Original articles

Nausea and vomiting in pregnancy: maternal characteristics and risk factors

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Summary

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Nausea with or without vomiting (NVP) is probably the most frequently reported medical complaint of pregnancy, but few studies have considered risk factors for its development. We used data from an ongoing epidemiological study of pregnancies in four regional centres. Mothers of infants with congenital malformations ($n = 17\,158$) and a sample of normal infants ($n = 5329$) were interviewed within 6 months of delivery by trained nurse-interviewers using a standardised questionnaire. For all risk factors investigated, odds ratios and 95% confidence intervals were calculated using multiple logistic regression, controlling for potential confounders.

The cumulative incidence (risk) of NVP was 67%. The risk of NVP and its timing during pregnancy were similar for mothers of malformed and normal infants, so data were combined. No changes in the NVP risk were observed over the 20-year study period. The risk decreased with increasing age, but increased with increasing gravidity. The risk also increased with increasing number of prior miscarriages. Further, within each gravidity category, the risk was higher for twin births than for singletons. Women who reported onset of NVP after the first trimester differed demographically from women whose NVP began earlier: they were less-well educated, had lower incomes, and were more likely to be black.

The finding that the number of prior pregnancies, both complete and incomplete, and number of fetuses independently appear to increase the risk of NVP suggests a fetal 'dose' effect. Together with selected demographic characteristics that differentiate early- vs. late-onset NVP, these findings warrant further investigation.

Keywords: *maternal nausea, pregnancy, gravidity, past obstetric history, maternal age, socioeconomic status, multiple pregnancy.*

Introduction

Nausea with or without vomiting (NVP) is probably the most frequently reported medical complaint of pregnancy, estimated to affect between 50% and 80% of women.[1–7] A variety of aetiological mechanisms have been proposed (e.g. hormonal, immunological, altered carbohydrate metabolism, vitamin B6 deficiency),[7–13] and it seems likely that there are multiple pathways that may lead to NVP. While many studies have examined various treatments for this condition[14–18] or the relationship between NVP and pregnancy outcome,[7,19,20] few studies have considered risk factors for the development of NVP itself. Among those that have, no clear consensus has emerged. For example, some studies have found younger mothers to be at a greater risk,[20–22] while others have reported no association with maternal age.[13] Traditionally, parity was believed to have no effect on NVP,[23] but more recent reports suggest an increased incidence among first pregnancies.[8,21,22] Although NVP is most common in the first trimester of pregnancy, some women experience these symptoms into the second trimester and sometimes

throughout pregnancy, and for a small proportion of women, NVP actually begins after the first trimester. Little is known about maternal or obstetric characteristics that may predict those women who are likely to have longer duration or later-onset NVP. Recognition of these characteristics may lead to better understanding of the aetiology of this very common condition.

As part of an ongoing programme to evaluate factors in pregnancy that may affect development of birth defects, we investigated potential risk factors for NVP occurrence, time of onset, and duration.

Methods

The Slone Epidemiology Center at Boston University has been conducting case–control surveillance of birth defects since 1976. The methods have been described elsewhere.[24,25] Briefly, infants with congenital malformations are identified in birth and tertiary care hospitals in the greater metropolitan areas of Boston, Philadelphia, Toronto, and San Diego. During the years 1983–85 and since 1992, a sample of non-malformed infants has also been included. Mothers of eligible subjects are interviewed within 6 months of the baby's birth by trained nurse-interviewers who use a standardised questionnaire. This study has been approved by Boston University Medical Center's Institutional Review Board and informed consent for the interview is obtained from all participants.

The interview elicits demographic information about the mother and detailed information regarding maternal illnesses and medications used during pregnancy. It also includes questions on a number of events related to pregnancy, such as high blood pressure, pre-eclampsia, vaginal bleeding, and diabetes (no distinction was made between gestational and pre-existing diabetes). Questions about NVP were introduced in 1983, and the present analysis therefore includes subjects interviewed between 1983 and 2003. The questionnaire has been modified somewhat over time, but in all versions, subjects were asked if they had experienced any of a list of specified events.

