



Hyperemesis Gravidarum and Maternal Age under 20 Years: A Cross Sectional Study

Siti Munawaroh^{1*}, Laurita Laras Pratiwi¹, Soetrisno²

¹ Medical Study Program, Medical Faculty, Universitas Sebelas Maret, Jl. Ir. Sutami 36 A, Ketingan Surakarta 57126 Indonesia

² Obstetric and Gynecologic Department, Medical Faculty, Universitas Sebelas Maret. Jl. Ir. Sutami 36 A, Ketingan Surakarta 57126 Indonesia

* Corresponding author

E-mail: munafkuns@staff.uns.ac.id

ABSTRACT

Background: Nausea and vomiting during pregnancy are common. When this happens excessively and interferes with activities, it is also called hyperemesis gravidarum. This situation can be detrimental to the mother and fetus, such as nutritional deficiencies, dehydration, electrolyte disturbances, weight loss during pregnancy, and an increased risk of childbirth, premature birth, and low birth weight. Many factors can cause the occurrence of hyperemesis gravidarum, one of which is the age of the mother under 20 years. This study aims to determine the relationship between hyperemesis gravidarum with maternal age under 20 years.

Method: a cross-sectional study with a fixed disease sampling method. Subjects were divided into two groups, there were 50 pregnant women with hyperemesis gravidarum and 50 pregnant women without hyperemesis gravidarum. This research was conducted in Dr. Moewardi Hospital, Surakarta. The independent variable being the mother's age under 20 years old and the dependent variable being hyperemesis gravidarum. The Fisher's Exact test was used to evaluate the data in SPSS. The participants in this study were 100 pregnant women,

Result: 12 of whom were under 20 and 88 of whom were between 20 and 35. The Fischer's Exact test yielded a p-value of 0.03, indicating that maternal age < 20 was related to hyperemesis gravidarum. Hyperemesis gravidarum is more common and has a higher risk in pregnant women under the age of 20.

Conclusion: There is a link between maternal age and the occurrence of hyperemesis gravidarum among women under the age of 20.

Keywords: *pregnancy, maternal age, hyperemesis gravidarum*

INTRODUCTION

Every pregnant woman will experience a process of body adjustment to pregnancy. The most common response is nausea and vomiting¹. In pregnancy, nausea and vomiting are common. Nausea

and vomiting are common in early pregnancy, beginning around the sixth week after the last menstrual cycle and lasting about ten weeks. 50-70 percent of pregnant women experience nausea and vomiting. However, there are times when

nausea and vomiting in pregnant women is so intense that everything they eat and drink is vomited, causing weight loss, decreased skin turgor and urinary volume, and acetonuria². If nausea and vomiting experienced interfere with daily activities or cause complications, it is called hyperemesis gravidarum (HG)¹.

Hyperemesis gravidarum rarely causes death, but the incidence is still relatively high. Sometimes, hyperemesis gravidarum that occurs continuously and is challenging to heal can make the patient depressed¹. Despite the low prevalence of causes of death, chronic nausea and vomiting might result in a loss of productive working time³. Hyperemesis gravidarum can result in significant morbidity for both the mother and the fetus, including weight loss, dehydration, electrolyte disturbances, and nutritional deficiencies, which can increase the risk of giving birth to a baby with low birth weight, premature birth, and an APGAR score of less than seven⁴.

Several risk factors are often associated with hyperemesis gravidarum, namely, nulliparity, the weight that is too low or too high before pregnancy, multiple pregnancies, fetal anomalies, history of hyperemesis gravidarum in previous pregnancies, gender of the female fetus, psychological conditions, and the age of the pregnant mother in the previous pregnancy under reproductive age⁵.

The mother's reproductive period for pregnancy is divided into 3 groups. First group, age < 20 years, at this time the mother is still too young to get pregnant; second, the age of 20-35 years, at this time the mother must regulate fertility (sparing pregnancies); and third, age > 35 years, at this time the mother has to prevent pregnancy because she is too old to get pregnant. The safest age for a mother to get pregnant is 20-35 years because in women from the age of 20, the

uterus and other body parts are really ready to accept pregnancy, also at that age women usually feel ready to become mothers. So, the age of the mother during pregnancy between 20-35 years has the least risk of pregnancy and childbirth⁶.

