The chance of recurrence of hyperemesis gravidarum: A systematic review

Caitlin R. Dean a,b,*, Claartje M. Bruin a, Margaret E. O’Hara b, Tessa J. Roseboom a, Mariska M. Leeflang c, René Spijker c,d, Rebecca C. Painter a

a Department of Gynaecology and Obstetrics, University Medical Centres Amsterdam, Amsterdam, the Netherlands
b Pregnancy Sickness Support, DG Normandy Way, Bodmin, Cornwall, PL31 1RB, UK
c Clinical Epidemiology and Biostatistics, University Medical Centres Amsterdam, Amsterdam, the Netherlands
d Cochrane Netherlands, Julius Center for Health Sciences and Primary Care, UMC Utrecht, Utrecht University, Heidelberglaan 100, Utrecht, the Netherlands

ARTICLE INFO
Article history:
Received 16 September 2019
Received in revised form 3 December 2019
Accepted 6 December 2019
Available online 20 December 2019

Keywords:
Hyperemesis gravidarum
Recurrence rate
Nausea and vomiting of pregnancy
Reproductive planning

ABSTRACT
Around 1% of pregnancies develop Hyperemesis Gravidarum (HG), causing high physical and psychological morbidity. Reports on HG recurrence rate in subsequent pregnancies vary widely. An accurate rate of recurrence is needed for informed reproductive decision making. Our objective is to systematically review and aggregate reported rates for HG subsequent to index pregnancies affected by HG. We searched databases from inception as per the protocol registered on PROSPERO. No language restrictions were applied. Inclusion was not restricted based on how HG was defined; reports of severe NVP were included where authors defined the condition as HG. We included descriptive epidemiological, case control and cohort study designs. Eligibility screening was performed in duplo. We extracted data on populations, study methods and outcomes of significance. A panel of patients reviewed the results and provided discussion and feedback. Quality was assessed with the JBI (2017) critical appraisal tool independently by two reviewers. We performed the searches on 1st November 2019. Our search yielded 4454 unique studies, of which five (n = 40,350 HG cases) matched eligibility criteria; One longitudinal and four population-based cohort studies from five countries. Follow-up ranged from 2 to 31 years. Definition of HG and data collection methods in all the studies created heterogeneity. Quality was low; studies lacked valid and reliable exposure, and/or follow-up was insufficient. Meta-analysis was not possible due to clinical and statistical heterogeneity. This systematic review found five heterogeneous studies reporting recurrence rates from 15 to 81%. Defining HG as hospital cases may have introduced detection bias and contribute to clinical heterogeneity. A prospective longitudinal cohort study using an internationally agreed definition of HG and outcomes meaningful to patients is required to establish the true recurrence rate of HG.

© 2019 The Author(s). Published by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).
Introduction

Hyperemesis gravidarum (HG) is a complication of pregnancy appearing at the extreme end of the pregnancy sickness spectrum. HG affects 1% of pregnancies. Unlike mild-moderate nausea and vomiting of pregnancy, which is a common, unpleasant, symptom of early pregnancy, HG can cause significant physical and psychological morbidity [1–3] and have a profound effect on quality of life [4].

The aetiology of HG is largely unknown and as yet there is no biomarker which can diagnose HG or predict the occurrence or severity of the disease in an individual [5]. A genetic aetiology would suggest that people affected would have a high chance of HG recurring in all pregnancies and recently a strong association between HG and genetic variants in two proteins was identified; growth and differentiation factor 15 (GDF15) and insulin like growth factor binding protein 7 (IGFBP7) [6]. These findings support previous reports identifying familial heredity causing a threefold increase in HG in people whose mother or sister experienced HG compared to those whose did not [7].

HG has been reported to recur in subsequent pregnancies following an affected one [8]. Appreciating the risk of recurrence enables families to plan for a prolonged period of maternal illness and evidence suggests that preventative measures such as early treatment may reduce the overall severity of the condition and holistic, practical planning of family life around the illness may reduce the biopsychosocial impacts [9,10]. Additionally, there are reports that people have terminated otherwise wanted pregnancies believing that they were unlikely to experience HG recurrence in a future pregnancy [11] and conversely, people who curtail future pregnancies believing there is no way to avoid HG in subsequent pregnancies [12]. Such significant life decisions warrant accurate information as a basis. Knowledge enabling advanced planning may help people feel more empowered which in turn may reduce the overall trauma and quality of life consequences of the condition [10].