Between 1988 and 1992, we asked about NVP as a single medical event, while before 1988 and after 1992, we asked about nausea and vomiting as separate entities. For each woman who reported NVP, we obtained information on its timing in pregnancy. Prior to 1987, women were asked to report the months of pregnancy in which NVP occurred. Subsequently, they were asked to provide specific start and stop dates, and based on either the date of their reported last menstrual period or their estimated due date, we calculated the months of pregnancy during which NVP was present. Based on previous research,[1] we defined a 'long duration' group as NVP which lasted >4 lunar months (independent of time of onset); we also defined a 'late onset' group as NVP that began after the first trimester.

The questions did not include any measure of severity of nausea and vomiting other than duration of symptoms. Small numbers of normal newborns have been included in the study since 1983, and in 1997 we began systematically enrolling a random sample of all births in Massachusetts. Odds ratios (OR) and 95% confidence intervals [CI] were calculated using multiple logistic regression, controlling for all other variables presented as well as year of interview and region.

Results

Information was available for the mothers of 17 158 malformed infants and 5329 normal infants. To

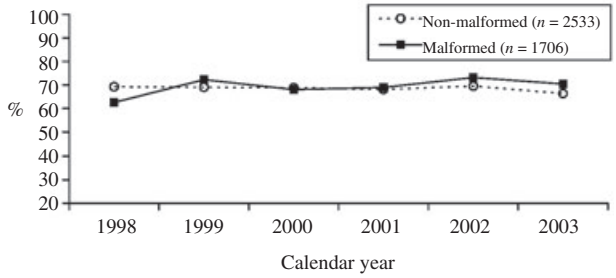

Figure 1. Risk of nausea and vomiting according to interview year, Massachusetts 1997–2003.

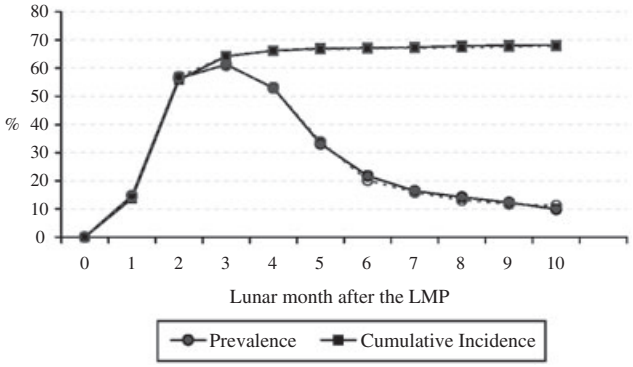

Figure 2. Prevalence and cumulative incidence of NVP during gestation for mothers of malformed (solid markers) and non-malformed infants (open markers), Massachusetts 1997–2003. LMP, last menstrual period.

Table 1. Demographic characteristics of women with and without nausea and vomiting of pregnancy

