

## OBSTETRICS

**Helicobacter pylori** infection: a predictor of vomiting severity in pregnancy and adverse birth outcome

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**BACKGROUND:** Nausea and occasional vomiting in early pregnancy is common. Why some women experience severe nausea and occasional vomiting in early pregnancy is unknown. Causes are multifactorial and only symptomatic treatment options are available, although adverse birth outcomes have been described. *Helicobacter pylori* infection has been implicated in the cause of nausea and occasional vomiting in early pregnancy.

**OBJECTIVE:** The purpose of this study was to investigate the association of *H pylori* with vomiting severity in pregnancy and its effect on birth outcome.

**STUDY DESIGN:** We assembled a population-based prospective cohort of pregnant women in The Netherlands. Enrolment took place between 2002 and 2006. *H pylori* serology was determined in mid gestation. Women reported whether they experienced vomiting in early, mid, and late gestation. Maternal weight was measured in the same time periods. Birth outcomes were obtained from medical records. Main outcome measures were vomiting frequency (no, occasional, daily) and duration (early, mid, late gestation), maternal weight gain, birthweight, small for gestational age, and prematurity. Data were analyzed with the use of multivariate regression.

**RESULTS:** We included 5549 Women, of whom 1932 (34.8%) reported occasional vomiting and 601 (10.8%) reported daily vomiting. Women who

were *H pylori*-positive (n=2363) were more likely to report daily vomiting (adjusted odds ratio, 1.44; 95% confidence interval, 1.16–1.78). *H pylori*-positivity was associated with a reduction of total weight gain in women with daily vomiting (adjusted difference, –2.1 kg; 95% confidence interval, –2.7 to –1.5); infants born to women with *H pylori* and daily vomiting had slightly reduced birthweight (adjusted difference –60g; 95% confidence interval, –109 – –12) and an increased risk of being small for gestational age (adjusted odds ratio, 1.49; 95% confidence interval, 1.04–2.14). *H pylori* and daily vomiting did not significantly affect prematurity rate.

**CONCLUSION:** This study suggests that *H pylori* is an independent risk factor for vomiting in pregnancy. In women with daily vomiting, *H pylori* is also associated with low maternal weight gain, reduced birth weight, and small for gestational age. Because effective treatments for severe nausea and occasional vomiting in early pregnancy are currently lacking, the effect of *H pylori* eradication therapy on nausea and occasional vomiting in early pregnancy symptom severity should be the target of future studies.

**Key words:** *Helicobacter pylori*, hyperemesis, nausea and vomiting in pregnancy, outcome, weight gain

Nausea and occasional vomiting in early pregnancy (NVP) affects 50–90% of pregnant women in the first half of gestation<sup>1</sup> and can impact greatly maternal wellbeing and quality of life.<sup>2</sup> When vomiting is severe or protracted or is accompanied by weight loss, dehydration, electrolyte disturbances, or hospitalization, it is referred to as hyperemesis gravidarum (HG).<sup>3</sup> In the absence of an internationally recognized definition, HG and severe NVP are likely to overlap in studies.<sup>4</sup>

In the Western world, severe NVP more often affects socially disadvantaged

women and those of non-Western ethnicity.<sup>5</sup> To date, there is no clear explanation for the risk differences between Western and non-Western ethnic groups. In a recent metaanalysis, colonization with the gastric bacterium *Helicobacter pylori* was associated positively with severe NVP (odds ratio [OR], 3.34; 95% confidence interval [CI], 2.92–4.81).<sup>6</sup> Interestingly, the *H pylori* prevalence in pregnant women of Western ethnicity is much lower than in women of non-Western ethnicity.<sup>7</sup> The association between *H pylori* and severe NVP has been replicated in several studies, but mainly in non-Western populations in which the prevalence of *H pylori* is high.<sup>8–10</sup> Three small studies on this topic that have been conducted in a Western setting reported conflicting findings.<sup>11–13</sup> Furthermore, some have suggested that more pathogenic variants of *H pylori*, such as cytotoxin-associated gene A (CagA)-positive strains are more

often found among women with severe NVP.<sup>14</sup> Several small studies have suggested that *H pylori* infection is associated not only with the presence of severe NVP but also associated positively with symptom severity<sup>8</sup> and persistence.<sup>10</sup>

Severe NVP has been associated repeatedly with adverse birth outcome, which includes low birthweight, small for gestational age (SGA), and prematurity<sup>15</sup>; however, the mechanism by which severe NVP may lead to adverse birth outcomes is not well understood. Weight loss or insufficient weight gain during pregnancy has been suggested to play a role,<sup>16,17</sup> although other factors such as the presence of *H pylori* on birth outcome has not been investigated.

In the present study, we investigated the hypothesis that *H pylori* is associated with vomiting severity in pregnancy and contributes to adverse birth outcomes in women with severe NVP. Furthermore, we investigated whether *H pylori*

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explains the marked ethnic differences in maternal daily vomiting incidence. The study was performed in a large prospective multiethnic cohort study in the Netherlands, the Generation R study.

