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Relationship Between β HCG Hormone Levels, Anxiety and Stress with Severe Degrees of Emesis Gravidarum

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Abstract

Emesis gravidarum is a common complaint of nausea and vomitting that felt by almost 90% of pregnant women. Emesis gravidarum, or better known as morning sickness, offen occur on first trimester of pregnancy. It bring on decrease quality of life pregnant women. It effects to physical and psychological health in pregnancy, family and social life, also their occupation. Etiology of emesis gravidarum is multifactors. This research aim is to analyze relationship between β HCG hormone level, anxiety and stress with severe degrees of emesis gravidarum on first trimester of pregnancy. Research used case control studied on 44 pregnant women on first trimester of pregnancy, each group was paired according to their gestational age. Research result show that there is a significant relationship between β HCG hormone level (p<0.001; OR 63.3; 95% CI 9.509-421.822) and anxiety (p<0.05; OR 4.9; 95% CI 1.325-18.205) with severe degrees of emesis gravidarum. Characteristic and demographics not entirely related to emesis gravidarum. Conclusion of this research is psychological and hormonal factors are related to severe degrees of emesis gravidarum. Dominant factors that caused severe degrees emesis gravidarum are multigravida and β HCG hormone levels in excess more than 49950 mui/dL.

Keywords: Emesis Gravidarum; β HCG Hormone Level; Anxiety; Stress; Nausea; Vomiting

1. Introduction

Emesis gravidarum is a common complaint by pregnant women. Some people know it by the term “morning sickness”. This complaint is often felt in first trimester of pregnancy, but it is possible that this condition will continue until third trimester of pregnancy [1, 2]. Emesis gravidarum has an impact on physical and mental health of pregnant women, family life, social life and environment of work [3, 4]. They decrease in both quality and quantity in working hours, threby reducing efficiency on their work [5, 6].

Emesis gravidarum occur almost happened to 35-91% on pregnancy and about 0.3-3.6% of them have more severe condition, called hyperemesis gravidarum [6-8]. Almost 32.7% pregnant women have nausea without vomiting and about 23.5% pregnant women with emesis gravidarum experiences this complaints untul third trimester of pregnancy

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[8]. Prevalence of emesis gravidarum is 63.5% in first timester, 33.8% in second trimester and 26.2% in third trimester of pregnancy [2, 3, 9]. Timing to start feel symptoms until duration of nausea and vomiting is different for each women.

Etiology of emesis gravidarum in not known for certain, but several studies have stated that this condition is due to multifactorial factors such as social enviroment, endocrin changes during pregnancy, digestive system disorders, hyperthyroidism, and psychosocial factors [2, 4, 5, 8, 10-12]. Other research have shown that there is relationship between risk factors with emesis gravidarum such as maternal age, parity, employment status, smoking, vitamin consumption and educational level [6, 7, 9, 13-15].

The effect of HCG on occurence of emesis gravidarum is still not known certaintly, but some experts statte that the mechanism includes an influence on simulation in the upper gastrointestinal tract or stimulating thyroid function due the findings of stuctural similarity with thyroid hormone (TSH). Stimulation of HCG in the upper digestive tract causes distension in the section, caused increasing of gastric acid secretion and accumulation of fluid in the intestinal lumen, which triggers emesis gravidarum [16-18]. Some opinion state that HCG stimulates the process of excretion in the gastrointestinal system. This condition can cause hyperthyroxinemia by showing symptoms of tachycardia, tremors, increased systolic, blood pressure, hyperreflexes, palpitations, depression and anxiety [1, 10, 16-18].

Besides being influenced by hormonal factors, emesis gravidarum is also influenced by psychological factors. Psychoanalytic theory describes nausea as a psychosomatic symptom. Nausea and vomiting are the body's reaction to rejection of unexpected situations and are also forms of communication that express hidden feelings [12]. Pregnancy is a time when a woman is very easily affected by several changes, both physical and psychological.

Emotional responses and physical manifestations of a disease will continuously be connected like a whole circle. On account of pregnant women with emesis gravidarum, the intensity of these complaints is related with the mother's emotional responses, for example, fear and anxiety about the wellbeing of herself and the child, sadness, depression and feeling of guilty towards her so life partner. These responses will affect the disease and the ability of pregnant women to acknowledge changes and physical manifestations [19].

