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ORIGINAL ARTICLE

Pregnancy and neonatal outcomes following hyperemesis gravidarum

R. L. Coetzee[1,2]*, B. Cormack[2], L. Sadler[3] and F. H. Bloomfield[4,5]

[1] *Department of Human Nutrition, University of Otago, Dunedin, New Zealand*
[2] *Nutrition Services, Auckland City Hospital, Auckland, New Zealand*
[3] *Women's Health, Auckland City Hospital, Auckland, New Zealand*
[4] *Newborn Services, Auckland City Hospital, Auckland, New Zealand*
[5] *The Liggins Institute, University of Auckland, Auckland, New Zealand*

Undernutrition during pregnancy is associated with detrimental pregnancy and neonatal outcomes, which can have long-term implications for the infant. Hyperemesis gravidarum may severely limit nutritional intake. The aim of this study was to investigate the effect of hyperemesis on pregnancy and neonatal outcome, particularly gestation length and infant size at birth. Seventy-five prospectively recruited women admitted to a tertiary level hospital in Auckland, with hyperemesis gravidarum between March 2003 and October 2005, were compared to 142 controls matched for age, parity, ethnicity and expected date of delivery. Data were obtained from electronic records and analysed by Student's *t*-test, χ^2, Wilcoxon, Fisher's exact tests and linear regression. Length of gestation, birth weight and crown-heel length were not different between participants and controls. Infants born to women with hyperemesis gravidarum had smaller head circumferences (*Z*-score mean (S.D.) 0.02 (0.16) *v.* 0.43 (0.11), $P = 0.04$ in all infants and -0.02 (1.24) *v.* 0.48 (1.29), $P = 0.01$ in-term infants). This study found hyperemesis gravidarum to be associated with smaller head circumferences in offspring. Given the reported associations between smaller head circumference at birth and lower cognitive ability and higher risk of cardiovascular disease in later life, further study is necessary to confirm these results and to determine whether there are any long-term implications for the offspring.

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Key words: head circumference, hyperemesis gravidarum, neonatal outcome, pregnancy outcome

Introduction

Undernutrition during pregnancy is associated with adverse pregnancy and neonatal outcomes, which can have significant long-term implications for the health and well-being of the infant.[1–5] For example, long-term follow-up of the offspring of women exposed to the Dutch Winter Famine has shown exposure to undernutrition *in utero* to be associated with decreased glucose tolerance and increased incidence of obesity and coronary artery disease at age 50.[4,6] Nausea and vomiting is a common symptom of pregnancy[7–9] but does not usually seriously affect maternal nutritional status.[10] However, hyperemesis gravidarum, a more severe and disabling condition[11,12] characterized by weight loss, intractable vomiting, ketonuria, electrolyte disturbances and hospitalization,[13–15] affects between 0.3% and 1.5% of pregnancies[13,15,16] and can severely limit nutritional intake[17] that can have serious implications for both mother and baby.[17–19] The onset of hyperemesis gravidarum typically occurs between 4 and 10 weeks of gestation and usually resolves by the 20th week; however, for some women, symptoms persist until delivery.[20–24] Given that studies in both humans and animals have shown undernutrition during pregnancy to be associated with poor pregnancy outcomes such as preterm delivery, low birth weight and small size at birth,[25–31] we hypothesized that hyperemesis gravidarum may result in reduced length of gestation and smaller infant size at birth. Although several studies have found hyperemesis gravidarum to be associated with preterm delivery, low birth weight, congenital abnormalities and neonatal death,[13,20,32–35] others have found no association between hyperemesis gravidarum and adverse pregnancy outcome.[16,32,36–38] Previous studies of hyperemesis gravidarum and pregnancy and neonatal outcomes vary in size and methodology, use birth weight as the only measure of infant size at birth, and are often limited by a lack of control for confounding factors such as ethnicity.[39–41] The aim of this study was to compare length of gestation and infant size at birth, including weight, crown-heel length and head circumference, between women admitted to hospital for hyperemesis gravidarum and controls matched for parity, age, ethnicity and estimated date of delivery.