The objective of this review is to establish the risk of recurrence of HG in a pregnancy subsequent to an affected one.

Methods

The review protocol was published in 2017 and followed the Joanna Briggs Institute (JBI) methodology for systematic reviews of descriptive epidemiological studies [13] [Available at: https://www.ncbi.nlm.nih.gov/pubmed/29135749]. No funding was received for this systematic review.

Patient involvement

Members of the patient advocacy group Pregnancy Sickness Support were first consulted to ensure the review question was considered meaningful and worthwhile, and then throughout the process for continued input. Additionally, two authors of the protocol and review (CD and MOH) are patient representatives for the condition.

Defining HG in the index pregnancy

Without an internationally recognised definition of HG, we included studies in which the authors describe nausea and vomiting in pregnancy as HG, regardless of how that diagnosis was defined or the care setting in which treatment was received. Studies in which people experienced nausea and vomiting during pregnancy, but were not diagnosed with HG were excluded. Subsequent pregnancies were not required to be consecutive and any pregnancy subsequent to the index one was considered.

Eligibility

Studies did not require non-HG pregnancy controls for the index pregnancy. Data on subsequent pregnancies must have been prospective; retrospective data on previous pregnancies were excluded. Inclusion was not restricted by geography, age of study or language.

Search strategy

The following databases were searched from inception using the search strategy outlined in Table 1: Embase, British Nursing

| Search | Terms |
|--------|-------|
| 1      | Pregnancy/ or pregnancy.mp. or pregnant*.mp. or Gestation*.mp. or Antenatal.mp. or Gravid*.mp. |
| 2      | Hyperemesis Gravidarum.mp. or Hyperemesis Gravidarum/ or Nausea/ or Nausea.mp. or Vomiting/ or Vomit*.mp. or Sickness.mp. |
| 3      | (Second or Subsequent or Successive or Recur* or Repeat or Next).mp. |
| 4      | 1 and 2 and 3 |
Reasons for exclusion

Two of the 31 articles were translated [18,19] but despite our efforts we were not able to obtain a valid translation of one paper [20]. Three conference abstracts were identified as for inclusion and the authors contacted for data or full manuscripts [21–23]. One author, of two abstracts, declined to provide further information [22,23] and the other was excluded following provision of further information [21].

We excluded 12 studies because they collected retrospective data rather than supplying prospective information to calculate a recurrence rate [19–21,24–32]. One reference was an abstract for an already excluded study [33]. One study contained overlapping data with another study from the same authors [34].

Study characteristics

Of the five included studies (see Table 2), four were large population-based database cohort studies in which three had been derived from documented hospital admissions [16,35,36] and one from a standardised form completed within a week of the birth by the attending midwife or doctor documenting maternal characteristics, pregnancy complications and birth outcomes [37]. The form does not specifically ask about pregnancy sickness or HG and so it is recorded verbatim in section B. The remaining study [12], was a cohort of people who had self-selected to take part in an online survey of the condition between 2003–2006 and were followed up in 2008 via email to see if they had a subsequent pregnancy.

The change of recurrence varies from 15.2 % in Trostgard, Stoltenberg [37] to 80.7 % in Fejzo [12]. Confidence intervals (CIs) for Fiaschi, Nelson-Piercy [35] and Nurmi [36] were not reported and so the lead authors were contacted to request further information. Fiaschi was able to provide confidence intervals but not an odds ratio (OR) as the data was no longer available. Nurmi was unable to provide an OR or CIs.

Discussion

Main findings

In this systematic review of five studies reporting 40,350 pregnancies from five countries occurring between 1967 and 2012, we found reported recurrence rate varied from 15 % to 81 %. We were unable to perform a meta-analysis and provide a summary recurrence rate due to heterogeneity (Fig 2).

