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Maternal characteristics largely explain poor pregnancy outcome after hyperemesis gravidarum

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ABSTRACT

Objective: To describe the characteristics of women who suffer from hyperemesis gravidarum, and explore the independent effect of hyperemesis gravidarum on pregnancy outcome.
Study design: In The Netherlands Perinatal Registry, we used all data on singleton pregnancies of at least 24 weeks and 500 g without congenital anomalies in the years 2000–2006. We examined the characteristics of women who suffered from hyperemesis gravidarum and their children.
Results: Women who suffered from hyperemesis gravidarum were slightly younger; more often primiparous, of lower socio-economic status, of non-Western descent and substance abusers; had more often conceived through assisted reproduction techniques and more often had pre-existing hypertension, diabetes mellitus and psychiatric diseases than women who did not suffer from hyperemesis gravidarum. Also, their pregnancies were more often complicated by hypertension and diabetes and they more often carried a female fetus. Pregnancies complicated by hyperemesis gravidarum significantly more often had an adverse outcome (prematurity or birth weight below the 10th percentile). The increased risk of adverse pregnancy outcomes after hyperemesis gravidarum was largely explained by the differences in maternal characteristics (crude OR 1.22 (95% CI 1.10–1.36), adjusted OR was 1.07 (95% CI 0.95–1.19)).
Conclusion: Hyperemesis gravidarum is associated with adverse pregnancy outcomes. This is largely explained by differences in maternal characteristics. Given the impact of the early environment on later health (which is independent of size at birth), studies that aim to assess the long-term consequences of hyperemesis gravidarum need to be given high priority.

1. Introduction

Nausea and vomiting in pregnancy is the most common pregnancy complication, affecting more than half of all women during the first trimester of pregnancy [1]. A more severe form of nausea and vomiting, known as hyperemesis gravidarum, is much less common, occurring in 0.5–3% of pregnancies [2–4] but is the most common cause of hospitalization in the first half of pregnancy and is the second only to preterm labour for pregnancy overall [5]. Both the aetiology and pathogenesis of hyperemesis gravidarum remain unknown [6,7].

Hyperemesis gravidarum generally occurs more often among young women in their first pregnancy, and many [2,4,8–10], but not all [7], studies found that babies born after hyperemetic pregnancies had lower birth weights. Young and primiparous women are known to have lighter babies, but none of the previous studies has taken this into account when investigating the outcome of pregnancies complicated by hyperemesis gravidarum. Therefore this study aims to investigate the independent contribution of hyperemesis gravidarum on pregnancy outcome. We describe the characteristics of women who suffer from hyperemesis gravidarum, as well as the neonatal outcomes of their babies, and investigate the independent role of hyperemesis gravidarum on pregnancy outcome.

2. Materials and methods

2.1. Netherlands Perinatal Registry

This was a population-based retrospective cohort study of all singleton deliveries after 24 weeks of gestation or more and a birth weight above 500 g in The Netherlands, between 2000 and 2006. Pregnancies with congenital anomalies (2.3%) were excluded. All

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information for this study was obtained from The Netherlands Perinatal Registry [11–15]. This registry contains population-based information on pregnancies, deliveries and (re)admissions of newborns. It is based on a validated probabilistic linkage of the national midwifery registry (LVR1), the obstetrics registry (LVR2) and the neonatology/paediatrics registry (LNR). The midwifery and obstetrics registries start at the first (booking) prenatal visit. If the child is admitted to a neonatal ward after birth, the information is collected in the neonatology registry. The registry contains information about the mother (demographic information, lifestyle, medical conditions), the pregnancy (the mode of conception, the course of pregnancy) delivery, and the baby, and covers 96% of all deliveries in The Netherlands.

2.2. Co-variates

We defined hyperemetic pregnancies as those pregnancies that were labeled during any time of pregnancy as complicated by hyperemesis gravidarum by the caregiver (either the midwife or the gynecologist). Information on parity, ethnicity, hypertension (pre-existing or pregnancy-induced), diabetes (pre-existing or pregnancy-related), thrombo-embolic disease, psychiatric disease (depression requiring medication, bipolar depression and all psychotic disorders), substance abuse (daily use of cannabis/opiates/benzodiazepines, and frequent use of hard drugs such as cocaine and heroin), and mode of conception (natural, IVF or other assisted reproduction techniques) all came from the medical records. The urbanization degree and socio-economic status were based on the four-digit postcode of the pregnant woman. Urbanization was based on the number of addresses per square kilometre and categorised as very urban ($\geq$2500 addresses/km^2), intermediate urban/rural (between 500 and 2500 addresses/km^2) and very rural ($<$500 addresses/km^2). The socio-economic status was categorised according to average price of housing based on postcode using data from The Netherlands Institute for Social Research in three categories (10th, 10–90, and $\geq$90th percentile).

