

Assessment of nausea and vomiting of pregnancy on antenatal clients of Addis Ababa

Tilahun Kuma¹, Lukman Yusuf¹, Shiferaw Negash¹

Abstract

Background: Nausea and vomiting of pregnancy (NVP) are common symptoms experienced during pregnancy. Both mild and severe symptoms can have significant morbidities and socioeconomic impact. Despite its frequency and associated distress, its exact cause is unknown. No study was done addressing this particular important issue in our country and this study will serve as a bench mark for future work on the topic in the Ethiopian context.

Objective: To assess nausea and vomiting of pregnancy on ANC (antenatal care) clients of three hospitals of Addis Ababa.

Methods: A descriptive facility based cross-sectional study, done in three teaching hospitals of Addis Ababa, the capital city of Ethiopia. Semi-structured questionnaires were administered to random sample of 384 pregnant women. Descriptive statistic was used to summarize data. P-value and ² test were used to measure associations.

Results: The prevalence of nausea and vomiting of pregnancy was 74.5%, with 4.4% being admitted for severe symptoms. It was found out that 91% had symptoms in the 1st trimester, 2.1% after mid pregnancy, and 85% were triggered by smell and taste. Primigravidity, nulliparity, excessive salivation and food aversion were significantly associated with nausea and vomiting connected with pregnancy. Significant associations were also observed between admission for severity and being unmarried, loss to work, affected relationship, more frequent vomiting, and early onset of symptoms. Severe frequency of vomiting was a major factor associated with admission for severity and loss to work.

Conclusion and recommendation: Nausea and vomiting of pregnancy found in this study were similar to other studies. Sensory stimuli were major trigger of symptoms and more frequent vomiting was linked with more admission. Importance of supportive measures, rest, counseling and advice on diet and life style modification needs to be underscored and early treatment of vomiting need to be considered. [*Ethiop. J. Health Dev.* 2013;27(3):200-207]

Introduction

Gastrointestinal and food-related disorders of pregnancy such as excessive salivation, food aversions, pica, nausea and vomiting in mild and extreme forms (emesis and hyperemesis gravidarum) are all principally symptoms of first and early second trimester pregnancy that can occasionally persist until term and delivery. Hyperemesis gravidarum is the most severe form of nausea and vomiting in pregnancy and is characterized by intractable nausea and vomiting that leads to dehydration, electrolyte and metabolic disturbances, and nutritional deficiencies that may require hospitalization. They are generally time-limited problems and usually improve and subside between the 14th and 16th weeks of pregnancy. In addition to altered physiological changes of pregnancy, causal factors could be attributed to some medical, surgical, and /or gynecological complications occurring at any time during the course of pregnancy. Out of all of these, nausea and vomiting are the commonest and clinically important ones. The severity of nausea and vomiting may affect the physical and psychological/emotional health of the pregnant women, as well as family, social and occupational functioning and the states of maternal role. Some women also considered termination of otherwise wanted pregnancies because of severe and prolonged nausea and vomiting (1, 2).

Many women lose time to both paid employment and housework with significant economic burden.

Approximately 8.6 million hours per year of paid employment and 5.8 million hours per year of housework were lost through pregnancy sickness symptoms in England and Wales (2). In the United States, severe nausea and vomiting accounts for over 285,000 hospital discharges annually (3). In 2002, in USA, the financial burden of severe nausea and vomiting was estimated to be about \$130 million. This figure was based on costs associated with an estimated annual average of 39,000 hospital admissions. It did not include physicians' fees or the loss of productivity at home or on the job or the cost of other patient treatment (4). In Germany, in 2005, the yearly cost of hospital admittances alone for hyperemesis gravidarum was about 28 million Euros, and the cost of lost working hours and outpatient treatment is not even included in this amount (5).