Method

Ethical approval was granted by the Northern Regional × Ethics Committee. Participants were prospectively identified women admitted to our hospital between March 2003 and

*Address for correspondence: F. H. Bloomfield, Liggins Institute, University of Auckland, Private Bag 92019, Victoria Street West, Auckland, 1142, New Zealand.
(Email f.bloomfield@auckland.ac.nz)

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October 2005, referred to a dietitian for hyperemesis gravidarum (International Classification for Diseases 10th edition (ICD-10) O21.0–O21.1 diagnosis codes) and who gave written informed consent to take part in a survey of nutritional issues surrounding hyperemesis gravidarum. Ethical approval to compare pregnancy and neonatal outcomes following these pregnancies with those of women who gave birth at the same time but who did not suffer from hyperemesis gravidarum was granted by the same committee under a different application. Standard treatment of women with hyperemesis gravidarum involved rehydration and electrolyte replacement, referral to a dietitian for nutritional assessment and education, prophylactic folic acid, pyridoxine, thiamine and anti-emetic prescription, including metaclopramide, cyclizine, prochlorperazine and ondansetron, in accordance with hospital policy but ultimately at the physician's discretion. Women were excluded from the survey if they had diabetes, were under 16 years of age, were taking methadone or non-prescribed drugs or were carrying twins, as multiple pregnancies have been associated with a higher incidence of hyperemesis gravidarum.[9] For each participant, two control women without hyperemesis gravidarum of the same parity, age category (⩽19, 20–24, 25–29, 30–34, 35–39 or ⩾40 years), ethnicity (European, Pacific Islander, Maori, Chinese, Indian or Other) and estimated date of delivery (to within 2 months) were retrospectively identified from the hospital database of all deliveries. If more than two appropriate matches existed, the first two with the closest match were selected, with priority given in the order of parity, age, ethnicity and then estimated date of delivery. As information on controls was abstracted from clinical records only, written consent was not required and not obtained.

Post hoc analysis to estimate the recruitment rate of women with hyperemesis gravidarum was performed using data retrieved from the hospital inpatient clinical coding database of all admissions during the study period coded as having hyperemesis gravidarum with metabolic disturbance (ICD-10 O21.1) and a length of stay of 3 or more days.

Maternal and infant data were gathered retrospectively from clinical notes. Where infant data were missing from maternal notes, they were retrieved from infant birth records and clinical notes where available. Maternal smoking status was categorized into three categories: non-smoking, smoking in the first trimester and smoking throughout pregnancy. Women who smoked before pregnancy and those who stopped smoking in the first trimester were categorized as smoking during the first trimester. Pre-pregnancy weight was generally based on recorded patient self-reported weight,[42] whereas height was extracted from prenatal records or from recorded self-reported height.[42,43] Where pre-pregnancy weight was not available, weight at the earliest gestation (under 8 weeks) was used as a surrogate.[44,45] Gestational weight gain at term was defined as the difference between final recorded weight at the last prenatal visit (after 36 completed weeks of gestation) and pre-pregnancy weight. If there was no recorded weight on admission, the first weight recorded for that hospital admission was used. Partial days of admission were counted as whole days and if readmission to hospital occurred on the same day as discharge, this was counted as the same admission. Estimated dates of delivery were derived from early ultrasound scans or, where early scan was unavailable, from last menstrual period or best clinical estimate.[46] In order to control for inconsistencies in recorded gestational age and to ensure uniformity between participants, gestational age at particular time points was calculated as the time between that particular date and that of 280 days before the estimated date of delivery. When two measurements for the same variable did not agree, the mean value was used.