Women's characteristics	NVP ($N = 14\,998$) *n* (%)	No-NVP ($N = 7489$) *n*	OR [95% CI]	Adjusted OR [95% CI][a]
Age (years)				
<21	1 133 (67.2)	553	1.00 Reference	1.00 Reference
21–25	2 829 (69.4)	1245	1.11 [0.98, 1.26]	0.97 [0.85, 1.10]
26–30	4 949 (67.2)	2414	1.00 [0.90, 1.12]	0.83 [0.73, 0.94]
31–35	4 207 (65.8)	2188	0.94 [0.84, 1.05]	0.72 [0.63, 0.83]
36–40	1 646 (64.3)	915	0.88 [0.77, 1.00]	0.64 [0.55, 0.75]
>40	230 (57.4)	171	0.66 [0.53, 0.82]	0.47 [0.37, 0.60]
Ethnic background				
White	12 475 (66.8)	6208	1.00 Reference	1.00 Reference
African origin	899 (63.7)	512	0.87 [0.78, 0.98]	0.78 [0.69, 0.88]
Asian	497 (66.5)	250	0.99 [0.85, 1.16]	1.01 [0.86, 1.19]
Native-American	37 (60.7)	24	0.77 [0.46, 1.28]	0.72 [0.43, 1.21]
Hispanic	883 (68.7)	402	1.09 [0.97, 1.24]	1.01 [0.89, 1.16]
Other	192 (68.6)	88	1.10 [0.86, 1.41]	1.07 [0.83, 1.38]
Pre-pregnancy weight (lb)				
<116	2 818 (66.3)	1431	1.00 Reference	1.00 Reference
116–130	4 261 (65.9)	2203	1.00 [0.92, 1.08]	0.98 [0.90, 1.07]
131–145	3 125 (67.1)	1534	1.05 [0.96, 1.15]	1.05 [0.96, 1.15]
>145	4 794 (67.6)	2301	1.07 [0.99, 1.16]	1.07 [0.98, 1.16]
Smokers				
Never	7 712 (67.3)	3755	1.00 Reference	1.00 Reference
During pregnancy	3 489 (63.6)	1998	0.85 [0.80, 0.91]	0.80 [0.74, 0.86]
Before pregnancy	3 791 (69.1)	1695	1.09 [1.02, 1.17]	1.06 [0.98, 1.13]
Education (years)				
<12	5 444 (66.3)	2772	1.00 Reference	1.00 Reference
12–15	3 991 (67.4)	1928	1.05 [0.98, 1.13]	1.09 [1.01, 1.17]
>15	5 563 (66.6)	2789	1.02 [0.95, 1.08]	1.11 [1.03, 1.21]
Income ($/year)				
<10 000	614 (65.4)	325	0.96 [0.83, 1.11]	1.03 [0.88, 1.21]
10 000–45 000	4 200 (65.2)	2241	0.95 [0.88, 1.02]	1.09 [1.00, 1.20]
>45 000	5 355 (66.5)	2699	1.00 Reference	1.00 Reference
Employment status				
Yes	11 056 (66.1)	5660	1.00 Reference	1.00 Reference
No	3 942 (68.3)	1829	1.10 [1.04, 1.18]	1.05 [0.98, 1.13]

[a]Adjusted for interview year in addition to all variables presented.
OR, relative risk.

determine whether NVP experiences differed between mothers of malformed infants and mothers of normal infants, we compared the risk of NVP in the random sample of 2533 Massachusetts mothers of normal infants born after 1997 (69%) with the risk for 1706 mothers of malformed infants (70%) born in Massachusetts in the same time period. These risks were not materially or statistically different between the two groups ($P > 0.20$) and ranged from 65% in 1998 to 68% in 2003 (Fig. 1). Further, the patterns of onset and monthly prevalence also did not differ between the two groups (Fig. 2). Therefore, all remaining analyses presented are based on mothers of malformed and non-malformed subjects combined, for a total population of 22 487.

Over the entire study period, the risk of NVP was 66.7%. For 5-year intervals beginning in 1983 (2003 included in the last interval), the risks were 69%, 62%, 65% and 68%. The apparent fluctuations in the risks are likely to be due to the modifications in the questionnaire.

Table 1 shows risks of NVP according to maternal demographic characteristics. There was a strong inverse relationship between age and the risk of NVP.

Table 2. Obstetric characteristics of women with and without nausea and vomiting of pregnancy