2.3. Statistical methods

We compared the characteristics of women with hyperemesis gravidarum to those of women without hyperemesis using a Chi square test or a *t*-test. Secondly, we compared characteristics of the babies born to these women. Analyses were repeated for the severe cases (the women with hyperemesis gravidarum who were hospitalized during gestation). Subsequently, we performed linear and logistic regression analyses to adjust for maternal and fetal characteristics and year of birth. We examined the association between hyperemesis gravidarum and pregnancy outcome for the total population and for the liveborns only.

3. Results

In the period 2000–2006, of the 1,199,218 singleton deliveries after more than 24 weeks of gestation in The Netherlands, 2190 (0.2%) were complicated by hyperemesis gravidarum (753 as indicated by the midwife without hospital admission) and 1437 by a gynecologist as requiring hospital admission (including 607 referrals from midwives).

Table 1 shows the maternal characteristics of the 1,197,028 women without hyperemesis, and those of the 2190 with hyperemesis. Women who suffered from hyperemesis gravidarum were slightly younger, more often primiparous, more often of non-Western origin, had a lower socio-economic status, and had more often conceived through assisted reproduction techniques. Also, they reported substance abuse more often and more often had a psychiatric illness, pre-existing hypertension and diabetes mellitus. They more often carried a female fetus.

Table 1
Demographic characteristics of women with and without hyperemesis gravidarum.

	Hyperemesis	No hyperemesis	*P* value
N	2190	1,197,028	
Age (SD)	29.4 (4.8)	30.4 (4.8)	<0.0001
Primiparous	49.6%	46.3%	<0.001
Non-Western ethnicity	28.7%	16.0%	<0.0001
Low socio-economic status (10th percentile)	13.2%	9.9%	<0.0001
Living in very urban areas	20.5%	19.5%	0.26
Pre-existing hypertension	0.87%	0.32%	<0.0001
Hypertension (pre-existing or pregnancy-related)	15.6%	8.5%	<0.0001
Diabetes mellitus (type 1 and type 2)	1.0%	0.5%	0.0005
Diabetes mellitus and gestational diabetes	1.8%	0.9%	<0.0001
Thrombo-embolic diseases	0.3%	0.2%	0.36
Psychiatric illness	2.1%	0.3%	<0.0001
Substance abuse during pregnancy	0.3%	0.1%	<0.0005
Assisted reproduction	2.4%	1.7%	<0.01
Female gender child	53.7%	48.8%	<0.0001

Table 2 shows the perinatal outcomes of pregnancies complicated by hyperemesis, and those without hyperemesis. Adverse pregnancy outcomes were more prevalent among women who had suffered from hyperemesis gravidarum. Women who suffered from hyperemesis gravidarum more often delivered prematurely and more often had a baby that was small for gestational age (<10th percentile). Perinatal mortality and NICU admissions did not differ.

The maternal characteristics associated with hyperemesis (age, parity, ethnicity, mode of conception, socio-economic status, hypertension, diabetes, psychiatric illness and drugs) are all known to be associated with adverse perinatal outcomes. Therefore, we investigated whether the association between hyperemesis gravidarum and adverse pregnancy outcome was attenuated by

Table 2
Pregnancy outcomes of hyperemetic and non-hyperemetic pregnancies.

	Hyperemesis	No hyperemesis	*P* value
N	2190	1,197,028	
Fetal mortality	0.2%	0.5%	0.06
Perinatal mortality	0.3%	0.6%	0.10
Birth weight in grams (SD)	3337 (587)	3453 (579)	<0.0001
Premature (<37 weeks)	7.6%	5.7%	<0.0001
Weight below 10th percentile	10.8%	9.8%	0.11
Adverse fetal outcome[a] incl mortality	17.9%	15.1%	0.0003
Liveborn babies only			
N	2186	1,191,519	
Neonatal mortality	0.14%	0.13%	0.96
Birth weight	3337 (587)	3459 (569)	<0.0001
Premature (<37 weeks)	7.6%	5.5%	<0.0001
Weight below 10th percentile	10.8%	9.7%	0.09
NICU admission	1.2%	0.9%	0.20
Apgar <7	2.3%	2.4%	0.77
Adverse fetal outcome[a] incl mortality	3.2%	3.0%	0.68

Fetal mortality, death during gestation and during labour divided by 1000 total births; neonatal mortality, death within first week after birth divided by 1000 live births.

[a] Adverse fetal outcome, prematurity (<37 weeks) or birth weight below p10 and/or perinatal mortality.