Hyperemesis gravidarum is linked to maternal age. This has something to do with pregnant women's mental health. According to research, mothers under the age of 20 or over the age of 35 are more prone to develop hyperemesis gravidarum. Hyperemesis gravidarum is linked to levels of chorionic gonadotropin, estrogen, and progesterone hormones in the mother's blood, hence gestational age is also a risk factor. One of the etiologies for hyperemesis gravidarum is a high amount of chorionic gonadotropin hormone. Because gonadotropin hormone levels in the blood are at their highest in the first trimester, nausea and vomiting are more likely. The number of gravida is another risk factor. Pregnant women who are pregnant for the first time will experience more stress than mothers who have already given birth, which can lead to hyperemesis gravidarum. Primigravida mothers have also not been able to adapt to the hormones estrogen and chorionic gonadotropin, which makes mothers who are pregnant for the first time more likely to experience hyperemesis gravidarum.^{7,8,9}

With the high incidence of hyperemesis gravidarum and the differences in results from previous studies, the authors are interested in examining the relationship between hyperemesis gravidarum and those under 20 years of age.

This study hypothesizes a link between hyperemesis gravidarum and pregnant women under the age of 20 years and that pregnant women under the age of 20 years have a higher risk of having hyperemesis gravidarum than pregnant women of reproductive age.

This study aims to see if there is a link between hyperemesis gravidarum and pregnant women under the age of 20.

METHODS

This study was a cross-sectional study employing an analytic observational technique. The study took place at Dr. Moewardi Hospital Surakarta. Fixed illness was used to recruit individuals in the group of pregnant women who had hyperemesis gravidarum, while random selection was used in pregnant women who did not have hyperemesis gravidarum. The sampling took place during September and October of 2016.

From January 2013 to September 2016, data from patient medical records were used in this investigation. It is used to examine the link between hyperemesis gravidarum and age under 20 years. Data were analyzed using SPSS 22.0 for Windows and the Fisher's Exact test method. Hyperemesis gravidarum was the dependent variable in this study, while under 20 years of age was the independent variable.

RESULT

The research subjects are diverse in terms of maternal age, parity, gestational age, abortion history, and anemia status. Table 1 provides a detailed description of these characteristics.

Table 1. Distribution of Research Subject Characteristics

Variable	Hyperemesis Gravidarum		Total
	Positif	Negatif	
Maternal Age			
<20 years	10	2	12
20-35 years	40	48	88
Parity			
Nullipara	25	22	47
Multipara	25	28	53
Gestational Age			
First trimester (≤12 weeks)	34	7	41

Trimester II&III (>12 weeks)	16	43	59
Riwayat Abortus			
Yes	5	8	13
No	45	42	87
Anemia Status			
Hb ≤11 g/dL	7	4	11
Hb >11 g/dL	43	46	89

The data in this study were analyzed using the Fisher's Exact test. This test examines the relationship between the statistical significance of the two variables. This study cannot use Chi-Square because there is one cell that has a value less than 5. This study observed the relationship between pregnant women under 20 years of age as the independent variable and hyperemesis gravidarum as the dependent variable.

The data of this study were analyzed using the SPSS 22.0 for Windows program. The results showed that ten pregnant women under 20 experienced hyperemesis gravidarum (10%) and did not experience hyperemesis gravidarum as many as two people (2%). While the maternal age of 20-35 years, those who experienced hyperemesis gravidarum were 40 people (40%) did not experience hyperemesis gravidarum as many as 48 (48%).

The Fisher's Exact test on the link between age under 20 years and the incidence of hyperemesis gravidarum yielded a significant result of $p = 0.03 (<0.05)$, indicating that the findings of this study were significant or statistically significant. Table 2 shows the results.

Table 2. Fisher's Exact Test Results for Hyperemesis Gravidarum Incidence and Age of Pregnant Women under 20 Years.