The organic, biochemical, metabolic and psychic changes and their subsequent complications can be immense thereby threatening the basic survival of women. Basically, all the body systems can be affected and multiple organ failures can be entered as complications in the extreme cases. Women with hyperemesis gravidarum can lose over 5% of their body weight; suffer fluid and electrolyte and acid base imbalances; and moreover risk nutritional deficiencies. In some instances long-lasting, very intensive vomiting, might in rare cases lead to esophageal mucosal injury/tear (a Mallory-Weiss syndrome), rupture of esophagus or spleen, choroid

¹Department of Obstetrics and Gynecology, College of Health Sciences, Addis Ababa University.

bleedings, transient hyperthyroxinemia, pneumothorax as well as neurological complications such as myelinolysis of the cerebellum or Wernicke encephalopathy caused by lack of vitamin B1 (6).

The exact etiologic factor for nausea and vomiting is unknown, but it is widely agreed that it is a multifactorial condition with genetic, physiological, behavioral, dietary, social, and psychological contributing determinants. The overall clinical symptoms are believed to be highly variable and tend to be affected by the age, marital status, place of residence, race/ethnicity, cultural, social, and educational status of the individual (7).

The full extent and implications of nausea and vomiting in pregnancy warrant early intervention, which is thought to decrease the severity and duration of the condition as well as prevent complications. However, because of to commonality of the condition and rarity in fatality, caused by it both care providers and pregnant women often tend to minimize the impact of NVP, thus the condition is often inadequately treated (7,8).

It is anticipated that this research will add to the growing body of knowledge about nausea and vomiting in pregnancy and contribute to bridging the information gap about this problem in our country as there have not been studies done addressing this particular important issue.

Materials

This study was done at three hospitals; Tikur Anbassa Specialized Hospital (SPRH), Ghandi Memorial Hospital (GMH) and St Paul's Hospital (SPH), all of them located in Addis Ababa. These particular facilities were chosen because they were technically and logistically accessible for this study. The descriptive facility-based cross-sectional study was conducted from June 1 to August 31, 2012 in order to assess nausea and vomiting of pregnancy on pregnant women attending antenatal care at the mentioned hospitals.

The participants were from Addis Ababa and its surrounding vicinities and consisted of all pregnant women who received antenatal care at those selected hospitals during that time. The sample size was calculated using the single population proportion formula and amounted to 384, where, the P was considered to be 0.5, the margin of error of 0.5 and 95% confidence level. Using a simple random sampling technique, every second woman was selected from those coming for ANC from Monday through Friday till the desired sample size was achieved.

The participants were recruited upon their appearance for their routine ANC follow up. All, except four study subjects, were of singleton intrauterine gestation. The four subjects with twin gestation were not significant to be considered separately. Subjects with severe nausea and vomiting but diagnosed to have concurrent medical or surgical illness were excluded during the recruitment

period. Each of the subjects was approached by an intern or a resident to explain the purpose of the study and to determine interest to participate in the study. The survey lasted for about 10 minutes and was completed by the client herself and/or by a trained data collector and returned while the subject was at the clinic for her scheduled prenatal visit. The completeness was checked by the respective interviewer immediately upon receiving the questionnaire. No pregnant woman refused to complete the questionnaire.

The semi-structured questionnaire contained both closed and open-ended questions which were adopted from similar researches done on the outcome of interest. It was pretested, refined and then translated into Amharic from the English. In addition to the questions used to assess NVP, the questionnaire also contained socio-demographic, obstetric and behavioral determinants.

No gestational age distinction was made as the intention was to assess NVP across the three trimesters. This survey was targeted only to the time of pregnancy based on the assumption that most women would remember their particular event of nausea and/or vomiting more clearly if surveyed during their pregnancies than after delivery.

Ethical approval was obtained from the Department of Research and Publication Committee, University of Addis Ababa, and permission to conduct the study in the chosen hospitals was secured from the responsible administrative body in each hospital.