Interpretation

The included studies showed significant clinical and statistical heterogeneity. Studies used diverse definitions for HG, which was the major contributor to heterogeneity. Fejzo et al. [12] found the highest estimate of recurrence of HG at 81 %. The study is a small cohort of self-selected participants followed up from a previous online survey on a charity website in which people reported their symptoms, treatments and outcomes from HG pregnancies. Only 33 % of the original cohort responded to the follow up request. HG was defined as symptoms causing significant weight loss and debility, typically requiring medication and/or IV fluids for treatment. The remaining four studies used birth registry data [37] hospital discharge data (ICD-10 codes) [16,35] or a combination of both [36]. Registraries and hospital data appear useful for pregnancy research, offering access to large population-based cohorts covering large time spans making them robust and reducing selection bias. However, it is vital that systematic validation of disease specific data is undertaken for credibility of

Index, CINAHL, MEDLINE, AMED, PsycARTICLES, PsychINFO, Global Health, Cochrane Pregnancy and Childbirth, SCOPUS. In addition to Google, the search for unpublished studies included: Pregnancy Sickness Support website, Hypermecis Education and Research Foundation website, NHS sites, British Library Explore (for British Theses) and Google scholar, Grey Literature Report and Open Grey for international Theses. Twitter was used to request knowledge of any relevant grey literature among active researchers and healthcare professionals. Key papers were hand searched for backwards citations.

Eligibility screening

Titles and abstracts were screened for eligibility by two independent reviewers (CD and CB) using Rayyan software [14] and those fitting the inclusion criteria were retrieved in full text for further eligibility screening by the two independent reviewers. Where possible, foreign language papers were translated with Google translate and then checked for accuracy by bilingual colleagues. Where there was doubt regarding inclusion a third reviewer (RP) was consulted. Data extraction of included studies utilized the standardized data extraction tool from JBI. Where possible authors were contacted for full texts or further information from published abstracts where full papers were not available.

Quality assessment

Methodological quality was assessed using standardized critical appraisal instruments from the JBI System for the Unified Management, Assessment and Review of Information, as available through the JBI (2017) critical appraisal tool downloads [15]. The tool uses 11 questions assessing: similarity of groups; validity, reliability and equality of exposure measurement; confounding factors and how they were dealt with; validity and reliability of outcome measurement; follow up duration and completeness; appropriate statistical analysis. We did not exclude papers based on low methodological scoring.

Data extraction

A data extraction form was generated from the JBI Reviewers Manual. Data extraction was completed by a single reviewer (CD). Authors were approached directly for additional details for data extraction and where possible these were provided.

Statistical analyses

As per the protocol we planned to conduct meta-analysis and assess heterogeneity using Chi-square and I2. In case of lack of studies or if heterogeneity prohibited meta-analysis, we had predefined that results would be presented narratively.

Results

Flow of in- and exclusion

We performed the search on 01-11-2019. Fig. 1 shows the Prisma flow chart of the selection process. The database searches yielded 8645 hits. Two additional references were obtained from other sources; one from hand searching key reference lists [16] and one from a public call for publications [17]. After removal of duplicates, we were left with n = 4454 unique papers. Eligibility screening of titles and abstract left n = 31 for full text assessment (Fig. 2).
such research [38]. The Medical Birth Registry Data of Norway (MBRN) generates ICD codes as used by Trogstad et al. [37], and has been validated for various birth outcomes such as early pre-term birth and birthweight, but not for medical conditions during pregnancy including hypertension [39]. While attempts have been made to validate the MBRN and ICD codes for HG, such efforts have been hampered by the lack of definition for the condition. While the Norwegian data appears to be valid for milder pregnancy sickness, they were not valid for severe pregnancy sickness or HG and nor were the ICD codes [40]. Validation studies of similar Nordic medical birth registries found that while common procedures, interventions and diagnoses are valid within the registries, occurrence of rarer complications and interventions of pregnancy could not be studied effectively with these registers.

Fig. 1. PRISMA flow diagram of selection process.

