

# A prospective study of nausea and vomiting during pregnancy

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**SUMMARY.** *The symptoms of nausea and vomiting in pregnancy were described by 363 pregnant women who kept daily symptom diaries. All delivered a single live baby. The majority of information collected was prospective, with the median day from last menstrual period to initial interview by the study midwife being day 57. It was found that 80% of women had symptoms, 28% experienced nausea only, while 52% had nausea and vomiting. The mean number of days from last menstrual period to onset and cessation of symptoms was 39 and 84, respectively, and 40% of women's symptoms ended abruptly. Cessation of symptoms occurred at approximately the same day from the last menstrual period whether they had begun earlier or later or whether they had been severe or mild. The median total number of hours of nausea per pregnancy in those 292 women experiencing symptoms was 56, with peak symptoms occurring in the ninth week. Eighty five per cent of women experienced days with two episodes of nausea. Fifty three per cent of episodes of vomiting occurred between 06.00 hours and 12.00 hours. The symptom complex can be defined as episodic daytime pregnancy sickness. Among the study population, 206 women were in paid employment. Seventy three of these women (35%) spent a mean of 62 hours away from their paid work because of symptoms of nausea and vomiting, showing the socioeconomic significance of this condition. The detailed information gathered should help in the investigation of the aetiology of nausea and vomiting during pregnancy.*

**Keywords:** *nausea; vomiting; pregnancy; morbidity.*

## Introduction

THE association between early pregnancy and symptoms of nausea and vomiting is generally accepted. However, there has been little research directed at finding out more about the symptom complex and developing an understanding of it. Since 1950, only about 30 articles have been published on this subject and most have been concerned with hyperemesis gravidarum.<sup>1</sup>

Features of the symptom complex that have been described include the gestational age of onset,<sup>2,4</sup> the variation in symptoms from pregnancy to pregnancy in the same patient<sup>3,5-7</sup> and the proportion of pregnant women who develop symptoms.<sup>8-13</sup> Little has been published on the manner of onset and cessation of symptoms, the daily pattern and variation in symptoms, the time of gestation when symptoms occur most commonly or the relationship between early and severe symptoms and total duration of symptoms.<sup>7</sup> The effect of nausea and vomiting on women's ability to carry out paid employment or housework is also an under-researched area.<sup>1,14</sup>

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Most published studies have been retrospective, reporting observations in women referred to hospital, the data being collected later on in the pregnancy,<sup>14</sup> or in some studies, months after the pregnancy.<sup>1</sup> These studies are likely to be biased towards more severe symptoms and less accurate because of their retrospective nature.

A large prospective collaborative study of more than 55 000 patients enrolled between 1958 and 1966 provided information on the symptom complex,<sup>5,15</sup> but detailed variations in the condition were not reported.

A prospective study in the United States of America used a well defined cohort of women.<sup>2</sup> However, the patient population was skewed towards the upper end of scales measuring socioeconomic status and the first interview was designed to occur during the 12th week of pregnancy. Jarnfelt-Samsioe and colleagues also carried out a prospective study but it did not provide detailed data on daily symptom patterns.<sup>4</sup>

In British general practice there is a defined population of mixed socioeconomic class, and patients suspecting pregnancy usually present in the surgery one or two weeks after their first missed menstrual period. This proves an ideal situation in which to obtain prospective data from early in pregnancy to investigate this well recognized, but under-researched symptom complex. This paper reports a study which aimed to describe a more complete clinical picture of nausea and vomiting in pregnancy.

## Method

The study was carried out in a seven partner urban teaching practice of 14 500 patients of mixed socioeconomic class. Approximately 5% of the practice population were from ethnic minorities. The study commenced on 1 May 1986 and continued for two and a half years. All patients first consulting about possible pregnancy who were registered with the practice at the time of their last missed menstrual period, and who were not requesting a termination of pregnancy, had the study explained to them by their general practitioner. Patients entered the study after a positive pregnancy test.