Variables of interest were transferred to Statistical Package for Social Sciences (SPSS ver. 20) system file. Data were cleaned and edited using frequency runs to check for errant and unusual values as well as logical inconsistencies. Data were summarized using appropriate descriptive statistics. P-value < 0.05 and χ^2 test were used to measure the strength of associations between the selected variables with the dependent variable (NVP).

Results

The age distribution of the study subjects ranged between 16 – 38 years, 164/384(68.8%) fell between the ages of 25 – 34 years with a mean age of 27.7 ± 4.37 years. Most were Amhara 165/384(43%) in ethnicity, partnered: 366/384(95.3%), completed elementary education: 265/384(69%); employed: 181/384(47.1%) and most 317/384(82.6%) intended to become pregnant (Table1).

The mean and median gestational age at the time of interview was 7.5 months (± 1.9 months) and 8 months respectively, (range 1.5-9 months), most, 290/384 (75.5%) were above 7 months and only 17/384 (4.4%) were in the first trimester. Premigravidity and GII-IV account for 111/384 (28.9%) and 247/384 (64.3%), respectively. One hundred six (27.6%) of the women had one or more history of abortion and 138/384 (35.9%) of them had at least one alive child (Table2).

Table 1: The socio-demographic and behavioral characteristics of participants

Participants characteristics	Number (384), Frequency(n)	Percent (%)
Age (year) = mean age 27.7±4.37		
<24	82	21.3
25-34	264	68.8
>35	38	9.9
Marital status		
Partnered	366	95.3
Non Partnered	18	4.7
Religion		
Christian	298	77.6
Muslim	86	22.4
Ethnicity		
Amhara	165	43.0
Oromo	90	23.4
Tigre	24	6.3
Gurage	80	20.8
Others	25	6.5
Living address		
Urban	365	94.3
Rural	22	5.7
Occupation		
Working	181	47.1
Not=working	204	52.9
Educational level		
8 th grade	119	31
9-12 th grade	162	42.2
College/University	103	26.8
Plan of pregnancy		
Planned	317	82.6
Not Planned	67	17.4
Living arrangement		
With husband or co tenant	372	96.9
Alone	12	3.1

Table 2: The obstetrical determinants

Obstetric variables	Frequency (n)	Percent (%)
Gestational age (months = mean 7.5 months ± 1.9 months, median 2)		
Total Numbers of Pregnancies		
1	111	28.9
2-4	247	64.3
+5	26	6.8
Parity		
Nulliparous	154	40.1
Primiparous	139	36.2
Multiparous	91	23.7
No of alive children		
None	164	42.7
One	138	35.9
2+	82	21.4
Abortion history		
No	278	72.4
Yes	106	27.6

Two hundred eighty six (74.5%) the women experienced nausea and/or vomiting during their index pregnancy and of these women, 64/384 (16.7%) had nausea only and 190/384 (49.5%) had both nausea and vomiting occurring together, and only 17/384 (4.4%) had severe NVP that required admission to a hospital. Excessive salivation and food aversion were reported in 159/384 (41.4%) and 216/384 (56.3%) respectively (Table 3).

Table 3: Prevalence of NVP and associated symptoms

Characteristics	Frequency(n)	Percent (%)
NVP symptoms		
Vomiting only	35	9.1
Nausea only	61	15.9
Nausea and Vomiting	190	49.5
No NVP symptoms	98	25.5
Total	384	100.0
Admitted for sever NVP (N=384)		
Yes	17	4.4
Total	384	100.0
Excessive salivation (Yes)		
	159	41.4
Pica/food craving (N=384) (Yes)		
	78	20.3
Food aversion (N=384) (Yes)		
	216	56.3

As shown in Table 4, 262/384 (91.6 %) of women had onset of NVP before the third month of pregnancy, and the mean gestational age for onset of NVP symptoms was 2.15 months ± 1.16. Of the women with NVP, 147/286 (51.4%) had an early pattern of symptoms, 168/286 (58.7%) had one to two episodes of vomiting per day and 243/286 (85%) were triggered by tasting and/or smelling. About 74 (25.9%) experienced loss work time (either paid job or housework) and 95 (33.2%) had affected marital relationships because of NVP.