Women's characteristics	NVP (N = 14 998) n (%)	No-NVP (N=7489) n	OR [95% CI]	Adjusted OR [95% CI][a]
Gravidity				
Primigravid	4 334 (64.2)	2417	1.00 Reference	1.00 Reference
Multigravid				
2	4 710 (66.7)	2349	1.12 [1.04, 1.20]	1.17 [1.09, 1.26]
3	3 090 (68.6)	1416	1.22 [1.12, 1.32]	1.34 [1.23, 1.46]
4+	2 864 (68.7)	1307	1.22 [1.13, 1.33]	1.43 [1.30, 1.57]
Sex				
Male	8 489 (66.1)	4360	1.00 Reference	1.00 Reference
Female	6 509 (67.6)	3127	1.07 [1.01, 1.13]	1.08 [1.02, 1.14]
Number of fetuses				
Single	14 464 (66.5)	7288	1.00 Reference	1.00 Reference
Twins	534 (72.7)	201	1.34 [1.14, 1.58]	1.38 [1.17, 1.63]
Planned pregnancy				
Planned	9 089 (66.6)	4553	1.00 Reference	1.00 Reference
Unplanned	5 198 (67.3)	2528	1.02 [0.99, 1.05]	1.01 [0.98, 1.05]
Uncertain	673 (66.0)	347	0.99 [0.92, 1.06]	1.01 [0.94, 1.08]
Urinary tract infection				
No	13 295 (66.2)	6778	1.00 Reference	1.00 Reference
Yes	1 703 (70.6)	711	1.22 [1.11, 1.34]	1.19 [1.08, 1.31]
Pre-eclampsia				
No	14 435 (66.5)	7258	1.00 Reference	
Yes	563 (70.9)	231	1.23 [1.05, 1.43]	1.22 [1.04, 1.42]
Vaginal bleeding				
No	11 351 (65.9)	5883	1.00 Reference	1.00 Reference
Yes	3 647 (69.4)	1606	1.18 [1.10, 1.26]	1.15 [1.08, 1.23]
Diabetes				
No	14 274 (66.8)	7080	1.00 Reference	
Yes	724 (63.9)	409	0.88 [0.78, 0.99]	0.88 [0.78, 1.00]
Seizure				
No	14 924 (66.7)	7446	1.00 Reference	
Yes	74 (63.3)	43	0.86 [0.59, 1.25]	0.80 [0.55, 1.17]
Oral herpes				
No	14 342 (66.7)	7172	1.00 Reference	1.00 Reference
Yes	656 (67.4)	317	1.04 [0.90, 1.19]	1.19 [1.08, 1.31]
Genital herpes				
No	14 778 (66.7)	7394	1.00 Reference	1.00 Reference
Yes	220 (69.8)	95	1.16 [0.91, 1.48]	1.19 [0.93, 1.52]
Other STD				
No	14 856 (66.7)	7413	1.00 Reference	1.00 Reference
Yes	142 (65.1)	76	0.93 [0.70, 1.23]	0.91 [0.69, 1.22]

[a]Adjusted for interview year in addition to all variables presented.
STD, sexually transmitted diseases; OR, relative risk.

Compared with women aged 20 or younger, the adjusted OR for women 40 or older was 0.47 [95% CI 0.37, 0.60], and the test for trend was highly significant ($P < 0.001$). The incidence of NVP was significantly lower in blacks, but did not differ appreciably with respect to pre-pregnant weight, income or employment status. Although there was a statistically significant (but borderline) elevation in risk among more educated women, the difference is not substantial. Women who smoked during pregnancy were significantly less likely to experience NVP than those who discontinued smoking or had never smoked.

Risks of NVP according to obstetric characteristics are presented in Table 2. No substantial differences

were observed for the sex of the infant, or whether the pregnancy was planned. Some conditions of pregnancy, such as herpes, pre-eclampsia, vaginal bleeding and urinary tract infections, were associated with small increases in the risk of NVP; diabetes was associated with a slight decrease in risk which was of borderline significance; and other conditions, such as seizures, and other sexually transmitted diseases, were not associated with the NVP risk.

We examined in detail the inter-relationships between NVP and parity, gravidity, and number of prior non-completed pregnancies. Because parity and gravidity are highly correlated, we included each separately in the multivariable model and found that gravidity had the stronger association of the two; therefore gravidity was retained in the model. With primigravid women as the reference group, the relative risk of NVP increased with each pregnancy to 1.43 [95% CI, 1.30, 1.57] for gravidity 4 or greater. To further explore the effects of increasing gravidity and increasing maternal age, we considered NVP in relation to gravidity according to 5-year age intervals (Fig. 3). In every age category, primigravidae had a lower incidence of NVP than multigravidae and within each gravidity category, the risk of NVP declined with age.

