Nausea and vomiting during pregnancy: A prospective study of its frequency, intensity, and patterns of change

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OBJECTIVE: Our purpose was to provide a detailed description of patterns of nausea and vomiting of pregnancy

STUDY DESIGN: A prospective study was performed with 160 women who provided daily recordings of frequency, duration, and severity of nausea and vomiting.

RESULTS: Seventy-four percent of women reported nausea lasting a mean of 34.6 days. "Morning sickness" occurred in only 1.8% of women, whereas 80% reported nausea lasting all day. Only 50% of women were relieved by 14 weeks' gestation; 90% had relief by week 22. Data based on the McGill Nausea Questionnaire indicate that the nausea experienced by pregnant women is similar in character and intensity to the nausea experienced by patients undergoing cancer chemotherapy.

CONCLUSIONS: Traditional teachings about nausea and vomiting of pregnancy are contradicted by our findings. Standardized tools for measuring the distribution, duration, and intensity of nausea are applicable to the study of nausea and vomiting of pregnancy and could be used in clinical trials to assess palliative measures. (Am J Obstet Gynecol 2000;182:931-7.)

Key words: Nausea, vomiting, complications of pregnancy

Nausea and vomiting during pregnancy has a pervasive, detrimental impact on women's family, social, and professional lives. 1 It is so common that it is used in the diagnosis of pregnancy.2 Not only is teratogenicity a concern, but common treatments and standard advice are not effective for all women and rarely provide complete relief.³ Clearly, the burden of discomfort from nausea and vomiting during pregnancy is great, as is the frustration of clinicians who would alleviate it. However, little work has been done to precisely and prospectively delineate its natural history—timing of onset, peak and resolution, duration, and variability in intensity throughout the day, from day to day, and from person to person. Knowledge of the patterns of nausea and vomiting during pregnancy are necessary preconditions to designing clinical trials of palliative therapy. Standardized instruments provide useful outcome measures. The Rhodes index of nausea and vomiting,4 which has been standardized, has previously been used in clinical trials of nausea and vomiting during pregnancy.5, 6 However,

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studies describing the pattern and course of nausea and vomiting during pregnancy have largely used instruments devised for each study, without verification of reliability and validity.⁷⁻⁹

This study was undertaken to provide a detailed description of the patterns of nausea and vomiting during pregnancy. We prospectively studied 160 expectant mothers, who recorded daily throughout gestation the frequency, intensity, and duration of nausea and provided weekly qualitative descriptions of nausea, using the McGill Nausea Questionnaire^{10, 11} (Fig 1). In addition, we report on palliative measures that were tried by our participants, as well as demographics, lifestyle factors, and the history of nausea as predictors of nausea and vomiting during pregnancy.

Methods

These data were collected as part of an extensive prospective study of correlates of nausea and vomiting during pregnancy. All women seeking prenatal care at an outpatient clinic of a McGill University teaching hospital in Montreal, Quebec, Canada and examined by one of us (Erica Eason, SM, MDCM) were invited at the first visit to participate in a study of nausea and vomiting in pregnancy. In accordance with university and hospital policies for human experimentation, informed consent was obtained before the assessment. The women who had hyperemesis gravidarum at presentation, as well as those who later miscarried, are not included in the study out of concern that their experience may represent a different

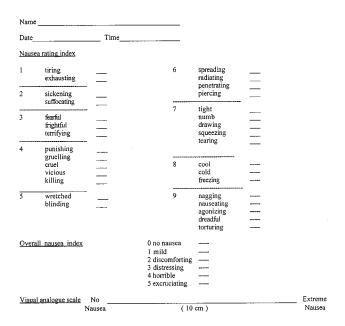


Fig 1. McGill Nausea Questionnaire. In nausea rating index rank value for each word is based on position of word in set; sum of rank values constitutes nausea rating index score. Overall nausea index is based on a scale of 0 to 5. Visual analog scale appears at bottom of questionnaire. (From Melzack R, Rosberger Z, Hollingsworth ML, Thirwell M. Can Med Assoc J 1985;133:755-9.)

hormonal environment (especially in the month before miscarriage).