Regarding relieving factors, 54/286 (18.9%) reported having used pharmacological methods of whom 50 (92.3%) used antiemetic medications. Among the traditional remedies used, lemon was the most frequented. Ninety seven (33.9%) of the women went to health institution for their symptoms with a Mean OPD visit of 1.82 ± 1.04 (range 1-4 days) and 55.7% of them were given medication to relieve symptoms. Among women having an OPD visits 17 (17.5%) were admitted for severe NVP and half of them were hospitalized for more than 7 days.

Table 4: Symptom characteristics and some impacts of nausea and vomiting of pregnancy in study participants

Characteristics	Frequency (n)	Percentage%
GA at onset of symptoms (months) = Mean 2.15 months ± 1.16		
Onset up to 2 months	196	68.5
> 2 up to 3 months	66	23.1
< 3 up to 5 months	18	6.3
> 5 months	6	2.1
Total	286	100.0
Pattern of symptoms		
Early	147	51.4
Late	66	23.1
Irregular	73	25.5
Total	286	100.0
No of vomiting per day		
1-2	132	58.7
3-4	72	32.0
5+	21	9.3
Total	225	100.0
Triggers of symptoms of NVP		
Smell only	90	31.5
Taste only	63	22.0
Both Taste & Smell	90	31.5
No Trigger	43	15.0
Total	286	100.0
Effect of NVP		
Loss to work (Yes)	74	25.9
Total	286	100.0
Marital relationship		
Yes	95	33.2
Total	286	100.0

Table 5: Measures taken to alleviate symptoms of NVP

What is used to ease NVP	Frequency (n)	Percentage %
None	220	76.9
Medication	54	18.9
Traditional remedies	12	4.2
Total	286	100.0
Mgt at outpatient		
Medication used	54	55.7
Non medication used	43	44.3
Total	97	100.0
Number of OPD visit = mean 1.82 ± 1.04 Range 1-4 days		
Admission to hospital (yes)	17	5.9
Total	286	100.0

No significant association was observed with the socio-demographic variables like age, ethnicity, place of residence, occupation, and educational level except marital status with NVP and severe NVP. Pregnant women, who were not partnered were significantly associated with NVP and severe NVP ($p < 0.05$). Some GI symptoms such as excessive salivation, pica and food aversion were also significantly associated with symptoms of NVP. Behavioral determinants such as living arrangement and plans of pregnancy were not significantly associated either with NVP or severe NVP (Table 6).

Table 6: Comparison of women with NVP and determinants of NVP

NVP	N	%	χ^2	df	p-value
GI symptoms					
Excessive salivation (Yes)	159	41.4	49.4	1	<0.0001
Pica (Yes)	78	20.3	8.31	1	0.004
Food aversion (Yes)	216	56.2	76.73	1	<0.0001
Marital status					
No partner	18	6.3	6.687	1	0.010
Partner	268	93.7			
Gravidity					
1	97	33.9	13.7	1	<0.0001
2+	189	66.1			
Parity					
0	132	46.2	17.1	1	<0.0001
1+	154	53.8			
Number of Children					
0	139	48.6	15.91	1	< 00001
1+	147	51.4			

Obstetrical variables such as primgravidity, nulliparity and having no live children were significantly associated with the outcome variable (NVP) ($p < 0.05$). However, gestational age at interview had no association with NVP.

Severe NVP was found to be significantly associated with loss of work, marital relationships, antiemetic use and also with more frequent episodes of vomiting with p value <0.05 (Table 7).