Women in the study were visited at home by the study midwife who obtained patient details. The midwife explained how to complete the daily symptom diary (which had been designed by the authors) and obtained the date of onset of symptoms, whenever that might have been, with up to two weeks' retrospective symptoms if they could be remembered accurately. Two-weekly contact was maintained with each patient to ensure that data were being accurately recorded. The women kept weekly records of how much time had been lost from paid employment and housework as a result of nausea and vomiting. The women completed the diaries until symptoms ceased, but were asked to contact the study midwife if symptoms recurred later.

Patients in the study were given no medication until 16 weeks of pregnancy unless their initial haemoglobin concentration was below 11 g dL<sup>-1</sup>, by agreement with the local consultant obstetricians. The pregnancy was dated from an accurate last menstrual period and confirmed or corrected for as many patients as possible by an ultrasound scan and the date of confinement.

All data collected were processed at Leicester University medical school using the SAS statistical package. Non-parametric tests were used throughout the analysis. The Mann Whitney U test was used to test for differences in total hours of nausea or

vomiting between those who did and who did not lose time from work or housework and those who did and who did not experience severe vomiting. The Kruskal Wallis one way analysis of variance was used to test the difference in duration of symptoms and day at which symptoms ceased for groups defined by the time at which symptoms started.

## Results

### Study population

A total of 456 women were recruited into the study. Twenty one women were then excluded as they presented after day 84 from their last menstrual period and it was felt that this was too late to record accurate data. The remaining 435 women were enrolled into the study and visited at home by the midwife.

A further 24 women were excluded from the study for reasons which developed after the initial interview. These were: refusal to cooperate, nine women; later termination of pregnancy, six; left practice and untraceable, five; unable to be contacted by study midwife, three; and admitted to hospital for ovarian cyst, one woman.

The following subgroups were excluded for the purposes of this analysis: miscarriage, 33 women; pregnant with twins, five; treated for symptoms of nausea and vomiting, three; stillbirth, three; hypothyroidism, two; insulin dependent diabetes, one; and ectopic pregnancy, one woman. The remaining 363 women who delivered a live single baby therefore comprised the study population.

The mean age at interview was 26 years, the youngest woman being 15 years old and the oldest being 40 years. Of the 363 women, 36.9% were primigravidae, 41.9% were gravida two, 13.5% were gravida three and the remaining 7.7% were gravida four or more. The study population reflected the socioeconomic and ethnic minority profile of the practice population. None of the women was being treated for low haemoglobin levels.

The median number of days from last menstrual period to initial interview with the study midwife was 57 (interquartile range 50 to 64 days). All diary data were collected prospectively except for 42 women who each also reported seven days' retrospective data and 16 women who each also reported 14 days.

### Symptoms of nausea and vomiting

For 266 women, episodes of nausea occurred before the initial interview. Twenty six women started their symptoms on or after the day of the initial interview. Seventy one women (19.6%) had no symptoms of nausea or vomiting throughout their pregnancy while 28.1% had nausea only, and 52.3% had nausea and vomiting. No-one had only vomiting.

**Onset and cessation of symptoms.** For the 292 women with symptoms, the mean day from the last menstrual period to the onset of symptoms was day 39 (median day 39, range eight to 79). For 72.2% symptoms started between days 29 and 49 from their last menstrual period (Table 1). The mean day for cessation of symptoms was day 84 from the last menstrual period (median day 81, range 44 to 213). Sixty per cent of women ceased having symptoms by the 84th day and 90.8% of women had ceased having symptoms by the 112th day (Table 1). For 38.6% of women, symptoms appeared to stop suddenly, that is, they had reported more than 14 hours of symptoms in the week prior to the cessation.

**Symptoms in previous pregnancies.** Of the 57 women who were multiparous and who had had over 100 hours of nausea, 36 (63.2%) stated they had had similar symptoms in a previous pregnancy. Of the 41 women who were multiparous who had had

**Table 1.** Time between last menstrual period and onset and cessation of symptoms of nausea and/or vomiting recorded by the 292 women experiencing symptoms at entry into the study.