Fig. 2. Forest plot for recurrence rates of hyperemesis gravidarum.
Furthermore, MBRN data was collected only on pregnancies progressing past 16 weeks gestation until 1998 and 12 weeks gestation after 1998 which, in the context of HG, would potentially miss cases ending in termination and miscarriage [40]. Fiaschi [35] utilised ICD-10 codes which are hampered by similar challenges around definition and validity. Validation studies addressing use of ICD-10 codes for uterine rupture and second trimester miscarriage found poor positive predictive values and low sensitivity and specificity resulting from a combination of over/under reporting of conditions, multiple codes for the same condition and an inability to secure the accuracy of reported data [41,42]. So, while hospital admission data has been validated for use in birth delivery research and general nausea and vomiting of pregnancy research it cannot be assumed to be valid for use in other early pregnancy complications and specifically HG. In the context of this review the problems with the definitions, data collection methods and ICD codes diminish the validity and internal reliability of these studies and we are unable to use them to generate a reliable rate to predict recurrence of HG.

Hospital admission as an objective definition for recurrence reporting can be further criticised due to well reported barriers to accessing secondary care specific to HG. In a 2015 charity report on termination for HG many respondents were denied any treatment at primary care level and were never admitted to hospital prior to the termination of pregnancy [43]. Conversely, people who receive high quality treatment in the community may not require admission if symptoms are managed sufficiently. In a recent UK study Gadsby, Rawson [44] found significant variation in treatment of nausea and vomiting of pregnancy between primary care practices and very few secondary care referrals despite multiple presentations to general practice. Members of our patient involvement panel expressed a strong view that hospital admission was an inadequate diagnostic criterion, particularly for second pregnancies where childcare issues meant people would have little choice but to tolerate more severe symptoms without admission to hospital.

External validity

The four large cohort studies [16,35–37] only included cases where the pregnancy continued to either 16 weeks [37], 20 weeks gestation [16] or delivery [35,36] and therefore excluded pregnancies ending in earlier miscarriage or termination. The rate of termination for HG has been cited as between 10–25% which could account for a reduction in the external validity of the cohort studies in which these cases would be excluded [11,43]. The report by Dean and Murphy [43] found the inability to care for other children was given as a key factor in the decision to terminate for over half the participants suggesting that subsequent pregnancies may have a higher termination rate then first pregnancies. Additionally, Fejzo et al. [12] found 37 of the 100 respondents to their follow up request said they were not willing to get pregnant again due to the risk of HG. Neither population would be represented by the large data sets used in these studies. However, Fiaschi et al. 2016 [35] found no difference in the rate of subsequent pregnancy between people with a history of HG and those without.

In 2017 O’Hara [17] explored 172 people’s experience of recurrent HG and, despite similar levels of symptom severity between pregnancies, she found that hospital admissions were reduced in subsequent pregnancies for a variety of factors. Increased support from healthcare professionals, family and friends in the later pregnancy helped them to cope without hospital admission but also the demands of childcare and a desire to not be separated from their other children meant people were reluctant to be admitted. Additionally, second- and third-line

| Study reference |
|------------------|
| Trogstad et al 2005 [37] |
| Fell et al 2006 [16] |
| Fejzo et al 2011 [12] |
| Fiaschi et al 2016 [35] |
| Nurmi et al 2018 [36] |

| Study design |
|---------------|
| Population-based database cohort study |
| Population-based database cohort study Canada 1988–2002 (14yrs) |
| Cohort study using online survey United States 2008 follow up from 2003 to 2006 (2–5yrs) |
| Population-based database cohort study United Kingdom 1997–2012 (15yrs) |
| Population-based database cohort study Finland 2004–2011 (7yrs) |

| Country |
|--------|
| Norway 1967–1998 (31 yrs) |

| Data collection period |
|------------------------|
| All documented singleton pregnancies >16 weeks with a 1st and 2nd pregnancy registered |
| All documented pregnancies >20 weeks with delivery of infant >500 g. |
| Self-reported symptoms severe enough to cause weight loss and require prescription medication or IV fluids/total parental nutrition/NG tube feeding or hospitalisation |
| Hospital admission coded with ICD-10 for primary diagnosis of HG. |
| All pregnancies ending in delivery with an HG discharge diagnosis within the first 20 weeks of pregnancy |