Management in the treatment of emesis gravidarum currently only focuses on pharmacological treatment by emphasizing biological causes and precluding other causative factors. Several studies have stated that there are more advantages in the management of disease by adapting the biopsychosocial model when compared with the biomedical model which just targets treatment based on the cause of changes in organ capacity and life structures. The purpose of this study is to analyze the relationship between levels of the hormone β HCG, anxiety and stress with severe degree of emesis gravidarum.

2. Material and methods

This study used an observational, analytic, case-control research design. The dependent variable in this study is severe degree of emesis gravidarum. The independent variables in this study are β HCG hormone levels, anxiety and stress. Confounding variables in this study are pregnancy planning, income, occupation, age, BMI, education level, gravida, marital status, previous history of emesis and smoking.

Sample in this study was taken by using a consecutive sampling technique with a total of 44 respondents, divided into 22 respondents belonging to the case group (women who experienced severe degree of emesis gravidarum) and 22 others who did not. Respondents in this study were paired according to gestational age per each group, so that the results of each case and control group consisted of 1 person with a gestational age of 6 weeks, 1 person of 7 weeks, 6 people of 8 weeks, 3 people of 9 weeks, 4 people of 10 weeks, 2 people of 11 weeks and 5 people of 12 weeks.

Assessment of the category of emesis gravidarum utilizes Modified Pregnancy Unique Quantification of Emesis and Nausea (PUQE) instrument. It is arranged as severe degree of emesis gravidarum if the score is >7. Stress utilizes Perceived Stress Scale instrument which has been translated into Indonesian. Anxiety assessment uses Zung Self-Rating Anxiety Scale instrument which is translated into Indonesian. Evaluation of β HCG hormone levels will be carried out through an ELISA assessment.

Data analysis used unpaired t test for data with a numerical scale. Data with a categorical scale were tested using chi square test and Kolmogorov Smirnov test. Multivariate analysis used logistic regression. Variable level of the hormone β HCG was transformed into a categorical scale by ROC analysis and the stress variable was transformed using the Rasch method.

3. Results and discussion

Table 1 Characteristic and Demography Respondents

Variable	Severe Degrees of Emesis Gravidarum (n = 22)	Normal pregnancy (n = 22)	P value	OR (95% CI)
Age				
Mean ± SD	24.95 ± 4.855	26.36 ± 5.233		
Median	24.50	25.50	0.360*	-
Interval	18	19		
Max-Min	36-18	36-17		
Pregnancy planning				
No	14 (63.6%)	7 (31.8%)	0.035**	3.750 (1.076-13.073)
Yes	8 (36.4%)	15 (68.2%)		
Income				
< RMW (IDR 3.100.000)	14 (63.6%)	13 (59.1%)	0.757**	1.212 (0.359-4.084)
≥ RMW (IDR 3.100.000)	8 (36.4%)	9 (40.9%)		
Occupation				
Does not work	8 (36.4%)	13 (59.1%)	0.131**	0.396 (0.117-1.334)
Yes	14 (63.6%)	9 (40.9%)		
Body Mass Index				
Underweight (< 18.5)	2 (9.1%)	1 (4.6%)	1.000***	-
Normal (18.5 – 22.9)	12 (54.5%)	12 (54.5%)		
Overweight (23-24.9)	8 (36.4%)	9 (40.9%)		
Education level				
Primary (grade 1-9)	4 (18.2%)	2 (9.1%)	1.000***	-
Secondary (grade 10-12)	13 (59.1%)	14 (63.6%)		
Higher (> grade 12)	5 (22.7%)	6 (27.3%)		
Gravida				
Multigravida	14 (63.6%)	6 (27.3%)	0.015**	4.667 (1.299-16.761)
Primigravida	8 (34.%)	16 (72.7%)		
Marital Status				
No	0 (0%)	0 (0%)	-	-
Married	22 (100%)	22 (100%)		
Previous history of nausea				
Yes	12 (54.5%)	6 (27.3%)	0.066**	3.200 (0.909 –11.268)
No	10 (45.5%)	16 (72.7%)		
Smoker				
Yes	15 (68.2%)	13 (59.1%)	0.531**	1.484 (0.431 –5.105)
No	7 (31.8%)	9 (40.9%)		