At the first prenatal visit women agreeing to participate filled out an initial questionnaire to provide demographic data and information about the current pregnancy and about their experience of nausea in the past (both related and unrelated to pregnancy). They also indicated whether they had any nausea in this pregnancy and, if so, its onset, timing, duration, and severity, together with any palliative measures they had tried. A booklet was provided in which to record once daily the intensity of nausea during four periods of the day and any vomiting episodes, beginning on the day after enrollment. Nausea accompanied by fever or acute diarrhea was not considered to constitute nausea and vomiting during pregnancy. The full McGill Nausea Questionnaire, requiring 2 to 3 minutes to answer, was completed weekly. Participants were contacted by telephone within 2 weeks of enrollment and periodically thereafter to verify that they understood how to complete the booklet and to encourage compliance. This level of contact was maintained until delivery and enabled us to follow those for whom nausea came in bouts. Completed booklets were returned in stamped, addressed envelopes provided by the researchers.

The McGill Nausea Questionnaire (Fig 1) was developed and evaluated by Melzack et al¹⁰ in response to the need for a valid and reproducible measure to evaluate therapies for nausea induced by cancer chemotherapy.

The questionnaire consists of three indexes of nausea, two quantitative and one qualitative. The quantitative components consisted of a rating of intensity by a numeric-verbal rating—the overall nausea index and a visual analog scale. The qualitative measure, which was the nausea rating index, consisted of sets of verbal affective and other descriptors of nausea, with each set ranked in order of increasing severity. The subject was asked to choose the word, if any, from each set that best described her nausea. A numeric index score, which was the nausea rating index score, was obtained by summing the rank values of the words selected. The full questionnaire was completed weekly, and the overall nausea index was used for the detailed daily nausea ratings.

Previous work by Melzack et al¹⁰ found this questionnaire to be a sensitive measure of the nausea and vomiting produced by chemotherapy drugs. The scores on all three indexes correlated significantly with the physicians' and nurses' overall nausea index estimates. All three scores discriminated between patients receiving low-nausea-producing chemotherapy (cisplatin) from those who received high-nausea-producing chemotherapy (5-fluorouracil).

Gestational age was calculated from the first day of the last menstrual period. When the last menstrual period was uncertain or when the gestational age estimated before 26 weeks by ultrasonography differed by >1 week from the estimate of gestational age by last menstrual period, the ultrasonographic estimate of gestational age was

Table I. Characteristics of study participants

	No.	%	Total
Age			
20-24 y	17	10.6	
25-29 y	60	37.5	
30-34 y	67	41.9	
35-39 y	16	10.0	160
Parity			
0	71	44.7	
1	62	39.0	
>1	26	16.3	159
Civil status			
Single	4	2.5	
Married or cohabiting	155	96.9	
Divorced or separated	1	0.6	160
Total family income			
<\$10,000	3	1.9	
\$10,000 to <\$20,000	7	4.4	
\$20,000 to <\$30,000	11	6.9	
\$30,000 to <\$40,000	28	17.5	
≥\$40,000	104	65.0	153
Education			
High school or less	32	20.0	
College	41	25.6	
University	52	32.5	
Postgraduate	32	20.0	157
Ethnic origin			
English Canadian	124	77.5	
French Canadian	27	16.9	
Immigrant	9	5.6	160

used. At least 95% of subjects had early ultrasonographic verification of gestational age.

Data were analyzed with the Statistical Package for the Social Sciences, release 4.1 (SPSS Inc, Chicago, Ill). The statistical procedures used were the Spearman correlation coefficient or multivariate regression analysis, as appropriate. Test results with P < .05 were considered to be statistically significant.