Table 7: Comparison of severe NVP and determinants of nausea and vomiting

Severe NVP	n	%	²	df	p-value, Fisher's
Marital status					
Partnered	14	82.4			
Non Partnered	3	17.6	6.471	1	0.039
Frequency of vomiting					
<5	12	70.6			
5+	5	29.4	8.76	1	0.013
Affected relationship					
No	6	35.3			
Yes	11	64.7	8.08	1	0.007
Loss of work Yes	17	100	51.8	1	<0.0001
Antiemetic use Yes	17	100	19.38	1	<0.0001

No significant difference for early severity and frequency of symptoms was observed when comparing those women who had less than 5 episodes of symptoms in up to 2 months from their LMP with those who had experienced more than 5 episodes of symptoms in up to 3 months from LMP. GA at onset of symptom showed no

association with pattern of symptom, admission for severity, medication or marital relationship.

A significant association was observed with early onset of symptoms and more frequent episodes of vomiting for those who lost time to work compared to those who lost no time from work with the p value <0.05 (Table 8).

Table 8: Comparison of loss of work and symptom characteristics of NVP

Variables	n	%	²	df	p-value
Onset of symptom					
Early onset(<2mo)	196	68.5			
Late onset(>2mo)	90	31.5	4.49	1	0.003
Frequency of vomiting					
<5	58	84.1			
5+	11	15.9	5.14	1	(Fisher's =0.044)

Discussion

The high prevalence of NVP in our study (74.5%), is similar to the rates (50%-90%) found in other studies (1, 2). The high prevalence supports that this is a normal physiologic occurrence in early pregnancy. The finding in our study that 9.8% of pregnant women experienced late NVP symptoms is in agreement with previous studies that showed approximately 10-32% of women experiencing late NVP symptoms (4, 6-8, 10).

The onset of symptoms in the 1st trimester (91.6%) and only 2.1% after 5 months of pregnancy observed in our study is in conformity with different studies reported, 90% onset of symptoms in first trimester and only 5% after 22 weeks of pregnancy (11, 12).

Similarly, the finding in our study that 16.9% had nausea only and 49.6% had both nausea and vomiting occurring together is comparable to the Gads by et al study which demonstrated that 25% had nausea only and 52% reported both nausea and vomiting (13).

The finding in our study of severe NVP, 6.1%, is lower than the Canadian and the Swedish reports of 19% and 17% respectively, (9, 14). This difference in the degree of severity is apparent because of the difference in methodology and definition of severity used, in our study, severe NVP was defined as a symptom that required hospital admission while in other studies a NVP

index scale measure was used for grading severity of nausea and vomiting.

NVP onset and severity decreased significantly with gestational age among women in the first and second trimesters of pregnancy. This is reasonable since the natural history of NVP is gradual improvement of symptoms as pregnancy progresses corresponding with the onset, peak and decline of maternal HCG levels. This association is well demonstrated in the present study as well.

It has been thought that symptoms of NVP occur mostly in the morning hours, which was indeed the most common period observed in our study subjects, where 147/286 (51.4%) of women experienced only morning symptom while 73 (25.5%) had symptoms at various times throughout the day (13, 14). A comparative analysis, however, is obviously difficult as daily diary registration of symptoms than self report as in our study was applied by others.

The study subjects of patients who had at least one episode of vomiting 167/286 (58.4%) in our subjects corresponds well with the previous findings of by Gads et al and the Tierson et al study. Associated gastrointestinal symptoms, including excessive salivation, food aversion and food cravings were found to be significantly related to reports of nausea and/or vomiting. The subjects, who

did not experience nausea and vomiting, reported the least number of gastrointestinal symptoms (16, 17).

The way in which a pregnant woman responded to the primary stimulus to nausea and vomiting of pregnancy depended on her susceptibility mediated by vestibular, gastrointestinal, olfactory, and behavioral pathways. Smell appeared to be a major trigger of symptom in our study (63%); this is comparable to Lacroix R et al, wherein 50% of women, olfaction appeared to be the primary mechanism involved that made nausea worse (18, 20).