	% of women (n = 292)
<i>Time between LMP and onset of symptoms (days)<sup>a</sup></i>	
≤ 21	6.9
22-28	6.5
29-35	21.3
36-42	27.1
43-49	23.7
50-56	8.2
57+	6.2
<i>Time between LMP and cessation of symptoms (days)</i>	
≤ 56	8.2
57-63	9.2
64-70	9.9
71-77	15.1
78-84	17.5
85-91	8.6
92-98	11.0
99-105	7.2
106-112	4.1
113+	9.2

n = number of women. LMP = last menstrual period. <sup>a</sup>Data missing for one patient.

no nausea in the current pregnancy, 24 (58.5%) stated they had had no or only slight nausea in a previous pregnancy.

**Symptom severity.** Two measures of the severity of symptoms were used – the total number of hours of nausea during pregnancy and the duration of symptoms in days from the start of symptoms. The median total number of hours of nausea per pregnancy in the 292 women suffering symptoms was 56 hours (interquartile range 22 to 139 hours). These symptoms lasted for a median of 41 days (interquartile range 28 to 56 days).

The week in which symptoms occurred most frequently was calculated for each woman experiencing symptoms. The median week of peak symptoms was nine (interquartile range eight to 10 weeks). Symptoms began to decrease after week 10. In only 34 women did symptoms become worse by more than seven hours in any week after week nine.

**Episodic nature of symptoms.** The total number of episodes of nausea recorded was 13 302. The times throughout the day when episodes of nausea occurred are shown in Table 2. The most common six-hour period for symptoms of nausea was between

**Table 2.** Total number of episodes of nausea and vomiting experienced by the 292 women, by time of day.

Time of day (hours)	% of total no. of episodes of:	
	Nausea <sup>a</sup> (n = 13 302)	Vomiting (n = 4071)
06.00-08.59	26.5	27.4
09.00-11.59	32.5	25.9
12.00-14.59	23.0	11.6
15.00-17.59	23.6	11.7
18.00-20.59	22.9	11.9
21.00-23.59	17.6	8.2
00.00-02.59	2.4	1.8
03.00-05.59	1.2	1.5

n = total number of episodes. <sup>a</sup>Percentages total more than 100% as episodes overlapping time periods were counted in each.

06.00 hours and 11.59 hours. The three-hour periods between 12.00 hours and 20.59 hours each had a similar percentage of symptoms of nausea. Eleven women (3.8%) only had symptoms of nausea between the 06.00 hours and 11.59 hours. A further three women only had symptoms of nausea between 15.00 hours and 23.59 hours. Thus 95.2% of women experienced symptoms both before and after midday.

Of the 190 women reporting vomiting, 48.4% had 10 or more episodes of vomiting, while 18.9% had 40 or more episodes. The time of day that women experienced episodes of vomiting is shown in Table 2; the pattern was similar to that for symptoms of nausea. Comparison of the total number of hours of nausea among those with severe vomiting (10 or more episodes of vomiting) and those with less severe vomiting, showed that the women experiencing severe vomiting had significantly more hours of nausea than those with less severe vomiting (median 136 hours, interquartile range 60 to 295 hours versus 41 hours, interquartile range 16 to 85 hours, Mann Whitney *U* test  $P < 0.001$ ).

**Number and length of episodes per day.** A total of 247 women (84.6%) experienced days with two episodes of nausea and 163 women (55.8%) experienced days with three or more episodes at some time in their pregnancy. Of the 13 296 episodes of nausea in which length was stated, 35.7% lasted between one and two hours and a further 35.3% lasted between two and four hours. To assess at which week of pregnancy women experienced the longest episodes of nausea, the percentage of all episodes which lasted four or more hours was calculated for each woman for each week. Week nine was the median week at which the longest episodes formed the greatest percentage of all episodes (interquartile range seven to 10 weeks). Only 21 women had the majority of their episodes lasting four hours or more after week 11.