* Analysis used unpaired t test; ** Analysis used chi square test; *** Analysis used Kolmogorov-Smirnov

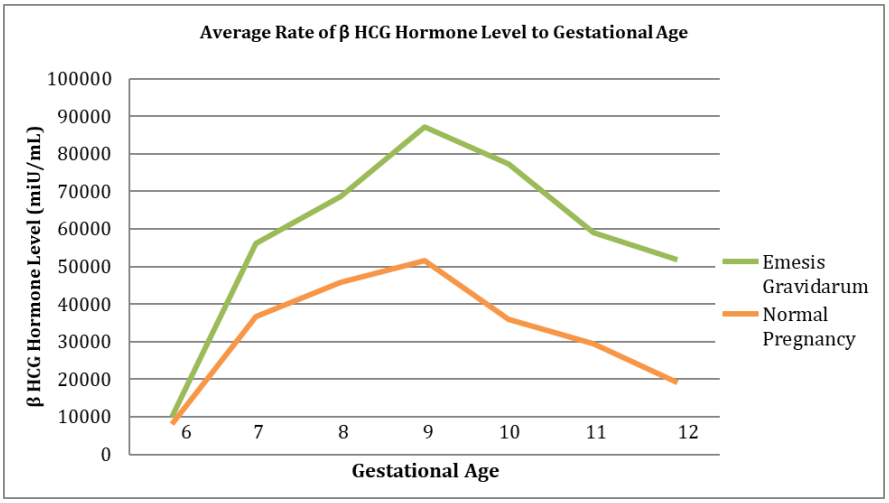

Figure 1 Average Rate of β HCG Hormonal Level to Gestational Age

According to figure 1, representation of increasing β HCG hormone levels significantly started on 7 until 10 week's pregnancy, with tag line on 9 weeks of pregnancy. Subsequently, it gradually descending until 12 weeks of pregnancy (gestational age observed in research).

According to table 1, average age on severe degrees of emesis gravidarum is 25 years old and on normal pregnancy is 26 years old. Founded that 36.4% respondents have not planning their pregnancy. On severe degrees of emesis gravidarum group, most of them are multigravida. Inversely proportional to normal pregnancy group, most of them are primigravida. Half of the pregnant with severe degrees of emesis gravidarum have experienced a similiar incident before. Only pregnancy planning and gravida that have significant relationship with severe degrees of emesis gravidarum. On 95% level of confidence, can be conclude that pregnant women whom have no planning on her pregnancy will be 3.75 times greater risk to get severe degrees of emesis gravidarum. So are with gravida, multigravida will be 4.667 times greater risk to get severe degrees of emesis gravidarum. On this research, age, income, occupation, body mass index, education level, marital status, previous history of nausea and smoker are not have meaningful relationship with severe degrees of emesis gravdarum.

Table 2 Transformation Variable β HCG Hormone Level and Stress

Variable	Severe Degrees of Emesis Gravidarum (n = 22)	Normal Pregnancy (n = 22)
β HCG hormone levels		
Median	66900	37100
Standard deviation	17483.194	13283.734
Range	79200	44210
Maximum-Minimum	89300-10100	52300-8090
Stress		
Mean (logit)	1.70	3.57
Standard deviation	5.38	5.01

* Analysis used *Rasch* model

Based on table 2, be known that on group with severe degrees of emesis gravidarum, range of β HCG hormone levels is 79200 miu/mL, while on normal pregnancy, range of β HCG hormone levels is 44210 miu/mL. Be observed on data, depicted pregnant women with emesis gravidarum have β HCG hormone levels higher than normal pregnancy.