Variable	HG		p-value	PR
	Positif	Negative		
Age <20 years	10	2	0.03	1,83 (1,3034-2,5788)
20-35 years	40	48		

The relationship between risk factors and effects obtained can be seen from the value of the Prevalence Ratio (PR). Based on the calculation of the prevalence ratio using table 4.2, the result is 1.83 (PR>1). So, this study can conclude that the age of pregnant women under 20 years can increase the risk of hyperemesis gravidarum by 1.83 times compared to the period of pregnant women at the age of 20-35 years.

DISCUSSIONS

The most obvious factor influencing the occurrence of hyperemesis gravidarum is the young age of pregnant women (<20 years)¹⁰. According to BKKBN (2012), a healthy reproductive age for pregnancy and childbirth is between 20-35 years. Pregnancy with less than 20 years tends to be unstable and not psychologically ready to accept the pregnancy, so it is easy to experience shock, depression, or stress¹¹. Because it is linked to the mother's psychological status, hyperemesis gravidarum frequently develops in woman under the age of 20. Because they still believe they are not ready to be a mother, being a mother at an early age creates psychological hardship⁸.

The age factor is one of the biological factors, which cannot be changed. The age factor is related to the psychological maturation process, where this psychological factor affects the mother's level of vulnerability to stress that can cause hyperemesis gravidarum. This stress can stimulate the brain's

vomiting region, resulting in extreme nausea and vomiting. Experts say that, aside from psychological issues, young women are still unable to handle an increase in the chorionic gonadotropin hormone, which induces nausea and vomiting⁹.

A person experiencing stress will increase the sympathetic nervous system to release adrenaline and cortisol. Higher cortisol and adrenocorticotropic levels were experienced in pregnant women with hyperemesis gravidarum¹², which indicates that hyperemesis gravidarum is associated with psychological and stress. Mental stress can cause excessive sympathetic nervous system activity to increase the production of trophoblast-derived tumor necrosis factor by the placenta. TNF, interleukin 1, and interleukin 6 regulate the production and release of hCG. hCG causes distention of the upper gastrointestinal tract. hCG under normal circumstances cannot stimulate nausea and vomiting because it cannot enter the cerebrospinal fluid. However, if serum hCG levels increase, it can affect the chemoreceptor trigger zone in the area posterior of the brainstem. Stimulation is transmitted to the motor nucleus of the vagus nerve, the nucleus ambiguus, and the lateral vestibular nucleus. Via the vagal afferent, it continues to the gastrointestinal tract, which causes vomiting¹¹. In addition, younger women have a lower threshold for nausea and vomiting¹³.

Nausea is the subjective sensation of wanting to vomit. Nausea is a conscious sensation caused by stimulation in the medulla region of the brain, which is linked to the vomiting center. Nausea is triggered by irritating impulses from the gastrointestinal system, motion sickness-related impulses from the lower part of the brain, and vomiting-initiating impulses from the cerebral cortex. from stomach and abdominal wall muscle contraction¹⁴.

Nausea and vomiting are experienced by almost 75-80% of pregnant women. 50% of pregnant women experience nausea and vomiting, 25% only experience nausea, and the rest do not experience nausea or vomiting. In humans, the motor response to vomiting is initiated by an uncomfortable feeling of nausea. The central nervous system has an important role in the physiology of nausea and vomiting by being the initial site for receiving and processing various vomiting stimulants. Nausea and vomiting in pregnancy are mechanisms to protect against teratogens, mutagens, and chemicals. This theory can explain why pregnant women feel or smell something that causes nausea and vomiting¹⁵.

According to many hypotheses, nausea, vomiting, and refusal of all incoming food and drink occur in hyperemesis gravidarum, and if this continues, it can lead to dehydration, an imbalance of electrolyte levels in the blood, and hypochloremic alkalosis. Furthermore, because the energy received from meals is insufficient, hyperemesis gravidarum causes carbohydrate and fat reserves to be depleted for energy, resulting in ketosis and the accumulation of acetone-acetic acid, hydroxybutyric acid, and acetone in the blood, resulting in acidosis. Furthermore, dehydration reduces blood flow to the tissues, reducing the availability of nutrients and oxygen while also accumulating hazardous metabolic chemicals in the blood. Then, as a result of vomiting and excretion through the kidneys, hyperemesis gravidarum can produce potassium deficit, which increases the frequency of vomiting and creates a difficult-to-break vicious cycle¹⁶. In severe, prolonged and frequent nausea and vomiting can cause the body to experience a deficiency of two important vitamins, namely thiamin and vitamin K. In thiamin deficiency, Wernicke's encephalopathy can occur, which is a