**Onset of symptoms and duration.** The women were divided into three groups: those who developed symptoms on or before day 28 from their last menstrual period, those developing symptoms between days 29 and 49, and those developing symptoms after day 49. The median and interquartile range of the duration of symptoms in days for these three groups, together with the median and interquartile range of the day symptoms ceased, are shown in Table 3. The day symptoms ceased was similar for the three groups. It follows that those whose symptoms started later had the symptoms for a significantly shorter time (Kruskal Wallis,  $P < 0.001$ ).

**Severity of early symptoms and duration of symptoms.** The relationship between early severity and duration of symptoms was investigated by comparing those women who had less than 36 hours of symptoms in all seven-day periods up to day 49 from their last menstrual period with those who had experienced more

than 36 hours of symptoms in any seven-day period up to day 49. There was no significant difference between the two groups for either the number of days the symptoms lasted or the day of cessation of symptoms.

**Time lost from paid work and housework.** Of the 363 women 206 (56.7%) were working at the time of the study. Of these women 52.4% were primigravidae as opposed to 36.9% primigravidae in the study overall. Women not working had a mean age of 25 years (standard deviation five years) compared with 26 years (standard deviation four years) for those working.

Of the 206 working women, 64.6% lost no time from work as a result of nausea and/or vomiting. The remaining 73 lost a total of 4528 hours of work; thus the mean amount of time lost per working woman in the study was 22.0 hours.

Comparison of the group of women who lost time from work with those who lost no time from work showed that those losing time had significantly worse symptoms in terms of greater total number of hours of nausea (Mann Whitney *U* test  $P < 0.001$ ) and a greater total number of episodes of vomiting (Mann Whitney *U* test  $P < 0.001$ ) (Table 4). Taking actual hours of work lost for working women there was a significant association between hours of work lost and both total number of hours of nausea suffered (Spearman rank correlation coefficient  $r = 0.51$ ,  $P < 0.001$ ) and total number of episodes of vomiting ( $r = 0.49$ ,  $P < 0.001$ ).

Data were also collected on hours of housework lost owing to symptoms of nausea and/or vomiting. A total of 93 women (25.6%) lost time from housework and half of these (46) also lost time from paid employment. A total of 3051 hours of housework

**Table 4.** Nausea and vomiting experienced by women having and not having time off work, and losing and not losing time from housework.

	Median (interquartile range)	
	Total no. of hours of nausea	Total no. of episodes of vomiting
<b>Women in paid employment</b>		
Having time off sick ( $n = 73$ )	100 (51 to 248)	9 (2 to 33)
Not having time off sick ( $n = 133$ )	20 (0 to 63)	0 (0 to 3)
<b>All women</b>		
Losing time from housework ( $n = 93$ )	121 (53 to 275)	9 (1 to 33)
Not losing time from housework ( $n = 270$ )	20.5 (0 to 66)	0 (0 to 5)

$n$  = total number of women in group.

were lost, a mean of eight hours per woman. Again, a significantly greater total number of hours of nausea (Mann Whitney *U* test  $P < 0.001$ ) and total number of episodes of vomiting (Mann Whitney *U* test  $P < 0.001$ ) were found in the group losing time from housework (Table 4).

## Discussion

The study obtained data on symptoms of nausea and vomiting in pregnancy from 363 women of varying parity, age and socio-economic status. The early initial interview (mean of 57 days from last menstrual period) has meant that, apart from the date nausea started which was frequently retrospective, detailed prospective data were obtained. It has therefore been possible to describe in detail the condition and some features of the natural history of nausea and vomiting in pregnancy.

**Table 3.** Duration of symptoms and cessation of symptoms, by time symptoms developed.

No. of days between LMP and start of symptoms	Median no. of days (interquartile range)	
	Symptoms lasted	After which symptoms ceased
<28 ( $n = 39$ )	61 (41 to 76)	82 (66 to 99)
28-49 ( $n = 210$ )	41 (28 to 53)	80 (89 to 95)
50+ ( $n = 42$ )	31.5 (15 to 45)	87.5 (74 to 102)

$n$  = number of women in group (data missing for one woman). LMP = last menstrual period.