Results

Of 200 potential subjects during the 2-year period beginning in May 1990, a total of 195 initially agreed to take part in the study and 180 (92%) completed it. Twenty participants miscarried, leaving 160 subjects with live births who are the basis of this report. Three women from this clinic who were admitted to the hospital for hyperemesis gravidarum during the study period are not study subjects. Of the 15 women not completing the study, 70% reported nausea, which is not significantly different from the 74% in those who completed it. Of the 20 who miscarried and for whom data are available (n = 14), 70% reported nausea.

Demographic characteristics of the 160 subjects are summarized in Table I. The average age of participants was 29.7 years, ranging from 21 to 39 years. More than 98% were white. Prospective self-recording of nausea and vomiting during pregnancy began at a mean of 8.2 weeks' gestation.





Fig 2. Timing of nausea during pregnancy. *Solid rule,* Onset of nausea; *shaded rule,* peak period; *dashed rule,* resolution of nausea

Prevalence and patterns of nausea and vomiting during pregnancy. Of the 160 subjects, 118 women (74%; 95%) confidence interval, 66%-80%) reported pregnancy-associated nausea either or both retrospectively and prospectively. Nausea was reported as early as the week of conception (ie, gestational age of 3 weeks), although the mean gestational age at onset was 5.7 weeks (median, 5 weeks). From the time that daily self-recording began, nausea lasted a mean of 34.6 days (95% confidence interval, 0-90 days; median, 27 days; range, 1-114 days). Vomiting began as early as a gestational age of 4 weeks. Sixty subjects (37.5%; 95% confidence interval, 30%-45% of all subjects; 50.8% of those with nausea) prospectively reported vomiting. Vomiting occurred on a mean of 5.6 days (95% confidence interval, 0-28 days; median, 3 days; range, 1-49 days). Vomiting occurred an average of 9.8 times.

The distribution of timing at onset, peak, and resolution of nausea in individual women is depicted in Fig 2. This distribution is derived from prospective recording except for events occurring before the study enrollment, in which case the retrospective report of the event is used. As expected, 90% of women destined to have nausea of pregnancy reported its onset by the 8th week of gestation, but 8 of the 118 noted nausea beginning only during or after the 10th week. Although the gestational age at which nausea was reported to be most severe (overall nausea index scores) varied, the modes of peak severity occurred at 11 and 13 weeks. Although 50% of women with nausea reported resolution by 14 weeks (the end of the first trimester), it was not until week 22 of gestation that nausea had resolved in 90% of women.

For each week of gestation the percentage of all subjects reporting nausea, together with its severity in af-

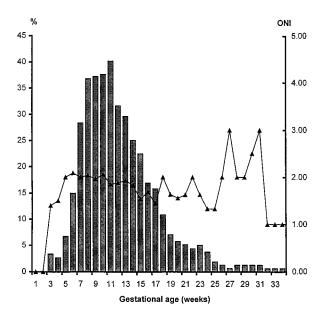


Fig 3. Percentage of women with nausea (*shaded bars*) and intensity of nausea (overall nausea index [*ONI*]) (*filled triangles*).

fected women as indicated by the overall nausea index, is depicted in Fig 3. Week 11 of gestation was the week in which the highest proportion of women, 40%, had nausea. This was also the peak week for vomiting. The ratings for mean nausea intensity (overall nausea index) among women with nausea were fairly constant, not only in the first trimester, when they ranged from 1.4 to 2.1 on a 5point scale, but throughout the pregnancy. Although the prevalence of nausea and vomiting during pregnancy is considerably decreased by the third trimester, in those still experiencing such, the intensity ratings stayed fairly constant (mean overall nausea index, 1.9) until nausea ended. (The three apparently higher severity ratings at late gestation represent ratings by a few women and are not significantly different from ratings for other weeks.) On the overall nausea index, the extreme ratings of "4, horrible" and "5, excruciating" were rarely used. We compared ratings by overall nausea index (a numeric and verbal measure) with those of the visual analog scale (a numeric measure). The two variables were shown to covary reliably (r = .92; P < .01).

