, have long been debated. Therefore, the mechanism and its contributing factors need to be explored more.

Previous studies have explored multiple factors that cause NVP, from individual characteristics (age, socioeconomic factor, parity), nutrition intake, and hormonal, and psychosocial factors (Retnowati, 2019; Zhang et al., 2020). Furthermore, gestational age has been linked to NVP incidence, yet, different findings have emerged. In some studies, earlier gestational age increased the incidence of NVP, whereas in others, greater gestational age was reported associated with a lower incidence of NVP (Erick et al., 2018; Nurmi et al., 2020; Zhang et al., 2020). However, among those studies, the true potential factors of NVP remain inconsistent.

Additionally, psychosocial, such as perceived social support impact the NVP severity (Bray et al., 2021). The social factor of NVP consists of a lack of family support and friends. Social support is an important factor of life quality in early pregnancy. It was reported that low social support is statistically correlated to a decline in life quality (Junandar et al., 2021). However, this positive relationship between family support and NVP is inconsistent across some studies. A nonsignificant effect of family support, particularly partner support on NVP levels was found in a large study in the UK (Roberts et al., 2023). These differing results may be due to variations in study settings, characteristics, and methods used.

Existing studies have focused on individual factors causing NVP, so some potential risk factors remain unclear. There was a lack of investigation exploring family support as the potential risk factor of NVP. This may allow women to have an essential protective domain from the benefits of the present study. Therefore, this study was aimed at assessing family support along with other risk factors of NVP among pregnant women in their trimester of gestational age. In addition, the prevalence of NVP was determined by a validated tool, based on the PUQE scale.

2. RESEARCH METHOD

A primary health center-based cross-sectional study was conducted in five Primary Health Centers in Semarang, Central Java. A total of 99 eligible subjects who visited those settings during August 2023 were interviewed. The inclusion criteria for this study were the following: pregnant, less than or equal to 12 weeks of gestational age. The criteria for exclusion were pregnant women with more than 12 gestational weeks. Written informed consent was obtained from all the subjects. The Ethical Committee of the Faculty of Medicine, University of Diponegoro approved the proposed study (120/EC/KEPK/FK-UNDIP/IV/2023).

The scale of NVP was measured by using the Pregnancy-Uniques Quantification of Emesin (PUQE). PUQE is a scoring system for nausea and vomiting during pregnancy, which focuses on three symptoms: nausea, vomiting, and retching over the past 24 hours (Hada et al.,

2021). The overall PUQE score is calculated by adding the three question scores, with each question scoring 1 to 5 points. The NVP was divided into mild (4 to 6), moderate (7 to 12), and severe (13 to 15) (Yilmaz et al., 2022).

Demographic information was obtained using a standardized questionnaire. The questionnaire was used to assess age, level of education, occupations, parity, and gestational age. A healthy reproductive stage was those aged 20 to 35, while those under 20 or older than 35 were considered risk reproductive age (Deatsman et al., 2016). Subjects who did not have any formal education or completed their junior high school were classed as low education, completed senior high school were assumed to be middle education levels, and higher education were subjects who graduated from universities.

Investigators confirm the gestational data based on the Maternal and Child Health book. To measure family support, we used the Multidimensional Paternal Perinatal Scale (MPPS), a recently developed tool based on the conceptual framework of paternal perinatal experience (Gemayel et al., 2021). The implementation of the developed questionnaire confirmed the construct validity and internal consistency. An individual anxiety level was assessed by using the Hamilton Anxiety Rating Scale (HARS), a psychological questionnaire used by clinicians to rate the severity of a patient's anxiety (Clark & Donovan, 1994; Hamilton, 1959). The anxiety level was divided into mild (7 to 14), moderate (15 to 27), and severe (more than 27).

Data analysis was conducted using SPSS. The mean and range were presented for continuous variables, while categorical variables were displayed in frequency and percentage. Bivariate and multivariate logistic regression analyses were used to determine the factors influencing NVP. A p-value less than 0.05 was considered statistically significant to increase the risk of NVP.