Infant growth parameters were converted to *Z*-scores using Australian normative data.[47] Small or large for gestational age was defined as a *Z*-score <-1.28 or >1.28, corresponding to $<$10th or $>$90th percentile, respectively. Low birth weight was defined as birth weight $<$2,500 g.[48]

Statistical analysis was performed using JMP 7.0 (SAS Institute Inc., Cary, NC, USA). Continuous data were checked for normality, transformed where appropriate and analysed by Student's *t*-test. Data that could not be satisfactorily transformed were analysed by non-parametric Wilcoxon test. The χ^2 and Fisher's exact tests were used to analyse frequency data. Linear regression analysis by least squares function was used to analyse associations between two continuous variables. Statistical significance was taken at the $P < 0.05$ level. Data are presented as mean (S.D.), median (range) or number (%) and unadjusted relative risk (RR; 95% CI) as appropriate.

Results

Of the 79 women with hyperemesis gravidarum identified through prospective recruitment into a survey of nutritional intake, four were excluded from this study: three gave birth to twins and in one adequate data could not be obtained. For one participant, only one control could be found who adequately met the matching criteria. Of the 149 matched controls, three were identified as having hyperemesis gravidarum in the index pregnancy and four had an incorrect parity recorded in the database and were consequently excluded. Two (2.7%) women with hyperemesis gravidarum terminated their pregnancy, one (1.3%) experienced a miscarriage at 8 weeks, one (1.3%) infant died *in utero* at 20 weeks, and data were missing for one (1.3%) infant, leaving data on 70 babies in the hyperemesis gravidarum group. In the control group, there was one (0.7%) neonatal death at 21 weeks and one (0.7%) stillbirth at 39 weeks, leaving data on 140 infants.

Maternal characteristics were similar in participants and controls with the exception of smoking in early pregnancy, which was less frequent in women with hyperemesis gravidarum (Table 1). Weight in early pregnancy was used as a surrogate for pre-pregnancy weight for two participants (weight obtained at 5.0 and 6.4 weeks) and 10 controls (weight obtained between 6.0 and 7.9 weeks).

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Table 1. *Maternal characteristics*

	Participants	*n*	Controls	*n*
Age at estimated date of delivery (years)[a]	30.8 (5.1)	75	30.9 (5.0)	142
Ethnic group[b]		75		142
Pacific Islander	30 (40.0)		55 (38.7)	
European	24 (32.0)		46 (32.4)	
Indian	11 (14.6)		24 (16.9)	
Maori	2 (2.7)		4 (2.8)	
Chinese	2 (2.7)		3 (2.1)	
Other	6 (8.0)		10 (7.1)	
Smoking in first trimester[b]	5 (7.0)*	71	24 (17.5)	137
Smoking throughout pregnancy[b]	2 (2.8)	71	12 (8.8)	167
Gravity[c]	2 (1–8)	75	3 (1–7)	142
1[b]	17 (22.7)		30 (21.7)	
⩾2[b]	58 (77.3)		112 (78.3)	
Parity[c]	1 (0–5)	75	1 (0–5)	142
0[b]	25 (33.3)		48 (33.8)	
1[b]	27 (36.0)		53 (37.3)	
⩾2[b]	23 (30.7)		41 (28.9)	
Height (cm)[a]	164.7 (5.7)	65	163.4 (7.5)	105
Pre-pregnancy weight (kg)[c]	70 (48–125)	65	66 (43–116)	23
Pre-pregnancy BMI (kg/m^2)[c]	26.2 (18.2–48.2)	58	27.2 (20.3–39.3)	22

BMI, body mass index.
n denotes the number of women for whom data were available.
[a] Data are presented as mean (S.D.).
[b] Data are presented as number (%).
[c] Data are presented as median (range).
*$P < 0.05$ compared with controls.

Median gestational age on first admission for hyperemesis gravidarum was 8.1 (5.7–14.9) weeks. Women had a median of 2 (1–8) admissions for hyperemesis gravidarum and spent a median of 6 (2–61) days in hospital due to hyperemesis gravidarum. Clinical data from these admissions are summarized in Table 2. Data on vomiting symptoms before admission were available for 73 participants. The median number of vomits per day in the week preceding hospital admission was 6 (1–20), with 36 (49.3%) women vomiting more than six times per day on average. Fifty-two of 62 (83.9%) women with hyperemesis gravidarum for whom sufficient data were available lost weight during their pregnancy. Median total weight loss during pregnancy (pre-pregnancy weight minus lowest weight during pregnancy) was 5.9 (0.8–17.0) kg or 8.2 (0.9–19.6) percent of pre-pregnancy weight.