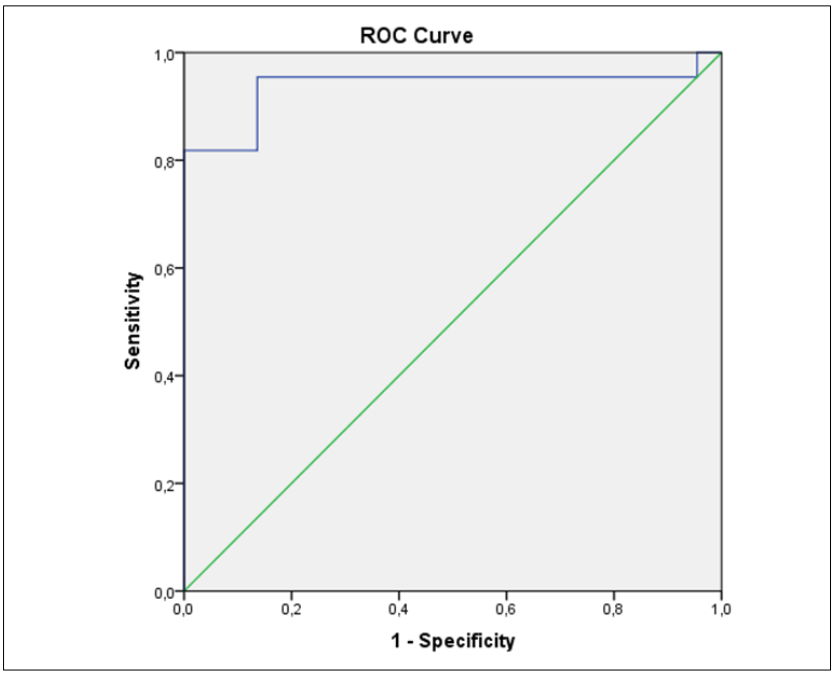

Figure 2 ROC Curve of β HCG hormone levels

Transformation variable β HCG hormone levels into catagorical scale used ROC analysis, get value cut off point is 49950 miu/dL with sensitivity 90.9% and speficity 86.4%, AUC value 93.8% (p=0.000).

Table 3 Relationship between β HCG hormone levels, anxiety and stress with severe degrees of emesis gravidarum

Variable	Severe Degrees of Emesis Gravidarum (n = 22)	Normal pregnancy (n = 22)	*P value*	OR (95% CI)
β HCG hormone levels				
≥ 49950 miu/mL	20 (90.9%)	3 (13.6%)	<0.001*	63.333 (9.509-421.822)
< 49950 miu/mL	2 (9.1%)	19 (86.4%)		
Anxiety				
Yes	13 (59.1%)	5 (22.7%)	0.014*	4.911 (1.325-18.205)
Normal	9 (40.9%)	17 (77.3%)		
Stress				
Yes	11 (50%)	13 (59.1%)	0.545*	0.692 (0.210-2.280)
No	11 (50%)	9 (40.9%)		

* Analysis used Chi Square test

Based on table 3, there is significant relationship between β HCG hormone levels and anxiety with severe degrees of emesis gravidarum (p=<0.001; p=0.004). On 95% level of confidence, can be conclude that pregnant women with β HCG hormone levels more or equal to than 49950 miu/mL will be 63.3 times greater risk to get severe degrees of emesis gravidarum. So are with anxiety, pregnant women with anxiety will be 4.9 times greater risk to get severe degrees of emesis gravidarum. On this research, stress not have meaningful relationship with severe degrees of emesis gravdarum.

Anxiety and stress are researched separately with different instruments. In the sence, anxiety is not an ongoing phenomenon by stress. Anxiety and stress determined by universal intrument (not specialized to pregnancy condition) and both of them are not attached to each other.

Based on table 4, acknowledge that β HCG hormone levels is not affected and affects mental health of pregnant women, related on stress and anxiety. In the condition of pregnancy with emesis gravidarum, β HCG hormone levels above of average from normal pregnancy, it is known only 13.6% women experience stress and anxiety related nausea and vomiting. Evens, in both of group the results are same. Respondents who do not experience stress and anxiety, it is illustrated that there is a possibility of experiencing severe degrees of emesis gravidarum if the level of the hormone β HCG is above the average for a normal pregnancy. This means that β HCG hormone levels are main factor caused emesis gravidarum.