Drawing women's attention to nausea and vomiting by using a daily diary may result in greater accuracy of reported symptoms. While vomiting is a clear end point, the reporting of which is unlikely to be affected, nausea must be a personal judgement, but there is no reason why this should influence the overall episodic pattern of symptoms. It has been found that patients who keep health diaries give more accurate information than those recalling symptoms.<sup>16</sup>

The days from last menstrual period to the start and cessation of symptoms have been described on several occasions.<sup>2,4</sup> In this study, for 72% of women symptoms were found to start between days 29 and 49 from last menstrual period and 80% to cease by day 99. Symptoms vary from pregnancy to pregnancy in the same woman.<sup>3,5-7</sup> The figures in this study suggest that about one third of women will have different symptoms in their successive pregnancies. The sudden cessation of symptoms in 39% of women was a surprising finding.

Cessation of symptoms occurred at approximately the same time, whether symptoms began early or late, and whether early symptoms were severe or mild. This may imply that one agent is involved in the aetiology of the condition and a different agent is responsible for its cessation. To identify this agent, blood samples could be taken from a woman when she has symptoms and compared with samples taken when she does not have symptoms, even on the same day, during weeks seven to nine of pregnancy when symptoms are most likely to be at their peak.

It has been thought that symptoms occur mostly in the morning<sup>17</sup> which could be taken as the six hours from 06.00 hours to 11.59 hours. In this study, this period was indeed the most common six-hour period for symptoms of nausea. Jarnfelt-Samsioe and colleagues found that 50% of women experienced peak symptoms of nausea in the morning and 36% felt sick throughout the day, while Vellacott's team found 19% complained of symptoms confined to the morning.<sup>1,14</sup> In this study, 4% of women had only morning sickness while 95% had symptoms before and after midday. The episodic nature of pregnancy sickness is rarely described.<sup>18</sup> Perhaps a more appropriate description of the condition would be episodic daytime pregnancy sickness.

The percentage of patients who had at least one episode of vomiting (52%) corresponds well with the previous findings of Tierson and colleagues<sup>2</sup> and Klebanoff and colleagues<sup>5</sup> (54% and 56%, respectively). The diaries showed that vomiting occurred with greater frequency in pregnancies in which there were more prolonged hours of nausea.

Jarnfelt-Samsioe and colleagues calculated that 12% of patients found ordinary work during pregnancy impossible.<sup>1</sup> In Vellacott and colleagues' study, 243 out of 500 women were employed.<sup>14</sup> Of these 183 (75%) complained of symptoms and 47% felt their job efficiency was reduced, with one in four actually needing time off work. The percentage of women working in the present study (57%) was similar to that in the control group in the Leicestershire perinatal study where 58% were working during pregnancy.<sup>19</sup> In the present study, 35% of working women needed 4528 hours away from their paid employment, a mean of 22 hours per working woman. A strong association was found between time lost to both paid employment and housework and the severity of pregnancy sickness symptoms. If these findings are applied to the population of England and Wales where 687 376 women gave birth in 1989 (Office of Population Censuses and Surveys data, 1989) and assuming 57% of women work during their pregnancy, then approximately 8.6 million hours per year of paid employment and 5.8 million hours per year of housework are lost through pregnancy sickness symptoms.

Observations of individual daily diaries appeared to suggest that during the period of maximum symptoms, although no two

pregnancies had exactly the same pattern, there was a consistent pattern to the daily timing, frequency and duration of episodes. It did not prove possible to quantify this statistically, but an overall predictable symptom pattern might suggest that the aetiology of the condition is organic. Prostaglandins E<sub>2</sub> released from decidual cells and macrophages of the decidua basalis, may be the main cause of the symptoms.<sup>20</sup> The symptoms may be suppressed by rising maternal serum levels of progesterone and cortisol, owing to their immunosuppressant properties.

The detailed information provided by this study should help in the investigation of the aetiology of nausea and vomiting during pregnancy.

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