Women with hyperemesis gravidarum were more likely to have spontaneous onset of labour than controls (76.9% *v.* 57.1%, $P = 0.006$; RR = 1.35, 95% CI = 1.11–1.64), but length of gestation was not significantly different between participants and controls (median (range) 40.1 (35.7–41.9) *v.* 39.7 (31.6–43.1) weeks, $P = 0.72$ in all deliveries, 40.2 (35.7–41.6) *v.* 39.9 (31.6–41.7) weeks, $P = 0.56$ in spontaneous deliveries and 40.1 (37.1–41.9) *v.* 39.9 (37.3–42.4) weeks $P = 0.84$ in deliveries at term). Infant weight, crown-heel length and head circumference at birth were not significantly different between groups (Table 3). However, infants of women with hyperemesis gravidarum had significantly lower head circumference *Z*-scores (mean (S.D.) 0.02 (0.16) *v.* 0.43 (0.11), $P = 0.04$; Table 3). In infants born at term, both absolute head circumference and head circumference *Z*-score were significantly lower in infants of women with hyperemesis gravidarum (median (range) 34.8 (30.2–38.0) *v.* 35.5 (31.0–39.0) cm, $P = 0.02$ and mean (S.D.) −0.02 (1.24) *v.* 0.48 (1.29), $P = 0.01$, respectively; Table 4).

Women with hyperemesis gravidarum who gave birth to infants with a head circumference small for gestational age ($n = 10$) had a greater percentage weight loss during pregnancy compared to women with hyperemesis gravidarum giving birth to infants with a head circumference appropriate for gestational age ($n = 35$; median (range) 8.9 (7.7–19.6) *v.* 7.9 (1.6–16.4) percent, $P = 0.03$). There were no other significant differences in either baseline demographic factors or pregnancy-related factors (listed in Table 2) between women with hyperemesis gravidarum who gave birth to infants with a head circumference small for gestational age and those who gave birth to infants with a head circumference appropriate for gestational age.

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Table 2. *Participants' admission and clinical data*

		n
Gestational age on first admission (weeks)[a]	8.1 (5.7–14.9)	73
Number of admissions for hyperemesis gravidarum[a]	2 (1–8)	75
Total length of stay (days)[a]	6 (2–61)	74
Presence of ketonuria[b]	74 (100)	74
Ketonuria +3[b]	50 (67.6)	74
Number of vomits per day[a,c]	6 (1–20)	73
Number of participants vomiting >6 times per day[b,c]	36 (49.3)	73
Number of participants receiving enteral nutrition[b]	11 (14.7)	75
Number of participants receiving intravenous vitamins[b]	17 (22.7)	75
Weight change at first admission (kg)[a,d]	−2.2 (−17.0–8.7)	58
Percentage weight change at first admission[a,d]	3.1 (−16.4–18.1)	58
Total weight change at term (kg)[a,d]	13.6 (−10.0–21.5)	28
Number of participants with weight loss during pregnancy[b]	52 (83.9)	62
Total weight loss during pregnancy (kg)[a,e]	5.9 (0.8–17.0)	52
Percentage total weight loss during pregnancy[a,d]	8.2 (0.9–19.6)	52

n denotes number of women for whom data were available.
[a] Data are presented as median (range).
[b] Data are presented as number (%).
[c] In the week preceding hospital admission.
[d] From pre-pregnancy weight.
[e] Pre-pregnancy weight minus lowest weight during pregnancy.

Post hoc analysis revealed that of all women admitted to our hospital during the study period and coded as having hyperemesis gravidarum with metabolic disturbance (ICD-10 O21.1) and a length of stay of 3 or more days, 33% participated in the survey of nutritional issues surrounding hyperemesis gravidarum and thus were identified as participants for the purpose of this study.