condition of central nervous system disorders characterized by dizziness, visual disturbances, ataxia and nystagmus. This disease can progress to severe and cause blindness, seizures and coma. In vitamin K deficiency, blood coagulation disorders occur and are also accompanied by epistaxis¹⁷.

After implantation, the hormone Human Chorionic Gonadotropin (hCG) is the first hormone that can be detected in the mother's blood and its levels increase in the first trimester. Human Chorionic Gonadotropin is a glycoprotein containing high carbohydrates produced by the placenta via the syncytiotrophoblast. High hCG levels are often associated with pregnancies with multiple fetuses¹⁸. Recent studies have also suggested that extravillous cytotrophoblasts also produce hCG due to the role of autocrine in modulating trophoblast invasion¹⁹. Several studies have shown that patients with hyperemesis gravidarum have higher hCG levels. In addition, hCG levels are associated with the severity of hyperemesis gravidarum²⁰. Human Chorionic Gonadotropin causes hyperemesis gravidarum by affecting the upper gastrointestinal tract or by stimulating thyroid function because hCG has a structure similar to TSH (Thyroid Stimulating Hormone)²¹.

In this study, statistical testing was carried out on the age variable under 20 years using the Fisher's Exact test by grouping the research subjects into two groups, namely hyperemesis gravidarum and not experiencing hyperemesis gravidarum. The results of the significance value $p=0.03$ ($p < 0.05$) means that there is a statistically significant relationship between pregnant women aged less than 20 years and the incidence of hyperemesis gravidarum. The results of this study are not following the research conducted by Mariantari (2014)²² with the title "The Relationship of Husband's

Support, Maternal Age, and Gravida to the Incidence of Emesis Gravidarum" where $p = 0.23$ ($p > 0.05$), which has no significant relationship between age and hyperemesis gravidarum. However, this study is under research conducted by Sumai (2014)²³ with the title "Factors Associated with the Incidence of Hyperemesis Gravidarum," where $p = 0.04$ ($p < 0.05$), which shows a statistically significant relationship between age and hyperemesis gravidarum.

Calculating the prevalence ratio in this study obtained the PR = 1.833 (PR > 1) results, which means that age under 20 years is a risk factor for hyperemesis gravidarum.

The limitation of this study is that it only examines age so that other confounding variables cannot be controlled. Other confounding variables that may affect the results in this study are education history, social support, economic status, history of contraceptive use. In addition, the selection of research designs carried out utilizing a cross-sectional approach cannot explain the causal mechanism of the variables studied because research subjects are taken at one time²⁴.

CONCLUSION

The age of pregnant women under 20 years has a statistically significant link with the occurrence of hyperemesis gravidarum. At Dr. Hospital, pregnant women under the age of 20 have a 1.83 times greater risk of hyperemesis gravidarum than pregnant women of reproductive age. Surakarta Moewardi.

ACKNOWLEDGEMENT

The authors would like to thank the Faculty of Medicine, Sebelas Maret University, and RSUD Dr. Moewardi, who have supported the implementation of this research.