3. RESULTS AND DISCUSSION

Table 1 shows the NVP, demographic, and health-related characteristics of the study subjects. This study assessed that 67.68% of subjects had moderate NVP, while 4.04% had severe NVP. The mean age was 27.9 with a range between 19 to 40 years old, and most studied subjects were categorized as healthy reproductive age (87.88%). The majority of pregnant women had middle formal education, employee, multigravida, and 12 weeks of gestational age. The mean of family support was 73.27 and higher among those who had good support (52.53%). The mean anxiety level was 14.21 and the majority was classed as mild anxiety (54.555).

Table 1. The Characteristics of Studied Subjects

Variable	Category	Frequency (N= 99)	Percentage
NVP	Severe	4	4.04
	Moderate	67	67.68
	Mild	28	28.28
Age (years)	Mean (Min-Max)	27.9 (19-40)	
	Unhealthy reproductive	12	12.12
	Healthy reproductive	87	87.88
Education	Low	4	4.04
	Middle	75	75.76
	Higher	20	20. 20
Occupation	Unemployed	46	46.46
	Employee	53	53.54
Parity	Prim gravida	36	36.36
	Multigravida	63	63.64
Gestational age	12 weeks	51	51.52
	<12 weeks	48	48.48

Family Support	Mean (Min-Max)	73.27 (20-84)	
	Low	47	47.47
	Good	52	52.53
Anxiety Level	Mean (Min-Max)	14.21 (1-28)	
	Severe	1	1.01
	Moderate	44	44.44
	Mild	54	54.55

Table 2 demonstrates the bivariate analysis of the associations between general variables and NVP. We simplified the NVP into 2 categories due to the small cell number in severe NVP, hence severe was included in the moderate category. These findings indicated that gestational age and anxiety level significantly influence NVP (p-value <0.05).

Table 2. Bivariate Analysis of Risk Factors for Nausea and Vomiting of Pregnancy.

Variables	**Category**	**NVP**		**p-value**
		Mild (N= 28)	**Moderate to Severe (N= 71)**	
Age of Respondent	Healthy reproductive	24 (27.6)	63 (72.4)	0,942
	Unhealthy reproductive	4 (33.3)	8 (66.7)	
Education	Low	3 (75)	1 (25)	0,306
	Middle	17 (22.7)	55 (77.3)	
	Higher	8 (42.1)	11 (57.9)	
Jobs	Employee	15 (28,3)	37 (69,8)	1
	Unemployed	13 (28.3)	33 (71.7)	
Parity	Primigravida	9 (25)	27 (75)	0,752
	Multigravida	19 (30.2)	44 (69.8)	
Gestational Age	12 weeks	19 (37.3)	32 (62.7)	0,041*
	<12 weeks	9 (18.8)	39 (81.2)	
Family Support	Good	16 (30.8)	36 (69.2)	0,723
	Deficient	12 (25.5)	35 (74.5)	
Anxiety Level	Mild	21 (38.9)	23 (61,1)1	0,019*
	Moderate	7 (15.9)	37 (84.1)	
	Severe	0	1 (100)	

** Significant at p-value<0.05*

The variables significantly related to NVP in Table 2 were used in multivariate logistic regression. Table 3 presents the statistically significant variables included in the final model of NVP. We also simplified the category of anxiety level, in which a small subject with severe anxiety merged with a moderate level to get a better analysis result.

Table 3. Final Model of Risk Factors for Nausea and Vomiting of Pregnancy.

Variable	**Category**	**OR**	**CI 95%**	**p-value**
Anxiety Level	Mild	3.337	1.240-8.982	0.017
	Moderate to severe	Ref.	1	
Gestational Age	12 weeks	2.462	0.954-6.356	0.063
	<12 weeks	Ref.	1	

This study investigated the prevalence of NVP and its contributing factors among pregnant women during their first trimester. We recruited women in early pregnancy, which perhaps have better captured early pregnancy conditions since NVP mostly (90%) began within the first trimester, primarily between the second and tenth week of gestation (Chan et al., 2011).