Table 4 Connection of β HCG hormone levels, anxiety and stress to each respondents

Group	Percentage of Respondents		
	Experiencing stress and anxiety	**Experiencing either stress or anxiety**	**Didn't experience both**
Severe degrees of emesis gravidarum	13.6%	72.8%	13.6%
Normal Pregnancy	9.1%	54.6%	36.3%

Table 5 Logistic regression analysis of β HCG hormone levels, anxiety, pregnancy planning, occupation, gravida and previous emesis history to severe degrees of emesis gravidarum

Variable	Koef. (β)	SE (β)	Wald	*P value*	Exp.B (95% CI)
Start model					
Multigravida	1.316	1.614	0.665	0.415	3.728(0.158-88.123)
Anxiety	1.484	1.183	1.575	0.210	4.410(0.434-44.786)
Precious nausea	1.344	1.752	0.589	0.443	3.836(0.124-118.782)
Unplanning pregnancy	0.419	1.256	0.111	0.739	1.520(0.130-17.813)
Workers	0.783	1.287	0.370	0.543	2.187(0.176-27.261)
β HCG hormone ≥ 49.950	4.161	1.316	10.002	0.002	64.116(4.865-844.901)
Constant	-4.627	1.759	6.921	0.009	
Last model					
Multigravida	2.063	1.172	3.096	0.078	7.868(0.791-78.294)
β HCG hormone ≥ 49.950	4.454	1.176	14.335	0.000	85.952(8.570-862.085)
Constant	-3.343	1.149	8..473	0.004	

In accordance to table 5, been found that dominant factor caused severe degrees of emesis gravidarum on this research are multigravida and pregnant women whom have β HCG hormone levels equal or more than 49950 miu/mL. Probability pregnant women whom have both of these risk factors to experience severe degrees of emesis gravidarum is 50.2%.

This research show that demographic and characteristics of pregnant women, not entirely related to emesis gravidarum. The only pregnancy planning, gravida and previous history of nausea are significantly related to severe degrees of emesis gravidarum[15, 16]. This is consistent with social psychology theory which stated that pregnancy planning is a condition that will affect pregnant women in adapting to changes and environment [19]. Unwanted pregnancy created its own spaces for psychology of pregnant women to refuse or even terminate their pregnancy [8, 20].

Emesis gravidarum is one of the complications of pregnancy caused by multifactorial factors, include endocrine and psychosocial factors [1, 5, 8, 9, 16]. Pregnant women with severe degrees of emesis gravidarum have β HCG hormone levels higher than normal pregnancy.

On perspective that hormonal changes are physiological condition in pregnancy, then additional information is needed also counseling to explain that on normal pregnancy, there will be increase β HCG hormone levels, which will be one of the factors caused emesis gravidarum. Therefore worries about problem arises affect mother's psychological during pregnancy can be eliminated.

Stimulation of HCG in upper digestive tract causes distention, causing an increase in gastric acid secretion and accumulation of fluid in the intestinal lumen, which trigger hyperemesis gravidarum [2, 21, 22]. Increasing on serum HCG will increase frequency of nausea and vomiting [2, 22, 23].

Hormonal changes that occur during pregnancy caused decrease of function of lower esophageal sphincter. These condition caused heartburn. Increasing progesteron during pregnancy will affect muscles OD stomach, and inhibit gastric emptying. Delayed gastric emptying can caused nausea and vomiting. It was also found that influence of electrical rhythm disturbances in the stomach can cause nausea [22]. Some opinions state that HCG stimulates process of excretion of gastrointestinal [11]. This condition can cause hyperthyroxinemia by showing symptoms of tachycardia, tremors, increased systolic, hyperreflexes, palpitations, depression and anxiety [7, 13].

Pregnant women who know the information hormonal changes hopefully can preparing their self to encourate these situation. Mental readiness on pregnancy women will affect acceptence their self of physical and psychological changes during pregnancy [23].

Emesis gravid arum is concluded is a form that shows the presence of somatic expression of psychological conflict or worsening of psychiatric conditions during pregnancy. Some experts research that gastrointestinal disorders caused by the interaction of brain when somebody experiences emotional stress and psychological immaturity [22, 23].