REFERENCES

1. Gunawan K, Manengkei P, Ocviyanti D Diagnosis dan tatalaksana Hyperemesis gravidarum. *J Indon Med Assoc*, 2011; 61 (11): 1-7.
2. Winkjosastro H. Ilmu Kebidanan. Jakarta : Yayasan Bina Pustaka Sarwono Prawirohardjo: 2009. p. 275
3. Goodwin TM. Hyperemesis gravidarum. *Obstet Gynecol Clin North Am* 2008; 35:401-17.
4. Ogunyemi. Hyperemesis Gravidarum. Medscape Drugs&Disease. *Medscape*; 2015.
5. Fell, Deshayne B. MSc1; Dodds, Linda PhD1; Joseph, K S. MD, PhD1; Allen, Victoria M. MD, MSc2; Butler, Blair MD2. Risk Factors for Hyperemesis Gravidarum Requiring Hospital Admission During Pregnancy. *Obstetrics & Gynecology*: February 2006 - Volume 107 - Issue 2, Part 1 - pp 277-284
6. BKKBN. *Pendewasaan usia perkawinan*. Badan Kependudukan dan Keluarga Berencana Nasional Lampung.2012. <http://www.BKKBN.go.id/>
7. Manuaba IBG,Manuaba IAC, Manuaba IBGF. Pengantar Kuliah Obstetri. Jakarta.EGC;2007
8. Vikanes A, Skjaerven R, Grjibovski AM, Gunnes N, Vangen S, Magnus P (2010). Recurrence of hyperemesis gravidarum across generations: Population based cohort study. *BMJ*, 340, c2050.
9. Yasa aril cikal. Hubungan antara karakteristik ibu hamil dengan kejadian hiperemesis gravidarum di RSUD Ujung Berung Periode 2010-2011. *J Fak Kedokt Univ Islam Bandung* [Internet]. 2012;1-64. Available from: <https://elibrary.unisba.ac.id/files2/Skr.12.00.10854.pdf>

10. BkbbN. *Pendewasaan Usia Perkawinan*. Lampung; 2012.
11. Guyton AC & Hall JE. *Buku Ajar Fisiologi Kedokteran*. Edisi 11. Jakarta EGC; 2008.
12. Decherney, AH, Goodwin TM, Nathan L, Laufer N. Lange. *Current Diagnosis and Treatment Obstetric and Gynecology*, 7th edition. Mc Graw Hill; 2008.
13. Winkjosastro H. Ilmu Kebidanan. Jakarta : Yayasan Bina Pustaka Sarwono Prawirohardjo; 2009. p. 275
14. American College of Obstetrics and Gynecology. Nausea and vomiting of pregnancy. *Obstetrics & Gynecology*. 2015. Volume:126 Issue 3.
15. Hanretty KP. *Obstetrics Illustrated*. Philadelphia : Churchill Livingstone, Inc : 2008. Chapter 7 : p.102
16. Cunningham FG, Leveno KJ, Gant NF, et al. *Williams Obstetrics 23rd Edition*. United States of America : McGraw-Hill Companies, Inc: 2010. Chapter 34 : p1113
17. Kuo SH, Yang YH, Wang RH, Chan TF, Chou FH. Relationships between leptin, HCG, cortisol, and psychosocial stress and nausea and vomiting throughout pregnancy. *PubMed*. 2010; 12(1):20-7.
18. Handschuh K, Guibourdenche J, Tsatsaris V, Guesnon M, Laurendeau I, Evain- Brion D, Fournier T. Human chorionic gonadotropin produced by the invasive trophoblast but not the villous trophoblast promotes cell invasion and is down-regulated by peroxisome proliferator-activated receptor- α . *Endocrinology* 2007; 148:5011–5019.
19. Tan PC, Tan NC, Omar SZ. Effect of high levels of human chorionic gonadotropin and estradiol on the severity of hyperemesis gravidarum. *Clinical Chemistry and Laboratory Medicine* 2009; 47:165-71.
20. Seow KM, Lee JY, Doong ML, Huang SW, Hwang JL, Huang WJ, Chang FY, Ho LT, Juan CC. Human chorionic gonadotropin regulates gastric emptying in ovariectomized rats. *Journal of Endocrinology* 2013; 216, 307–314
21. Mariantari Y, Lestari W, Arneliwati. Hubungan Dukungan Suami, Usia Ibu, dan Gravidarum terhadap Kejadian Emesis Gravidarum. *JOM PSIK* 2014; Vol 1 No. 2.
22. Sumai E, Keintjem F, Manueke I. *Faktor-faktor yang Berhubungan dengan Kejadian Hiperemesis Gravidarum*. Poltekkes Kemenkes Manado 2014; Volume 2 No 1
23. Sastroasmoro, S. 2011. *Dasar-Dasar Metodologi Penelitian Klinis*. Jakarta : Sagung Seto