Contrary to most reports, of the socio-demographic variables studied, only not being partnered showed significant association with NVP/severe NVP. Similarly, contrasting results were obtained compared to other reports with regards to the association between NVP and race/ethnicity, unintended pregnancy, and place of residence. These differences may have resulted from the difference in methodology, that is, some of these studies that found such associations were focused on severe NVP (hyperemesis gravidarum) or vomiting alone (16, 19, 21-24),

In conformity with other studies, nullipara women, primigravida women, or those with no child were found to be significantly associated with NVP. This may be due to stress and exposure to high levels of HCG for the first time (25, 26, 28).

NVP can have a significant impact on family life, on the ability to perform usual daily activities and on social functioning. In addition, the presence and severity of NVP have been shown to have an impact on the quality of life of pregnant women. We found significant association between severe NVP and negatively affected marital relationships. We observed a strong association between loss of work time and the severity in frequency of pregnancy symptoms and severe NVP. In one study it was calculated that 12% of patients found ordinary work during pregnancy impossible. In another study, 57% of women were working during pregnancy and about 35% needed time off from their paid employment and 25% needed time away from their house work (13, 14, 30, 34).

Regarding what women used to ease nausea and vomiting, most (76.9%), in our subjects did not take antiemetics or alternative medications or non-drug alternatives or traditional remedies to alleviate their symptoms. This is may be from the fact that most women may feel NVP as a sign of early pregnancy and is temporary requiring no treatment as such. In our study medication was used in about 18.9%, of whom 91.6% used anti-emetics. This is similar to Lacasse et al report, where, 20.4% reported that they used anti-emetic medications. It is shown that the severity of NVP was the factor most closely related to women's decisions to take antiemetic medication. The same studies affirmed significant association between the use of antiemetic

medications to ease NVP and hospital admission for severe nausea and vomiting connected with compared to women who did not use antiemetic medications. This may be due to physicians' decision to use antiemetic medications which may be as consequence of severe nausea and vomiting symptoms at their presentation to clinic (31, 40).

In our study, 14 (82.4%) out of 17 women with severe NVP were admitted at or before 2 months of gestation and 8 (47.1%) of them had readmission for recurrence of severe symptoms. It was observed that the peak incidence of admission for hyperemesis gravidarum was reported to be between 8-12 weeks (57%), while only 5% were admitted before eight weeks of gestation and 25% of the patients required re-admission to hospital because of the recurrence of symptoms for the mere reason that some of the patients may have been discharged too soon (41). This disparity could be explained by the difference in methodology and the characteristics of the population.

In conclusion, three fourth of women had symptoms of nausea and/or pregnancy and severe symptoms were reported in 4.4% only, which is comparable to the currently available body of literature. The strong associations observed between severe NVP and marital status, frequency of vomiting, early onset of symptom, loss of work time, and marital relationship. Gestational age was described in months, because of the design of the study (retrospective) and none of the subjects could preferentially describe the GA in weeks as observed in the preparatory phase. As most of the respondents were in advanced gestation during the interview, with no custom of keeping health diary or menstrual calendar, the possibility of information (recall) bias cannot be excluded. Severity measured on admission criteria could miss those without admission but yet could have had significant perceived morbidity. From this cross-sectional study, it is impossible to determine causal relationships. Hence, whether these are methodological artifacts or are etiologically significant findings requires further investigation and a large-scale prospective national study.

Acknowledgments

We would like to express our sincere gratitude and appreciation to all residents, interns, and gynecologic OPD nurses of the three hospitals for their invaluable support during the data collection and to all others who have directly or indirectly contributed towards the realization of the study.

References

1. Gadsby R, Barnie-Adshead T. Review: severe nausea and vomiting of pregnancy: should it be treated with appropriate pharmacotherapy? *The Obstetrician & Gynecologist* 2011;13:107-111.
2. Philip B: Hyperemesis Gravidarum: Literature Review. *Wisconsin Medical Journal* 2003; 102(3): 46-51.