Discussion

In this matched cohort study, there were no differences in length of gestation or birth weight between women with hyperemesis gravidarum and controls. However, we report that head circumference in offspring of women with hyperemesis gravidarum is significantly reduced. The additional finding that women with hyperemesis gravidarum who bore offspring with a head circumference small for gestational age had suffered greater pregnancy weight loss than those who bore offspring with a head circumference appropriate for gestational age may implicate a nutritional deficit in this association. If these findings are real, they may have important long-term implications for the infants of women with hyperemesis gravidarum, given the reported associations between smaller head circumference at birth and lower cognitive ability[49–51] and higher risk of cardiovascular disease in later life.[52] Furthermore, there also have been reports of behavioural disorders among infants born to women with hyperemesis gravidarum[24] and associations between nausea in pregnancy with early childhood temperament and behaviour problems at 12 years of age.[53] There are, to our knowledge, no long-term follow-up studies of offspring of women of hyperemesis gravidarum. Although our study did not find an association between hyperemesis gravidarum and decreased gestation length or birth weight, it is now clear that an adverse intrauterine environment can have long-term consequences for health independent of size at birth in both human and animal studies.[3,54,55] Thus, long-term follow-up of offspring is indicated, and in light of our findings of a reduced head circumference this should include assessment of neurodevelopmental and neuropsychological outcomes.

Although there have been a number of studies evaluating the effects of hyperemesis gravidarum on pregnancy and neonatal outcomes, we could identify only two matched cohort studies.[32,38] Although slightly smaller than the study by Tan *et al.*[38] our study is comparable in size to most previous observational cohort studies.[18,35–37,56] A search of MEDLINE (1950 to November 2010) and Web of Science (1898 to November 2010; English language; search terms: 'hyperemesis gravidarum', 'pregnancy outcome' and 'neonatal outcome') revealed no other study investigating crown-heel length and head circumference at birth in infants born to women with hyperemesis gravidarum. However, we did find one study, which compared pregnancy outcomes in women with any nausea and vomiting in pregnancy, with women who did not report any nausea in early pregnancy and which reported a small, statistically non-significant, reduction in head circumference at birth in infants born to women with any nausea and vomiting in pregnancy.[10] Previous studies

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Table 3. *Neonatal outcomes*

	Participants	*n*	Controls	*n*	RR (95% CI)[a]
Gestational age of all infants (weeks)[b]	40.1 (35.7–31.9)	70	39.7 (31.6–43.1)	140	
Gestational age of infants with spontaneous births (weeks)[b]	40.2 (35.7–41.6)	50	39.9 (31.6–41.7)	79	
Preterm birth (all infants)[c]	3 (4.3)	70	9 (6.4)	140	0.67 (0.19–2.35)
Preterm birth (spontaneous births)[c]	2 (4.0)	50	2 (2.5)	79	1.58 (0.23–10.86)
Infant sex		70		140	
Male[c]	41 (58.6)		79 (56.4)		1.04 (0.81–1.33)
Female[c]	29 (41.4)		61 (43.6)		0.94 (0.67–1.31)
Birth weight (g)[b]	3440 (1980–4815)	62	3540 (1010–5250)	140	
Low birth weight[c]	1 (1.6)	62	7 (5.0)	140	0.32 (0.04–2.57)
Birth weight *Z*-score[d]	0.15 (1.06)	62	0.36 (1.16)	140	
Small for gestational age[c]	4 (6.5)	62	9 (6.4)	140	1.00 (0.32–3.14)
Placental weight (g)[d]	668 (161)	49	671 (155)	133	
Crown-heel length (cm)[b]	51.0 (45.0–56.0)	61	52.0 (37.0–58.0)	137	
Crown-heel length *Z*-score[d]	0.19 (0.83)	61	0.30 (1.07)	137	
Head circumference (cm)[b]	34.5 (30.2–38.0)	61	35.5 (26.5–39.0)	137	
Head circumference *Z*-score[d]	0.02 (1.28)*	61	0.43 (1.27)	137	
Head circumference small for gestational age[c]	10 (16.4)	61	11 (8.0)	137	2.04 (0.92–4.55)
Head circumference large for gestational age[c]	12 (19.7)	61	31 (22.7)	137	0.87 (0.48–1.57)
1 min Apgar score[b]	9 (2–10)	62	9 (0–10)	140	
1 min Apgar score <7[c]	7 (11.1)	62	14 (10.0)	140	1.13 (0.48–2.66)
5 min Apgar score[b]	10 (7–10)	62	10 (4–10)	140	
5 min Apgar score <7[c]	1 (1.6)	62	2 (1.4)	140	1.13 (0.10–12.22)
Resuscitation[c]	7 (11.3)	62	9 (6.6)	137	1.72 (0.67–4.40)
Congenital abnormality[c]	3 (4.9)	61	15 (11.0)	137	0.45 (0.13–1.49)
Admitted to neonatal intensive care[c]	3 (5.3)	57	16 (11.7)	137	0.45 (0.14–1.49)