## Methods

### Study population

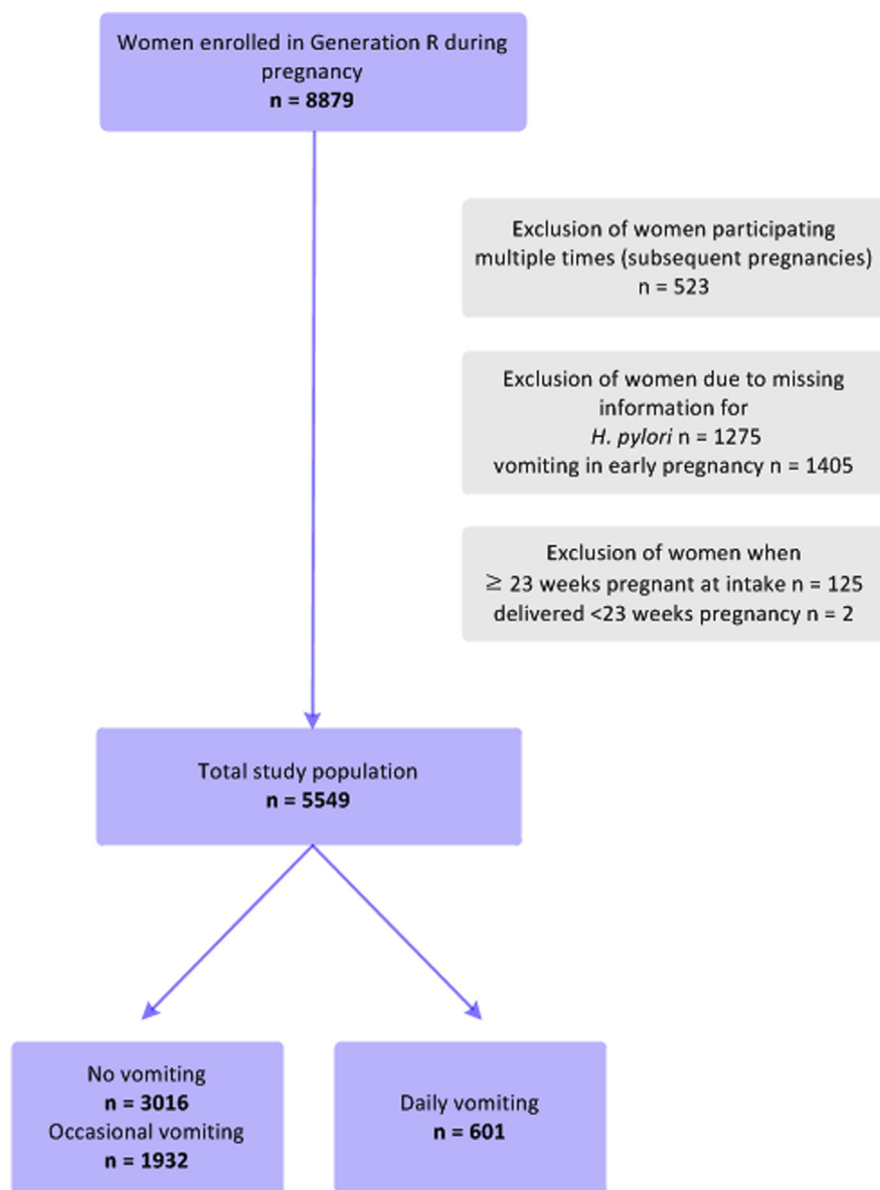
This study was embedded in the Generation R study, which is a population-based, prospective cohort study from early pregnancy until young adulthood. Approval of the Generation R Study was obtained from the Central Committee on Research that involves Human Subjects in the Netherlands via the Medical Ethics Committee of the Erasmus Medical Center, Rotterdam. All participants provided written informed consent. The study is still ongoing and conducted in Rotterdam, which is the second largest city of the Netherlands with a multiethnic community. Study design and aims have been described in detail elsewhere.<sup>18</sup> In brief, 8879 pregnant women were enrolled from 2002–2006. Women underwent physical examinations (measurement of height and weight) and filled out questionnaires in early, mid, and late gestation. These questionnaires contained information on medical history, socioeconomic background, lifestyle, and current pregnancy. The number of physical examinations and questionnaires received was dependent on the gestational age at enrolment. Serum samples were obtained during mid gestation.<sup>19</sup>

In this study, 5549 women with complete data on vomiting status in early gestation and *H pylori* serology in mid gestation were included. Women enrolled after 22 weeks gestation with no information on previous vomiting status were excluded, because vomiting that starts after this gestational age is likely to have other underlying causes. Women were also excluded if they participated multiple times in subsequent pregnancies or delivered at <23 weeks gestation (Figure 1).

### Definition of daily vomiting

There is no internationally recognized definition for severe NVP or HG. In this study, women were asked in every questionnaire whether they experienced vomiting for the past 3 months.

**FIGURE 1**  
Flow diagram of participant selection



Women were included if information on *H pylori* serology and vomiting status in early pregnancy was available.

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Answers ranged from “never” to “daily” on a 1–5 scale (never, less than once a week, once a week, few times a week, daily). If daily vomiting has been present for 3 months at study enrollment, women were considered to have severe NVP. When vomiting occurred <1 time each week, once a week, or few times a week, women were considered to have occasional vomiting. Because occasional vomiting in pregnancy is considered

physiological, women with no vomiting and occasional vomiting were considered the reference group, despite the fact there were some statistical differences in baseline characteristics between women with no vomiting and occasional vomiting (Table 1).

### Symptom severity

Symptom severity was explored according to vomiting frequency (no, occasional,

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