| HG definition |
|---------------|
| HG cases: 4796 Controls: 542442 HG described as pregnancy nausea and vomiting associated with ketosis and >5% weight loss. Also via ICD-8 as 638.0, 638.9 or 784.1. |
| HG cases: 447 Controls: 83910 Admission to hospital prior to 24 weeks gestation for HG |
| Self-reported surveys |
| Hospital Episodic Statistics data. |
| Medical births register (completed following delivery) and Hospital discharge register |

| Participants |
|--------------|
| Norwegian |
| All documented singleton pregnancies >16 weeks with a 1st and 2nd pregnancy registered |

| Data collection |
|-----------------|
| Reported on standardised form completed by midwife/physician within one week of delivery, form does not specifically ask about HG so would be recorded as verbatim description under “other” and subsequently coded according to ICD-8 as above |
| The Nova Scotia Atlee Perinatal Database data which records all antepartum admissions during pregnancy. Data abstracted by trained coders. |
| Hospital records |
| Medical births register (completed following delivery) and Hospital discharge register |
medications, such as ondansetron and steroids, were more commonly used in subsequent pregnancies and so although severe symptoms were still experienced, they were better controlled to avoid the need for admission. Based on the diagnostic criteria which lead to ICD code generation for HG in subsequent pregnancies within the included population-based cohort studies it is likely that recurrence is underestimated due to the lack of early pregnancy loss inclusion and reduced admissions identified by O’Hara.

Strengths and limitations

Among the strengths of this study, are a published protocol, the broad scope, and complete patient involvement throughout the review from inception of the question to interpretation of the finding. A significant limitation of the study is the lack of studies with suitable, homogeneous definitions of HG and data collection methods which decreased external validity through exclusion of potentially important cases.

Conclusion

While this review cannot provide a definitive rate for people to base important reproductive decisions on, a history of HG remains a substantial risk factor and healthcare professionals can advise people that the risk of recurrence is high enough to warrant pre-pregnancy planning.

A large prospective cohort study for HG is needed to follow people through their reproductive lives to establish the nature and course of the condition and the rate of recurrence in subsequent pregnancies. However, recruitment for such a study would need careful consideration and would be significantly aided by an internationally agreed definition for the condition so as not to rely on arbitrary criteria such as hospital admission [45].

Statement of author contribution

Contribution to authorship: CD was lead author throughout conception, planning, carrying out and writing up. CB assisted with abstract screening. MOH provided patient input during conception, planning, analysis and write up. TJR provided supervision throughout. ML assisted with statistical analysis of results and forest plot generation. RS conducted the searches. RCP provided supervision throughout. All authors reviewed the manuscript.

Funding

No funding was received.

Declaration of Competing Interest

There are no conflicts of interest to declare.