The prevalence of moderate to severe and mild NVP was 71.7% and 28.3% respectively among 99 subjects. The analysis showed that women with greater gestational age and mild anxiety were more likely to experience NVP during their pregnancy (Schetter & Tanner, 2012).

Pregnant women with greater gestational weeks were associated with a higher incidence of NVP in this study, which is inconsistent with previous similar studies. A hospital-based retrospective study in China reported an inverse association where greater gestational age correlated with a lower number of NVP cases (OR= 0.95; 0.93-0.97) (Zhang et al., 2020). Nevertheless, NVP results from multiple metabolic and endocrine factors (Lee & Saha, 2011). The most contributing factor is human chorionic gonadotropin (hCG). This may be associated with the incidence of NVP and the peak of hCG production, which occurs between 12 and 14 weeks of gestation in 90% of women (Royal College of Obstetricians and Gynaecologists, 2016). These sources legitimate the findings of the present study that women with 12 gestational weeks are more likely to increase the risk of NVP by 2.5 times than those with earlier gestational (<12 weeks).

Human chorionic gonadotropin (hCG) is a pregnancy hormone that has been widely recognized as an essential factor in the pathogenesis of NVP (Davis, 2004; Niemeijer et al., 2014). In a prospective study in Malaysia, it was found that hyperemesis gravidarum in first-trimester women resulted in poor short-term outcomes, supported by increased serum hCG levels (Tan et al., 2009). High levels of hCG and beta-hCG increase the severity of NVP (OR= 1.47; 1.11–1.95) (Dekkers et al., 2019). Elevated levels of hCG may cause nausea and vomiting through the hCG receptor located in the posttrauma of the human brain stem. These hormonal changes, particularly the direct effects of hCG, are responsible for the symptoms of NVP (Bustos et al., 2017).

Despite altered reproductive hormones, psychological factors may contribute significantly to the progression of NVP (Liu et al., 2022). Some studies have shown that elevated depressive symptoms in the first trimester and a history of depression were independently associated with the incidence of NVP (Dekkers et al., 2019; Taguchi et al., 2022). Possible adverse psychological factors associated with NVP include depression, anxiety, mood disorders, and stress (Hizli et al., 2012; Uguz et al., 2012). In this study, most of the subjects experienced mild and moderate anxiety levels in the twelve weeks of pregnancy. Those detected with mild anxiety are more likely to develop moderate to severe NVP by three times than moderate to severe anxiety. These results are consistent with a similar cross-sectional study in which those with mild NVP were less stressed than those with moderate to severe NVP (Şahin et al., 2022). This study supports the claim that stress levels may be associated with the severity of NVP and proves the pattern that nausea and vomiting during pregnancy may be the result of a strong effect of anxiety (Tan et al., 2014; Wang et al., 2020). Nonetheless, surprisingly, mild anxiety had a larger effect on NVP than moderate to severe levels of anxiety. This is caused by the fact that NVP is a multifactor incidence, anxiety is not sufficient to cause NVP without interaction with other potential factors.

Although the proposed study may be close evidence of multiple factors for developing NVP by exploring demographic, health-related characteristics, and psychological factors, some limitations should be acknowledged. First, a larger sample size may facilitate more precise findings in a cross-sectional study. Second, the outcome, NVP presented a small number of severe NVP, hence the investigators simplified it into two categories in which severe merged to moderate level of NVP. This decision may present misclassification and may have underestimated the true association.

4. CONCLUSION

The present study shows that gestational age and anxiety level are associated with the incidence of NVP among pregnant women during their first trimester. The findings highlight

the importance of controlling psychological factors despite other health-related conditions during earlier pregnancy. Further studies with an assessment of multiple potential factors to track NVP development are needed to clarify how these findings may change over time.

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