The mean score on the qualitative measure, the nausea rating index, during the peak (eleventh) week for nausea was 7.6, of a possible 31. The mean score on the overall nausea index during this week was 1.85.

The distribution of nausea throughout the day is depicted in Fig 4. Although 80.2% of women reported nausea in the morning, "morning sickness" (ie, nausea limited to mornings alone) occurred in only 1.8% (95% confidence interval, 0%-7%) of affected women. Nausea and vomiting during pregnancy lasted until afternoon in 3.7%, until after suppertime in 4.7%, and all day long in

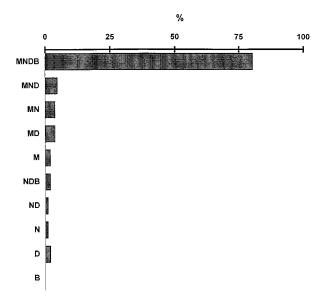


Fig 4. Daily pattern of nausea during pregnancy. *M*, Morning; *N*, noon; *D*, dinnertime; *B*, bedtime.

80% (95% confidence interval, 71%-87%). The 10 remaining women reported no morning nausea but had nausea at various other times throughout the day.

A further analysis of the day-to-day patterns of nausea was carried out to assess the persistence of nausea. Once prospective recordings began, 23 women indicated nausea on an uninterrupted daily basis, with an average duration of 44.6 days for this group. Twenty women reported a cessation of nausea lasting at least a day. This group averaged 24.7 days with nausea, 5.5 days without, and then 3.8 days with nausea again. The remainder had ≥2 periods (≤20 periods) of at least a day without nausea before it finally resolved. There was no difference in gestational age at the onset of nausea between women who had persistent nausea and those who had intermittent nausea.

Demographics, history of nausea, and lifestyle choices. Three sets of multiple regression analysis with the forward selection method were carried out to examine whether demographics, history of nausea, and lifestyle variables could predict who would be nauseated and the intensity of nausea (overall nausea index). In the first series age, height, and weight during the first trimester were predictive neither of nausea and vomiting during pregnancy nor of overall nausea index scores. Because most women (n = 143) were married or cohabited, we have insufficient power to assess the importance of marital status. Women with less education (grade school or high school) were significantly more likely to report nausea and vomiting during pregnancy ($R^2 = .07$; F = 12.1; P < .0001) and had higher intensity scores (overall nausea index) ($R^2 = .05$; F = 8.4; P < .01). An income range of

Table II. Palliative measures

Method used		Efficacy						
	Helpful		Somewhat helpful		Not helpful			
	No.	%	No.	%	No.	%		
Mental concentration	10	8.4	29	24.5	17	14.4		
Dry foods	34	28.8	41	34.7	9	7.6		
Clear liquids and carbonated drinks	20	16.9	41	34.7	14	11.8		
Going outside	24	20.3	23	19.4	11	9.3		
Lying down	36	30.5	34	28.8	22	18.6		
Medication	5	4.2	1	0.8	4	3.3		

\$30,000 to \$40,000 (in contrast to incomes of <\$30,000 and of >\$40,000) significantly predicted those who reported nausea (R^2 = .09; F = 4.2; P < .05); this group accounted for 9% of the variance in predicting scores on the overall nausea index (R^2 = .09; F = 7.2; P < .01). Finally, women who worked part-time (in contrast to those who worked full-time, were students, worked at home, or were unemployed) accounted for 13% (R^2 = .13; F = 6.0; P < .01) of the variance in scores on the overall nausea index.