References

[1] Fiaschi L, Nelson-Piercy C, Gibson J, Szatkowski L, Tata LJ. Adverse maternal and birth outcomes in women admitted to hospital for hyperemesis gravidarum: a population-based cohort study. Paediatr Perinat Epidemiol 2018;32(1):40–51.
[2] Mullin PM, Ching C, Schoenberg F, MacGibbon K, Romero R, Goodwin TM, et al. Risk factors, treatments, and outcomes associated with prolonged hyperemesis gravidarum. J Matern Fetal Neonatal Med 2012;25(6):632–6.
[3] Mitchell-Jones N, Gallos I, Farren J, Tobias A, Bottomley C, Bourne T. Psychological morbidity associated with hyperemesis gravidarum: a systematic review and meta-analysis. BJog 2017;124(1):20–30.
[4] Dean CR, Bannigan K, Marsden J. Reviewing the effect of hyperemesis gravidarum on women's lives and mental health. Br J Midwifery 2018;26(2):109–10.
[5] Nienmeijer MN, Grooten JJ, Vos NB, Bais MJL, van der Post JA, Mol BWL, et al. Diagnostic markers for hyperemesis gravidarum: a systematic review and metaanalysis. Am J Obstet Gynecol 2012;211(2):150.e1–e15.
[6] Fejoz MS, Sazonova OV, Sathiyasagarsuri JF, Hallgrimsmóttir IB, 23andMe Research Team, Vavic V, et al. Placenta and appetite genes GDF15 and IGBP7 are associated with hyperemesis gravidarum. Nat Commun 2019;10(1178):1–9.
[7] Vikanes Å, Skjærven R, Grifjóhová AM, Gunnès N, Vangen S, Magnus P. Recurrence of hyperemesis gravidarum across generations: population-based cohort study. BMJ 2010;340:c2050.
[8] Royal College of Obstetricians and Gynaecologists. The management of nausea and vomiting of pregnancy and hyperemesis gravidarum. London: Royal College of Obstetricians and Gynaecologists; 2016.
[9] Koren G, Maltepe C. Preemptive Diclectin therapy for the management of nausea and vomiting of pregnancy and hyperemesis gravidarum. Am J Obstet Gynecol 2013;208(1):520–5.
[10] Dean CR, Helping women prepare for hyperemesis gravidarum. Br J Midwifery 2014;22(12):847–52.
[11] Poursharif B, Korst L, MacGibbon K, Fejoz M, Romero R, Goodwin T. Elective pregnancy termination in a large cohort of women with hyperemesis gravidarum. Contraception 2007;76(6):451–5.
[12] Fejoz MS, MacGibbon KW, Romero R, Goodwin TM, Mullin PM. Recurrence risk of hyperemesis gravidarum. J Midwifery Womens Health 2011;56(2):122–6.
[13] Dean CR, Bannigan K, O’Hara M, Painter RC, Marsden J. Recurrence rates of hyperemesis gravidarum in pregnancy: a systematic review protocol. JBI Database System Rev Implement Rep 2017;15(11):2659–65.
[14] Ouzzani M, Hannay M, Fedorowicz Z, Elmargarmid A, Rayyan - a web and mobile app for systematic reviews. Syst Rev 2016;5(201):1–10.
[15] The Joanna Briggs Institute. Critical appraisal tool downloads. Available from: http://joannabriggs.org/research/critical-appraisal-tools.html.
[16] Bell DR, Dodds I, Joseph KS, Allen VM, Butler B. Risk factors for hyperemesis gravidarum requiring hospital admission during pregnancy. Obstet Gynecol 2006;107(2):277–84.
[17] O’Hara M. Experience of hyperemesis gravidarum in a subsequent pregnancy. MIDIRS 2017;27(1):309–19.
[18] Huirle B. Nausea and vomiting during pregnancy: prevalence, etiology, evaluation, treatment recommendations. Schweizer Zeitschrift für Gynäkologie. 2011;161:29–30.
[19] Cribari Z, Ouldamer L, Body G, Bacq Y. Hyperemesis gravidarum: a ten-year French retrospective study of 109 patients. Presse Médicale 2015;44(1): e13–22.
[20] Buss A. The tendency to recurrence in hyperemesis gravidarum. Harefuah 1964;67:84–7.
[21] Hameroff A, Mniarji V, Talus P, Nacharaju V, Charles C, Price N, et al. Prostaglandin levels in pregnant women with and without hyperemesis gravidarum. Reprod Sci 2017;24(1 Supplement 1):121A–2A.
[22] Fassett MJ, Peltier MR, Getahun D. Hyperemesis gravidarum: risk of recurrence in subsequent pregnancies. Reprod Sci 2017;24(1 Supplement 1):85A–6A.
[23] Fassett MJ, Wing DA, Shaw SF, Im TM, Getahun D. Recurrence risk of hyperemesis gravidarum in successive pregnancies. Reprod Sci 2019;26(1 Supplement 1):94A–5A.