We then considered whether the effect of gravidity was present according to whether past pregnancies were completed or not. We found that the risk of NVP increased with both, and was more marked for past pregnancies that were not completed. For women with four or more incomplete pregnancies, the OR was 1.35 [95% CI, 1.07, 1.71] compared with 1.15 [95% CI, 1.01, 1.30] for ≥4 completed pregnancies. NVP was also associated with the number of fetuses in the index pregnancy; although not statistically different for every point, within each gravidity group, the risks of NVP were greater for twin births than for singleton births (Fig. 4). We had no information about occurrence of NVP in previous pregnancies.

We considered whether the timing of onset or the duration of NVP might distinguish subgroups of women with unique or different characteristics. There were 4559 women (20%) who fell into the long duration category of NVP, and 1016 women (4.5%) who were considered late onset. Tables 3 and 4 present risks for these subgroups of NVP according to maternal characteristics (the risks for the shorter duration and earlier onset, are included in both tables for purposes of comparison).

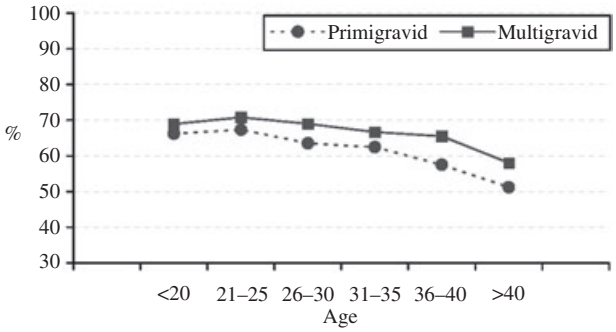

Figure 3. Risks of nausea and vomiting in index pregnancy among 6751 primigravid and 15 736 multigravid women according to age, 1983–2003.

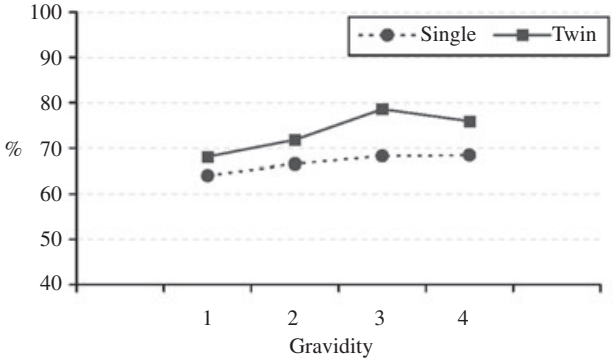

Figure 4. Risks of nausea and vomiting of pregnancy for 21 752 singleton and 735 twin births according to parity.

Longer duration, like shorter duration, was more common among younger women and women with lower income levels. Of note, it was also related to greater pre-pregnant weight. Long-duration NVP was more frequent among multigravidae, women carrying a multiple gestation, and, marginally, among women whose pregnancy was unplanned. No smoking effect was observed.

For late-onset NVP, the median duration was 2 months. In contrast with early-onset NVP, late-onset NVP (Table 4) was associated with unplanned pregnancy, lower levels of education, lower income levels, and black ethnicity. Because women with these demographic characteristics may tend to present late for obstetric care, we examined the timing of the first obstetric visit in relation to late-onset NVP to determine if late start of prenatal care might in some way have influenced reporting of later dates of onset of NVP. There were 10 000 women for whom the date of the first prenatal visit was available, 3324 of whom had

Table 3. Duration of nausea and vomiting according to selected women's characteristics