Stress and anxiety are mental health disorders that happens almost to everyone especially pregnant women. This condition is normally occured to everyone because their worried about reality does not accordance to expectation. Stressor not always being bad effect on their mental health. When someone can figure it out, then it will bring positive change [5, 23].

It same goes for pregnant women, when their get pressure from perceived changes during pregnancy, thus adaptability are needed. Stress during pregnancy related to biological changes on body. Mental readiness before and during pregnancy will help the adjustment that occur, of course this thing also supported with care and interpersonal relationship from husband and family.

Anxiety is emotional disorders that can led onset physical and mental symptoms. On first trimester, pregnant women feel irritable and anxious about their pregnancy. Changes in character can be described by changes in appetite patterns. This situation can stimulate hypothalamus pituitary adrenal and central nervous system. Progressively, production of ACTH, cortisol and CRH will increase. Trustworthy caused stress and anxiety during pregnancy [4, 20].

Type of supported not only limited get by family, support from health professional also give impression to pregnant women on dealing with their pressure. Quality midwifery care should noticed their condition by biopsychosocial. This means that attention is needed to not only physical health condition but also mental health [23].

Result of the study, proven that half of pregnant women get stress, so on management midwifery care have to screening mental health on pregnant women. By doing this, it will provide opportunities to pregnant women to resolve their problem and adapting their self to pressure and changer during pregnancy. Therefore quality life during pregnancy improved and generate child who have well-being in physical and mental health [23, 24].

Midwives on primary care health facility can giving information and counseling about stress and anxiety during pregnancy [24, 25]. In addition, information about health education to the public regarding mental disorders such as stress and anxiety that are different from insanity will help implement sountermeasures in an effort to refer to psychiatrist and psychologist [23].

4. Conclusion

There are associated between β HCG hormone levels and anxiety with severe degrees of emesis gravidarum on first trimester pregnancy. Dominant factors can cause severe degrees of emesis gravidarum are β HCG hormone levels equal or more than 49950 miu/mL and multigravida.

Compliance with ethical standards

Acknowledgments

In Implementation, this research has limitations including use of measuring instruments for mental disorders are still using universal tools, not specifically for pregnant women. Besides that, anxiety and stress only measured by self-evaluation tools by respondents, and not re-examined with regarding to hormone related to stress, so this is likely to be refraction on diagnosis stress and anxiety.

Disclosure of conflict of interest

There is no instance in this study where the researcher used her authority to suppress the research's subject and other authors cooperate voluntarily rather than using their positions or authority to exert pressure each other.

Statement of informed consent

In this study, researcher allowed research's subject to select whether or not to participate. Prior to data collection stage, research's subject was explained about the research information and sign an informed consent as a form of consent to participate in the study without compultion.

References

[1] Verberg MFG, Gillott DJ, Al-Fardan N, Grudzinskas JG. Hyperemesis Gravidarum, a Literature Review. Human Reproduction Update. 2005;11(5):527-239.

[2] O'Connor KA, Holman DJ, Brindle E, Miller RC, Barsom SH, Wood JW. Pregnancy-Related Sickness in Rural Banglades: Symptomps and Their Link with Reproductive Hormones. Human Reproduction Update. 2004.

[3] Lee NM, Saha S. Nausea and Vomiting of Pregnancy. Gastroenterol Clin North Am. 2011;40(2):309-34.

[4] Heitmann K, Nordeng H, C. HG, Solheimsnes A, Holst L. The Burden of Nausea and Vomitting During Pregnancy: Severe Impacts on Quality of Life, Daily Life Functioning nd Willingness to Become Pregnant Again-Results From a Cross-Sectional Study. BMC Pregnancy and Childbirth. 2017;17(75).

[5] Locock L AJ, Rozmovits L. Women's Responses To Nausea and Vomiting in Pregnancy. Midwifery. 2008;24(2):143-52.

[6] Kallen B, Lundberg G, A A. Relationship Between Vitamin use, Smoking and Nausea and Vomiting of Pregnancy. Acta Obstetricia et Gynecologica Scandinavica. 2003;82:916-20.