[24] Fejoz MS, Ching C, Schoenberg FP, MacGibbon KW, Romero R, Goodwin TM, et al. Change in pregnancy and recurrence of hyperemesis gravidarum. J Matern Fetal Neonatal Med 2012;25(8):1241–5.
[25] Kamalak Z, Köşüş N, Köşüş A, Hızlı D, Ayrım A, Kurt G. Is there any effect of demographic features on development of hyperemesis gravidarum in the Turkish population? Turk J Med Sci 2013;43(6):995–9.
[26] Koren G, Maltepe C. Pre-emptive therapy for severe nausea and vomiting of pregnancy and hyperemesis gravidarum. J Obstet Gynaecol 2004;24(5):530–3.
[27] Majerus PW, Guze SB, Delong WB, Robins E. Psychotic factors and psychiatric disease in hyperemesis gravidarum: a follow-up study of 69 vometers and 66 controls. Am J Psychiatry 1960;117(5):421–9.
[28] Maltepe C, Koren G. Pre-emptive diclectin treatment for nausea and vomiting of pregnancy: results of a randomized controlled trial. Birth Defects Res (Part A) – Clin Mol Teratol 2012;94(5):327.
[29] Tan IV, Jacobsen KH. Risk factors for hyperemesis gravidarum. Curr Womens Health Rev 2010;6(4):309–17.
[30] Tylden E. Hyperemesis and physiological vomiting. J Psychosom Res 1968;12(1):85–93.
[31] Hall RE. The treatment of hyperemesis gravidarum with chlorpromazine. Am J Obstet Gynecol 1956;71(2):285–90.
[32] Fejoz MS, Arzy D, Tian R, MacGibbon KW, Mullin PM. Evidence GDF15 plays a role in familial and recurrent hyperemesis gravidarum. Geburtshilfe Frauenheilkd 2018;78(9):866–70.
[33] Koren G, Maltepe C. Preemptive Diclectin therapy for the management of nausea and vomiting of pregnancy and hyperemesis gravidarum. Am J Obstet Gynecol 2005;293:Suppl. 1:S50.
[34] Magtira A, Paik Schoenberg F, MacGibbon KW, Tabsh K, Fejoz MS. Psychiatric factors do not affect recurrence risk of hyperemesis gravidarum. J Obstet Gynaecol Res 2015;41(4):512–6.
[35] Fiaschi L, Nelson-Piercy C, Tata LJ. Hospital admission for hyperemesis gravidarum: a nationwide study of occurrence, recurrence and risk factors among 8.2 million pregnancies. Hum Reprod 2016;31(August 8):1675–84.
[36] Nurmi M, Rautava P, Cissler M, Vahberg T, Polo-Kantola P. Recurrence patterns of hyperemesis gravidarum. Am J Obstet Gynecol 2018;219(5):469.e1–469.e10.
[37] Trogstad L, Stoltenberg C, Magnus P, Skjaerven R, Irgens L. Recurrence risk in hyperemesis gravidarum. BJOG 2005;112(12):1641–5.
[38] Langhoff-Roos J, Krebs L, Klungsoyr K, Bjarnadottir RI, Kallen K, Tapper AM, et al. The Nordic medical birth register—a potential goldmine for clinical research. Acta Obstet Gynecol Scand 2014;93(2):132–7.
[39] Moth FN, Sebastian TR, Horn J, Rich-Edwards J, Romundstad PR, Asvold BO. Validity of a selection of pregnancy complications in the Medical Birth Registry of Norway. Acta Obstet Gynecol Scand 2016;95(5):519–27.
[40] Vikanes Å, Magnus P, Vangen S, Lomsdal S, Gjeibovski AM. Hyperemesis gravidarum in the Medical Birth Registry of Norway – a validity study. BMC Pregnancy Childbirth 2012;12(15):1–6.
[41] Thisted DL, Mortensen LH, Hvidman L, Rasmussen SC, Larsen T, Krebs L. Use of ICD-10 codes to monitor uterine rupture: validation of a national birth registry. Eur J Obstet Gynecol Reprod Biol 2014;173:23–8.
[42] Sneider K, Langhoff-Roos J, Sundtoft IB, Christiansen OB. Validation of second trimester miscarriages and spontaneous deliveries. Clin Epidemiol 2015;7:517–27.
[43] Dean C, Murphy C. I could not survive another day: improving treatment and tackling stigma: lessons from women’s experiences of abortion for severe pregnancy sickness. London: Pregnancy Sickness Support and BPAS; 2015.
[44] Gadsby R, Rawson V, Dziadulewicz E, Rousseau B, Collings H. Nausea and vomiting of pregnancy and resource implications: the NVP Impact Study. Br J Gen Pract 2019;69(680):e217–23.
[45] Roseboom TJ, Painter RC, Grooten IJ, van’t Hooft J. Development of a definition and core outcome set for studies in hyperemesis gravidarum. Available from:. 2015. http://www.comet-initiative.org/studies/details/805.