Women's characteristics	Typical duration *N* (%)	OR [95% CI][a]	Long duration *N* (%)	OR [95% CI][a]
Number of fetuses				
Single	10 043 (46.7)	1.00 Reference	4396 (20.21)	1.00 Reference
Twins	371 (50.48)	1.37 [1.15, 1.64]	163 (22.18)	1.53 [1.24, 1.90]
Gravidity				
Primigravid	3 118 (46.2)	1.00 Reference	1210 (17.9)	1.00 Reference
Multigravid	7 296 (46.4)	1.21 [1.2, 1.6]	3349 (21.2)	1.42 [1.30, 1.55]
2	3 337 (47.3)	1.14 [1.06, 1.23]	1366 (19.4)	1.25 [1.13, 1.38]
3	2 101 (46.6)	1.26 [1.15, 1.38]	985 (21.9)	1.55 [1.38, 1.73]
4+	1 858 (44.6)	1.32 [1.19, 1.45]	998 (23.9)	1.76 [1.56, 1.98]
Planned pregnancy				
Planned	6 553 (48.0)	1.00 Reference	2523 (18.5)	1.00 Reference
Unplanned	3 371 (43.6)	1.00 [0.96, 1.03]	1816 (23.5)	1.08 [1.04, 1.13]
Uncertain	468 (45.9)	1.00 [0.94, 1.14]	204 (20.0)	1.03 [0.94, 1.13]
Education (years)				
<12	3 506 (42.7)	1.00 Reference	1927 (23.5)	1.00 Reference
12–15	2 729 (46.1)	1.11 [1.02, 1.20]	1256 (21.2)	1.03 [0.93, 1.14]
>15	4 179 (50.0)	1.17 [1.07, 1.27]	1376 (16.5)	0.92 [0.83, 1.02]
Age (years)				
<21	722 (42.8)	1.00 Reference	409 (24.3)	1.00 Reference
21–25	1 842 (45.2)	0.99 [0.87, 1.15]	983 (24.1)	1.00 [0.93, 1.14[
26–30	3 450 (46.9)	0.87 [0.76, 1.00]	1488 (20.2)	0.81 [0.69, 0.96]
31–35	3 049 (47.7)	0.79 [0.68, 0.91]	1153 (18.0)	0.69 [0.58, 0.82]
36–40	1 179 (46.0)	0.72 [0.61, 0.84]	465 (18.2)	0.66 [0.54, 0.81]
>40	170 (42.4)	0.56 [0.43, 0.73]	59 (14.7)	0.42 [0.30, 0.59]
Income ($/year)				
<10 000	383 (40.8)	1.01 [0.85, 1.21]	227 (24.2)	1.10 [0.89, 1.35]
10 000–45 000	2 793 (43.4)	1.06 [0.96, 1.17]	1400 (21.7)	1.21 [1.08, 1.37]
>45 000	4 000 (49.7)	1.00 Reference	1345 (16.7)	1.00 Reference
Smokers				
Never	5 432 (47.4)	1.00 Reference	2266 (19.8)	1.00 Reference
During pregnancy	2 213 (40.3)	0.76 [0.70, 0.82]	1271 (23.2)	0.91 [0.8, 1.01]
Before pregnancy	2 764 (50.4)	1.09 [1.01, 1.18]	1021 (18.6)	0.97 [0.88, 1.07]
Ethnic background				
White	8 827 (47.3)	1.00 Reference	3635 (19.5)	1.00 Reference
African origin	512 (36.3)	0.67 [0.58, 0.76]	382 (27.1)	1.06 [0.91, 1.24]
Asian	349 (46.7)	0.96 [0.80, 1.14]	148 (19.8)	1.15 [0.92, 1.43]
Native-American	20 (32.8)	0.61 [0.34, 1.11]	17 (27.9)	1.05 [0.56, 1.98]
Hispanic	569 (44.3)	0.98 [0.85, 1.13]	309 (24.1)	1.21 [1.02, 1.43]
Other	128 (45.7)	0.99 [0.76, 1.30]	62 (22.1)	1.15 [0.83, 1.59]
Pre-pregnancy weight (lb)				
<116	1 997 (47.0)	1.00 Reference	819 (19.3)	1.00 Reference
116–130	3 094 (47.9)	0.99 [0.90, 1.08]	1164 (18.0)	0.98 [0.88, 1.10]
131–145	2 214 (47.5)	1.02 [0.93, 1.12]	903 (19.4)	1.13 [1.00, 1.27]
>145	3 109 (43.8)	0.96 [0.88, 1.05]	1673 (23.6)	1.36 [1.22, 1.52]

[a]Adjusted for interview year in addition to all variables presented.

no NVP and 497 of whom had late-onset NVP. We found that among these women the OR for late-onset NVP relative to no NVP was elevated: 1.85 [95% CI 1.20, 2.84] among women whose first prenatal visit occurred in the sixth lunar month or later, compared with women whose first visit occurred within the first trimester. However, when the analysis was restricted to women whose first visit occurred during the first trimester, the associations with education, income and race remained.