3. Fejzo MS, ChunYu Ching, Schoenberg FP, Macqibbon K, Romero R, Goodwin TM et al. Change in Paternity and Recurrence of Hyperemesis Gravidarum. *J Matern Fetal Neonatal Med* 2012;25(8):1241-45.
4. Miller F. Nausea and vomiting in pregnancy: the problem of perception—is it really a disease! *Am J Obstetric Gynecol* 2002;186:S182-183.
5. Bühling KJ. Nausea and hyperemesis gravidarum. *Gynakol Geburtsmed. Gynakol Endokrinol* 2008;4(1):36–48.
6. Krzyscin M, Gryzmislowski M, Dera A, Breborowicz GH. Nausea and vomiting in pregnancy. *Archives of Perinatal Medicine* 2009;15(4):209-14.
7. Kaplan B, Friedman S, Erman A, Bar J, Hod M, Gabbay U, et al. Hyperemesis Gravidarum: A Review. *J Reprod Med* 1994;39:605-12.
8. O'Brien B. et al. Nausea and Vomiting during Pregnancy: Effects on quality of women's Lives. *Birth* 1992;19(3):138-43.
9. Jennifer K. Nausea and Vomiting in Pregnancy: Prevalence and Relationship with Psychosocial Determinants of Health; (Unpublished doctoral thesis), University of Saskatchewan, Saskatoon, Saskatchewan, 2010.
10. Broussard CN, Richter JE. Nausea and vomiting of pregnancy: *Gastroenterol Clin North Am* 1998;27(1):123-51.
11. Davis M. Nausea and Vomiting of Pregnancy; An Evidence-based Review. *J Perinat Neonat Nurs* 2004;18(4):312-28.
12. Sherman PW, Flaxman SM. Nausea and vomiting of pregnancy in evolutionary perspective. *Am J Obstet Gynecol* 2002;186:S190-7.
13. Gadsby R, Barnie-Adshead AM, Jagger C. A prospective study of nausea and vomiting during pregnancy; *British Journal of General Practice* 1993;43:245-48.
14. Jarnfelt-Samsioe A, Samsioe G, Velinder GM. Nausea and vomiting in pregnancy - a contribution to its epidemiology. *Gynecol Obstet Invest* 1983;16:221-29.
15. Nyaruhucha CN. Food cravings, aversions and pica among pregnant women in Dar es Salaam, Tanzania. *Tanzan J Health Res* 2009;11(1):29-34.
16. American College of Obstetricians and Gynecologists (ACOG) and Practice Bulletin No.52. Nausea and Vomiting of Pregnancy. *Obstetric Gynecology* 2004;103(4):803-14.
17. Lacasse A, Rey E, Ferreira E, Morin C, Bérard A. Epidemiology of nausea and vomiting of pregnancy: Prevalence, severity, determinants, and the importance of race/ethnicity. *BMC Pregnancy and Child birth* 2009;9:26.
18. Bayley TM, Dye L, Jones S, DeBono M, Hill AJ. Food cravings and aversions during pregnancy: Relationships with nausea and vomiting. *Appetite* 2002;38(1):45-51.
19. Goodwin TM. Nausea and vomiting of pregnancy: An obstetric syndrome. *Am J Obstetric Gynecology* 2002;186:184-89.
20. Lacroix R, Eason E, Melzack R. Nausea and vomiting during pregnancy: A prospective study of its frequency, intensity, and patterns of change. *Am J Obstet Gynecol* 2000;182:931-37.
21. Swallow B, Lindow S, Masson E, Hay D. Women with nausea and vomiting in pregnancy demonstrate worse health and are adversely affected by odours. *J Obstet Gynaecol* 2005;25(6):544-49.
22. Loannis M, Andrea G, Franz K. Review article; Nausea and Vomiting in Pregnancy. *Dtsch Arztebl* 2007;104(25):1821–26.
23. Jordan V. The incidence of hyperemesis gravidarum is increased among Pacific Islanders living in Wellington. *N Z Med J* 1995;108(1006):342-44.
24. Gadsby R, Barnie-Adshead, A. Nausea and vomiting of pregnancy; a literature review: *Pregnancy Sickness Support* 2011; [www.pregnancysicknesssupport.org.uk].
25. Walker A, Walker B, Jones J, Verardi M, Walker C. Nausea and vomiting and dietary cravings and aversions during pregnancy in South African Women. *Br J Obstet Gynaecol* 1985;92:484-89.
26. Jueckstock JK, Kaestner R, Mylonas I. Managing hyperemesis gravidarum: A multimodal challenge, *BMC Med* 2010;8:46.
27. Verberg MFG, Gillott D J, Al-Fardan N, Grudzinskas JG. Hyperemesis gravidarum, a literature review; *Human Reproduction Update* 2005;11(5):527–39.
28. Smith C, Crowther C, Beilby J, Dandeaux J. The impact of nausea and vomiting on women: A burden of early pregnancy. *Aust NZ J Obstetric Gynaecol* 2000;40(4):397-401.
29. Tierson FD, Olsen CL, Hook EB. Nausea and vomiting of pregnancy and association with pregnancy outcome. *Am J Obstetric Gynecology* 1986;155(5):1017-19.
30. Mullin PM, Ching CY, Schoenberg F, MacGibbon K, Romero R, Goodwin TM et al. Risk factors, treatments, and outcomes associated with prolonged hyperemesis gravidarum. *J Matern Fetal and Neonatal Med* 2012;25(6):632-36.
31. Cheryl LA, Michele AK, Suzanne C, Cathy B, Margaret H, George WT, et al. The burden of illness of severe nausea and vomiting of pregnancy in the United States. *Am J Obstet Gynecol* 2002;186: Issue 5, Supplement 2, Page S220-S227.
32. Mazzotta P, Stewart D, Atanackovic G, Koren G, Magee LA. Psychosocial Morbidity among Women with nausea and vomiting of pregnancy: Prevalence and association with anti-emetic therapy. *J Psychosom Obstetric Gynecol* 2000;21:129-36.
33. McCormack D, Scott-Heyes G, McCusker CG. The impact of hyperemesis gravidarum on maternal mental health and maternal-fetal attachment. *J Psychosom Obstetric Gynaecol* 2011;32(2):79-87.