RR, relative risk.
n denotes number of infants for whom data were available.
[a] Data are presented as unadjusted RR (95% CI).
[b] Data are presented as median (range).
[c] Data are presented as number (%).
[d] Data are presented as mean (S.D.).
*$P < 0.05$ compared with controls.

have focused on birth weight as the only measure of infant size at birth; however, this is only a crude measure of foetal growth.[1,30,57,58] Broekman *et al.*[49] suggest that even small differences in size at birth, similar to those seen in this study, within the normal range, can have a clinically significant implications for intelligence in childhood. The finding of smaller head circumferences in infants born to women with hyperemesis gravidarum in this study indicates that hyperemesis gravidarum may have effects on neonatal outcomes not previously measured in this population group. Conflicting results of previous studies may be due to differences in diagnostic criteria[13–15,33] and consequent differences in severity of hyperemesis gravidarum,[33,59,60] as well as a lack of control for confounding factors such as ethnicity.[39–41] The tight matching criteria and the use of two controls for each participant in this study meant that parity, age, ethnicity and expected date of delivery were well controlled for. In addition, maternal pre-pregnancy body mass index (BMI) and offspring sex also were well matched between the groups; thus smaller head circumference is unlikely to be related to maternal pre-pregnancy BMI or an increased incidence of female offspring in the hyperemesis group. Although both a low and high BMI have been associated with and increased incidence of hyperemesis gravidarum,[32,37,61,62] results are inconsistent[56,59,60,63] and the potential underlying mechanisms unclear.[62] Similarly, some previous studies have reported a greater incidence of female offspring in pregnancies affected by hyperemesis gravidarum,[34,56] whereas others have found no significant difference.[15,16] A further strength to this study is in the diagnosis and management of women with hyperemesis gravidarum. As recruitment of study participants took place in only one hospital, as opposed to multi-centre recruitment used in a number of previous studies,[13,32,34,38] diagnosis and management of women with hyperemesis gravidarum was standardized, thus reducing the potential for heterogeneity to confound results. Furthermore, participants were identified prospectively. Hospital policy was to refer all women diagnosed with hyperemesis gravidarum to a dietitian,

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Table 4. *Gestational age and birth size of infants born at term*

	Participants	*n*	Controls	*n*	RR (95% CI)[a]
Gestational age (weeks)[b]	40.1 (37.1–41.9)	67	39.9 (37.3 to 42.4)	130	
Birth weight (g)[b]	3465 (1980–4815)	59	3580 (2040–5250)	130	
Low birth weight[c]	1 (1.7)	59	2 (1.5)	130	1.10 (0.10–11.91)
Birth weight *Z*-score[d]	0.16 (1.07)	59	0.39 (0.10)	130	
Small for gestational age[c]	4 (6.8)	59	7 (5.4)	130	1.26 (0.38–4.14)
Crown-heel length (cm)[b]	52.0 (45.0–56.0)	58	52.0 (45.5–58.0)	127	
Crown-heel length *Z*-score[d]	0.19 (0.83)	58	0.31 (1.06)	127	
Head circumference (cm)[b]	34.8 (30.2–38.0)*	58	35.5 (31.0–39.0)	127	
Head circumference *Z*-score[d]	−0.02 (1.24)*	58	0.48 (1.29)	127	
Head circumference small for gestational age[c]	10 (17.2)	58	10 (7.9)	127	2.44 (0.96–4.97)
Head circumference large for gestational age[c]	11 (19.0)	58	31 (24.4)	127	0.78 (0.42–1.44)