[7] Petry CJ, Ong KK, Beardsall K, Hughes IA, Acerini CL, Dunger DB. Vomiting in Pregnancy is Associated with a Higher Risk of Low Birth Weight: a Cohort Study. BMC Pregnancy and Childbirth. 2018;18(133).

[8] Bustos M, Venkataramanan R, Caritis S. Nausea and Vomiting of Pregnancy-What's New? Autonomic Neuroscience : Basic & Clinical. 2017;202:62-72.

[9] Gadsby R, Ivanova D, Trevelyan E, Hutton JL, Johnson S. Nausea and Vomitting in Pregnancy is Not Just 'Morning Sickness': Data From a Prospective Cohort Study in The UK. British Journal of General Practice. 2020;70(697):e534-e9.

[10] Einarson T, Piwko C, Koren G. Prevelance of Nausea and Vomiting of Pregnancy in The USA: A Meta-Analysis. J Popul Ther Clin Pharmacol. 2013;20(2):e163-e70.

[11] Clark SM, Costantine MM, Hankins GDV. Review of NVP and HG and Early Pharmacotherapeutic Intervention. Obstetric and Gynecology Int. 2012;2012.

[12] Buckwalter JG SS. Psychological factors in the etiology and treatment of severe nausea and vomiting in pregnancy. Am J Obstet Gynecol. 2002;186:S210-S4.

[13] Yoo A, Zaccaro J. Falsely Low Serum hCG Level in a Patient With Hydatidiform Mole Caused by the "High-Dose Hook Effect". Laboratory Medicine. 2000;31(8):431-5.

[14] McCarthy FP, Khashan AS, North RA, Baker PN, Dekker G, Poston L, et al. A Prospective Cohort Study Investigating Assosiations Between Hyperemesis Gravidarum and Cognitive, Behavioral and Emotional Well-Being in Pregnancy. PLoS ONE. 2011;6(11).

[15] Zhang H, Wu S, Zeng J, Liu Z. Risk Factors of Prolonged Nausea and Vomiting During Pregnancy. Risk Manag Healthc Policy. 2020;13:2645-54.

[16] Mamesah I, Loho M, Suparman E. Relationship Betwen BMI and B-HCG Levels with Hyperemesis Gravidarum in Manado, Indonesia. Majalah Obstetri & Ginekologi. 2019;27(3).

[17] Kasande AJ, Eze ED, Ezekiell I, Rabiu KM. Alteration of Human Chorionic Gonadotropin Levels among Pregnant Women with Morning Sickness Attending Antenatal Care Services at Ishaka Adventist Hospital, Uganda. Journal of Biosciences and Medicines. 2017;5(8).

[18] Shaheen AGAA, Wafa YAE-S, El-Omda FAE-A. Effect of High Levels of Human Chorionic Gonadotropin and Estradiol on Degree of Hyperemesis Gravidarum. Al-Azhar International Medical Journal. 2021;4(7):17-23.

[19] Munch S. Women's Experiences with A Pregnancy Complication: Causal Explanations of Hyperemesis Gravidarum. Social Work in Health Care. 2002;36(1):59-75.

[20] Mancuso RA SC, Rini CM, Roesch SC, Hobel CJ. Maternal Prenatal Anxiety and corticotropin-Releasing Hormone Associated With Timing of Delivery. Psychosom med. 2004;66(5):762-9.

[21] Gomes CF SM, Lourenço I, Martins D, Torres J. Gastrointestinal diseases during pregnancy: what does the gastroenterologist need to know? Ann Gastroenterol. 2018;31(4):385-94.

[22] Broussard CN RJ. Nausea and vomiting of pregnancy. Gastroenterol Clin North Am. 1998;27(1):123-51.

[23] Guideline G-t. The Management of Nausea and Vomiting of Pregnancy and Hyperemesis Gravidarum. Royal Collage of Obstetricians and Gynaecologists: NICE Accredited; 2016.

[24] Jin J. Treatments for Nausea and Vomiting During Pregnancy. JAMA. 2016;316(13):1420.

[25] Sukeningsih L, Winardi B, Kusumaningrum T. Effect of Counseling on Frequency and Severity of Nausea and Vomiting in Pregnancy (NVP). Indonesian Midwifery and Health Science Journal. 2020;4(3).