Table 4. Onset of nausea and vomiting according to selected women's characteristics

Women's characteristics	Early onset *N* (%)	OR [95% CI][a]	Late onset *N* (%)	OR [95% CI][a]
Number of fetuses				
Single	13 382 (61.5)	1.00 Reference	998 (4.6)	1.00 Reference
Twins	514 (69.9)	1.47 [1.25, 1.74]	18 (2.5)	0.82 [0.50, 1.33]
Gravidity				
Primigravid	3 948 (58.5)	1.00 Reference	368 (5.5)	1.00 Reference
Multigravid	9 948 (63.2)	1.30 [1.22, 1.38]	648 (4.1)	0.89 [0.77, 1.04]
2	4 414 (62.5)	1.20 [1.12, 1.30]	277 (3.9)	0.83 [0.70, 0.99]
3	2 886 (64.1)	1.37 [1.26, 1.49]	188 (4.2)	0.97 [0.80, 1.18]
4+	2 648 (63.5)	1.47 [1.34, 1.61]	183 (4.4)	0.96 [0.77, 1.18]
Planned pregnancy				
Planned	8 525 (62.5)	1.00 Reference	523 (3.8)	1.00 Reference
Unplanned	4 702 (60.9)	1.02 [0.98, 1.05]	454 (5.9)	1.10 [1.02, 1.18]
Uncertain	634 (62.2)	1.03 [0.96, 1.11]	36 (3.5)	0.93 [0.77, 1.11]
Education (years)				
<12	4 887 (59.5)	1.00 Reference	515 (6.3)	1.00 Reference
12–15	3 724 (62.9)	1.10 [1.02, 1.19]	247 (4.2)	0.85 [0.72, 1.01]
>15	5 285 (63.3)	1.12 [1.04, 1.21]	254 (3.0)	0.77 [0.64, 0.93]
Age (years)				
<21	980 (58.1)	1.00 Reference	144 (8.5)	1.00 Reference
21–25	2 570 (63.1)	1.01 [0.89, 1.15]	244 (6.0)	0.92 [0.72, 1.18]
26–30	4 600 (62.5)	0.87 [0.76, 0.99]	318 (4.3)	0.77 [0.60, 0.99]
31–35	3 987 (62.4)	0.78 [0.68, 0.89]	204 (3.2)	0.60 [0.46, 0.80]
36–40	1 546 (60.4)	0.70 [0.61, 0.82]	87 (3.4)	0.64 [0.46, 0.89]
>40	209 (52.1)	0.51 [0.40, 0.65]	19 (4.7)	0.69 [0.41, 1.18]
Income ($/year)				
<10 000	537 (57.2)	1.00 [0.85, 1.18]	66 (7.0)	1.29 [0.91, 1.80]
10 000–45 000	3 845 (59.7)	1.06 [0.96, 1.16]	320 (5.0)	1.41 [1.14, 1.75]
>45 000	5 091 (63.2)	1.00 Reference	237 (2.9)	1.00 Reference
Smokers				
Never	7 182 (62.6)	1.00 Reference	482 (4.2)	1.00 Reference
During pregnancy	3 146 (57.3)	0.79 [0.74, 0.85]	326 (5.9)	1.07 [0.91, 1.26]
Before pregnancy	3 563 (65.0)	1.06 [0.99, 1.14]	207 (3.8)	0.99 [0.83, 1.19]
Ethnic background				
White	11 662 (62.4)	1.00 Reference	768 (4.1)	1.00 Reference
African origin	776 (55.0)	0.75 [0.66, 0.85]	111 (7.9)	1.30 [1.02, 1.66]
Asian	466 (62.4)	0.98 [0.83, 1.15]	24 (3.2)	0.84 [0.54, 1.30]
Native-American	32 (52.5)	0.72 [0.42, 1.23]	5 (8.2)	1.28 [0.48, 3.42]
Hispanic	767 (59.7)	0.94 [0.83, 1.08]	96 (7.5)	1.52 [1.17, 1.98]
Other	178 (63.6)	1.06 [0.82, 1.36]	12 (4.3)	0.94 [0.51, 1.75]
Pre-pregnancy weight (lb)				
<116	2 594 (61.1)	1.00 Reference	213 (5.0)	1.00 Reference
116–130	3 985 (61.7)	0.99 [0.91, 1.07]	254 (3.9)	0.86 [0.70, 1.05]
131–145	2 899 (62.2)	1.05 [0.95, 1.15]	211 (4.5)	1.10 [0.89, 1.35]
>145	4 418 (62.3)	1.06 [0.97, 1.15]	338 (4.8)	1.11 [0.91, 1.34]