Women with nausea during a previous pregnancy were significantly more likely to report nausea and vomiting during the index pregnancy ($R^2 = .17$; F = 33.6; P < .0001) and to have high scores on the overall nausea index (R^2 = .04; F = 7.4; P < .01). A history of medication-related nausea also predicted nausea and vomiting during pregnancy ($R^2 = .20$; F = 6.3; P < .01) but not nausea intensity. A history of nausea when ill, while under stress, with menstrual cramps, while using oral contraceptives, or while traveling was unrelated to nausea and vomiting during pregnancy or to intensity scores. Whether the mothers of the study subjects had had nausea during pregnancy was unrelated to the study subjects' current experience with nausea and to their scores on the overall nausea index; the number of previous children of the study subjects was also unrelated.

Nineteen women smoked cigarettes during pregnancy; smoking was not associated with either nausea or vomiting during pregnancy or with scores on the overall nausea index. However, among the women who smoked, the reported number of cigarettes smoked predicted nausea and vomiting during pregnancy ($R^2 = .05$; F = 8.1; P < .01). Alcohol consumption also was not associated with nausea and vomiting during pregnancy or with scores on the overall nausea index.

The occurrence of nausea and vomiting did not predict the sex or birth weight of the child.

Palliative measures. The 118 women who reported nausea and vomiting during pregnancy were asked to identify any palliative measures they had tried and to rate their effectiveness. We evaluated a total of six broad categories that were derived from previous work on nausea

and vomiting during pregnancy.^{1, 8} The most commonly used and effective interventions were (1) modification of the diet to dry foods and carbonated drinks and (2) time spent outside in the fresh air or reduction of mobility (Table II).

Comment

This prospective study of 160 women used daily self-recording of symptoms and the McGill Nausea Questionnaire, a previously validated tool (Melzack et al¹⁰), to provide detailed descriptive information on severity and timing of nausea and vomiting throughout the day and throughout the pregnancy.

In this study the prevalence of nausea (74%) and vomiting (37.5%) during pregnancy is comparable to that found in other studies. Gadsby et al,⁸ reporting prospectively on 363 women, noted an 80% prevalence of nausea and 52% of vomiting. Vellacott et al⁹ reported nausea during the first trimester in 56% of the 500 women they studied. Klebanoff et al,¹² using data collected monthly during pregnancy for the Collaborative Perinatal Project, reported vomiting in 56% of pregnant women.

Nausea and vomiting during pregnancy are commonly believed to disappear by the end of the first trimester. 13-16 However, our data show that the prevalence is greatest at 11 weeks' gestation, and the severity in those affected peaks at 11 to 13 weeks. Although the prevalence gradually declines in the second trimester, only half of women with nausea and vomiting during pregnancy were completely relieved by 14 weeks' gestation, and it was not until gestational week 22 that nausea had resolved in 90% of affected women. These findings corroborate those of Gadsby et al,8 who found that in 9.2% of women the symptoms did not resolve until after 16 weeks; Klebanoff et al,12 who found that 9% vomited after 22 weeks; and Vellacott et al,9 who found that 73% of their sample continued to have symptoms after week 12. It is important that caregivers be aware of this aspect of the natural history of nausea and vomiting during pregnancy, to avoid setting women up for anger and disappointment when the symptoms persist.

In women with ongoing nausea in the second and third trimesters, the intensity of nausea did not abate; rather, it remained fairly stable, with the mean weekly ratings on the overall nausea index for nauseated women mostly between 1.4 and 2.0 on a 5-point scale. The relative rarity of ratings on the overall nausea index of 4 (horrible) or 5 (excruciating) in the context of pregnancy is somewhat surprising in view of the severity of symptoms. We considered the possibility that women may be reluctant to choose ratings associated with words expressing such negative feelings in association with pregnancy, either because of their genuinely positive feelings about being pregnant or lest they be considered to be reacting badly to it. However, the high correlation (r = .92) between the visual measure (visual analog scale) and the verbal measure (overall nausea index) suggests that the women did not tend to be influenced by the negative verbal descriptors of the overall nausea index and that their scores were reliable across assessment methods. We conclude that nausea and vomiting during pregnancy are fairly stable in terms of their intensity in each individual and may be more akin to an all-or-none phenomenon. This may be helpful in directing research toward understanding the mechanisms of nausea and vomiting during pregnancy.