34. Bozzo P, Einarson TR, Koren G, Einarson A. Nausea and vomiting of pregnancy (NVP) and depression: Cause or effect? *Clin Invest Med* 2011;34(4):245.
35. Jennifer RN. Nausea and Vomiting in Pregnancy. *N Engl J Med* 2010;363:1544-50.
36. Gazmarian JA, Peterson R, Jamieson DJ, Schild L, Adams MM, Franks AL, et al. Hospitalization during pregnancy among managed care enrolls. *Obstet Gynecol* 2002;100(1):94-100.
37. Marlena S. Fejzo MS, Brecht A, MacGibbon DK, Romero R, Goodwin TM, et al. The impact of and risk factors for HG: Treatment, genetics and epidemiology: Hyperemesis Education and Research (HER) Foundation [cited 2013]; Available at: URL: https://www.pregnancysicknesssupport.org.uk/documents/conference_papers/The_impact_of_and_risk_factors_for_HG.pdf
38. Vutyavanich T, Kraissarin T, Ruangsri R. Ginger for nausea and vomiting in pregnancy: Randomized, double-masked, placebo-controlled Trial; *Obstetric and Gynecol* 2001;97(4):577-82.
39. Mario F. Nausea and vomiting in early pregnancy. *Clinical Evidence* 2009; 6:1405.
40. Lacasse A, Rey E, Ferreira E, Morin C, Be´rard A. Nausea and vomiting of pregnancy: What about quality of life? *BJOG* 2008;115:1484–93.
41. Fairweather DV. Nausea and vomiting in pregnancy. *Am J Obstet and Gynecol* 1968;102(1):135-175.