[a]Adjusted for interview year in addition to all variables presented.

In contrast with early-onset NVP, late-onset NVP was marginally more common in singleton pregnancies, primigravid women, and was not associated with increasing gravidity.

Discussion

Similar to most studies of NVP,[1–7] we found the overall risk of this condition to be about 67%. Of note, the risk,

timing of onset, and duration of NVP were virtually identical for mothers of both normal and malformed infants, and the risk was relatively unchanged over the 20 years of this study. We also found that NVP most often began during the second lunar month and persisted for less than 4 months.

This study was large enough to provide stable estimates for many potential risk factors for NVP. Several reports had identified an increased risk in younger women,[21,22] in multiparous women[22] and for multiple births,[3] although these studies left unclear whether these effects were independent of each other. We, too, found these same characteristics to be associated with increased risks of NVP, and we further found that these effects are, indeed, largely independent. These results, in combination with the results for multiple fetuses and completed pregnancies, suggest that the aetiology of NVP may be related to physiological factor(s) associated with both the pregnancy history and the current pregnancy.

On the other hand, our data do not support other risk factors that have been suggested in previous studies. We did not confirm relationships between overall occurrence of NVP and increased pre-pregnant weight,[21,22] black race, or low education, or a strong relationship with female sex of the infant.[3,26] These differences may result from the fact that some of these studies focused on severe NVP (hyperemesis gravidarum)[22,26] or vomiting alone.[21] Although we found that women who smoked during pregnancy were less likely to experience NVP, we could not determine whether this was due to the fact that women who were experiencing NVP were more likely to discontinue smoking.

When we examined NVP by duration and onset, we found some notable differences. Long-duration NVP increased with increasing pre-pregnant weight. Women with late-onset NVP were considerably more likely to be less educated and have lower incomes. Because these factors tend to be related to socio-economic status, we considered whether this association was due to such women presenting for prenatal care relatively late in pregnancy. While we did find that women presenting in the third trimester were more likely to report late-onset NVP than women who presented in the first trimester, we also found that the associations with education and income were evident among women who presented in the first trimester. Further, we are unaware of any evidence to suggest that earlier prenatal visits would have precipitated NVP, or that access to medical care would affect recall of pregnancy events. Although the association between late-onset NVP and low socio-economic status does not appear to be explained by late presentation for prenatal care, it is unclear how lower socio-economic status might lead to late-onset NVP. With respect to other risk factors, primigravid women were at a slightly higher risk of late-onset NVP than multigravid women. This may in part be a reflection of the fact that these women do not recognise nausea as a pregnancy event at its initial occurrence. No smoking effect was observed among these women.

NVP is a common condition that has a significant impact on quality of life for those who experience it.[6,27] While many hypotheses have been proposed, its aetiology remains unclear.[8] The study reported here is one of the largest to consider risk factors for NVP and to distinguish between early- and late-onset NVP. There appears to be an increased risk of NVP associated with the number of liveborn fetuses delivered, whether these result from multiple singleton births or a single pregnancy with multiple infants. The slightly higher risk of NVP observed among women with a history of miscarriage, if true, would seem to suggest that gravidity and parity may be independently related to the risk of NVP. Further, late-onset and long-duration NVP appear to have somewhat different risk factors. Whether these are methodological artefacts or are aetiologically significant requires further investigation.

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