The McGill Nausea Questionnaire provides both qualitative (the nausea rating index) and quantitative (the overall nausea index and the visual analog scale) indexes of nausea. The clinical meaning of the nausea scores obtained in this study may be best grasped in light of the nausea scores obtained in an earlier study in which the same questionnaire was used with cancer patients undergoing chemotherapy. 10 Patients given cisplatin, with high nausea-producing potential, reported a score on the overall nausea index of 10 (on a scale of 0-31) and a mean overall nausea index of 3.6. Those receiving 5-fluorouracil, which has low nausea-producing potential, reported a mean nausea rating index of 3.3 and an overall nausea index of 1.8. By contrast, in our study at 11 weeks' gestation, when nausea prevalence and vomiting frequencies were maximal, the mean nausea index score was 7.6 and the mean overall nausea index score was 1.85. Thus nausea and vomiting during pregnancy were comparable in severity to those induced by moderately nausea-producing cancer chemotherapy.

It is commonly believed that nausea and vomiting during pregnancy are worst on awakening and will usually not outlast the morning. 17 Our findings concerning the daily distribution of nausea indicate that <2% of women had nausea only in the mornings; for most women nausea lasted throughout the day. This finding corroborates that of Gadsby et al, 8 who reported a fairly uniform distribution of nausea throughout the waking hours; only 3.8% of their sample had nausea limited to the hours between 6 AM and noon. Similarly, DiIorio et al 18 found

from 7-day diaries that nausea was equally likely to be present throughout the waking hours. Vellacott et al⁹ reported that only 19% of women with nausea and vomiting during pregnancy had symptoms confined to the morning. These figures suggest that the term *morning sickness* is misleading and should be avoided when one is referring to nausea and vomiting during pregnancy.

The finding that 23% of our study group had uninterrupted daily nausea for an average of 44.6 days, 20% had one interruption of nausea, and the rest had more intermittent symptoms suggests that these groups may differ in physiologic, psychologic, or environmental parameters in ways that may be relevant to our future understanding of nausea and vomiting during pregnancy.

Previous work relating nausea and vomiting during pregnancy to demographic variables has shown mixed results. Vellacott et al⁹ and Fitzgerald¹⁹ did not find a relationship between nausea and vomiting during pregnancy and educational level, income level, marital status, or age. Klebanoff et al, 12 in a much larger study, found that younger age and less education were significantly associated with vomiting in early pregnancy. Our findings show a significant relationship between three variables—low educational level, middle to low income, and part-time work—and nausea and vomiting during pregnancy. The same three variables also significantly predicted nausea intensity scores. Taken together, these results suggest that social demographic variables are important in predicting a small yet significant portion of cases of nausea and vomiting during pregnancy. Likewise, women with a history of nausea during pregnancy were shown to report nausea and vomiting during subsequent pregnancies and high nausea intensity scores.

The most effective and commonly used palliative measures reported in the literature and confirmed in our study were rest, eating carbohydrates, and drinking carbonated drinks. ^{1, 6, 7} That 20% of our sample had not tried these measures before being questioned about them suggests that reviewing the measures with patients may prove beneficial.

Our fairly homogeneous sample limits the generalizability of these findings. Further transcultural work may shed light on the role of biologic and other determinants of nausea and vomiting during pregnancy.

A multitude of etiologic theories involving physiologic and psychologic mechanisms have been advanced to explain nausea and vomiting during pregnancy, but none has been satisfactory.^{1, 13} This study provides data regarding the actual day-to-day fluctuations and the course of nausea and vomiting during pregnancy, which may be useful in guiding future research. Just as the pain of labor was widely underestimated in the past and has been shown by objective pain ratings to be comparable to the worst pain experienced in other contexts, this study demonstrates that the nausea and vomiting

experienced by pregnant women are comparable to what is thought to be the worst nausea, that of cancer chemotherapy.

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