RR, relative risk.
n denotes number of infants for whom data were available.
[a] Data are presented as unadjusted RR (95% CI).
[b] Data are presented as median (range).
[c] Data are presented as number (%).
[d] Data are presented as mean (S.D.).
*$P < 0.05$ compared with controls.

and the dietetic service conducted a survey of nutritional issues surrounding hyperemesis gravidarum from March 2003 to October 2005, which required informed, written consent. Women were thus screened to confirm that they did indeed have hyperemesis gravidarum. We estimated that the women prospectively recruited accounted for 33% of the total admitted for 3 or more days and receiving ICD-10 O21.1 diagnostic codes. However, this does not necessarily reflect the recruitment rate into the survey, as some of these women may have been admitted for reasons other than hyperemesis gravidarum and therefore may not have been referred to the dietetic service. Furthermore, the profile of women with hyperemesis gravidarum in this study is similar to those reported in the literature,[13,18,20,32,33,36,38] and the use of matched controls helps to eliminate any bias as a result of an apparently low recruitment rate.

Although this study has considerable strengths, results should also be viewed in light of its limitations. The observational nature of the study means that associations cannot confer causality, and even though participants were matched for obvious confounders, there is potential for residual confounding. The causes of foetal growth restriction, for example, are multi-factorial[64,65] and differences in infant head circumference at birth attributed to hyperemesis gravidarum may also be influenced by other factors not measured in this study. For example, maternal psychological distress, which is also commonly associated with hyperemesis gravidarum,[11,12] has been associated with a reduced foetal head circumference *in utero*.[66] Nevertheless, studies assessing the influence of maternal nutritional status on foetal growth have found newborn length and head circumference to be positively associated with weight gain and maternal thigh skinfold measurement in mid-pregnancy, independent of maternal pre-pregnancy anthropometry,[30,67] and are consistent with the association between a greater percentage weight loss during pregnancy in mothers with hyperemesis gravidarum and the incidence bearing offspring with a head circumference small for gestational age in this study. There is also evidence to suggest that nutritional insults during pregnancy can result in permanent changes in foetal development, which in turn affect foetal growth.[2,57,68] Such events may occur in women with hyperemesis gravidarum as a result of poor nutritional intake in early pregnancy[17,24] and may explain the smaller head circumferences in infants born to women with hyperemesis gravidarum in this study. The low incidence of various outcomes and missing data for particular variables limits the confidence in detecting differences in some neonatal outcomes between women with hyperemesis gravidarum and controls. Although the actual differences in head circumference between infants born to women with hyperemesis gravidarum and infants born to controls are small, the incidence of giving birth to an infant with a head circumference small for gestational age in the hyperemesis group was twice that of the control group (although not statistically significant). Furthermore, this study is likely to underestimate the actual significance of these results given that all women in this study were diagnosed and treated for hyperemesis gravidarum, whereas globally, many women are likely to go undiagnosed or treated less aggressively.[12,24]

In conclusion, hyperemesis gravidarum was not associated with altered length of gestation, birth weight or crown-heel length but was associated with smaller head circumferences in offspring. Further study is necessary to confirm these results and long-term follow-up of infants born to women with

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hyperemesis gravidarum is needed to determine whether hyperemesis gravidarum has any long-term implications for the infant.

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Statement of Interest

None.

Ethical considerations

Ethical approval for this study was granted by the Northern Regional × Ethics Committee (Ethics No. NTX/07/102/EXP) on 4th October 2007. Ethical approval for the survey of nutritional issues surrounding hyperemesis gravidarum conducted by the dietetic service was granted by the same committee under a different application (AKX/02/00/313 'Study of women admitted to National Women's Hospital with hyperemesis gravidarum') on 28th November 2002.

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