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## International Colloquium on Hyperemesis Gravidarum 2024

***6–7 November 2024, Ventura, California, USA***

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# CONTENTS

***International Colloquium on Hyperemesis Gravidarum 2024***

## 001

**GDF15 and the pathogenesis of pregnancy sickness**

Stephen O'Rahilly MD FRS
MRC Metabolic Disease Unit, Institute of Metabolic Science, University of Cambridge, Cambridge, UK
so104@cam.ac.uk

GDF15 was identified in 1999 by Breit as a member of the TGF beta superfamily produced by a wide range of cells in response to cellular stressors. Breit showed that it reduced food intake through actions in the hindbrain and subsequently several groups identified its receptor; a heterodimer of GFRAL and Ret. In 2000 Breit reported that GDF15 levels were elevated in thvalente plasma of pregnant women and that placental expression of *GDF15* was high. In 2017/18, Fejzo *et al*. reported that genetic variants close to GDF15 were strongly associated with Hyperemesis Gravidarum and that women with HG had higher circulating levels of GDF15 and the O'Rahilly lab, working independently, found that women who vomited in pregnancy had higher levels of GDF15 than those who did not. In 2019, our collaborators at Pfizer reported that GDF15 administration was aversive in mice.

The O'Rahilly and Fejzo labs collaborated to discover the following

1. Using, for the first time, an assay that reliably measured GDF15, we established that levels of GDF15 in maternal plasma were significantly higher both in women with HG vs controls (at ~9 weeks gestation) and in a separate study in women reporting vomiting in pregnancy vs those who did not (at ~15 weeks gestation). There was, however, substantial overlap in GDF15 levels between affected and unaffected women so, alone, GDF15 levels could not fully explain HG.
2. Using a natural labelling experiment, we established that >95% of the GDF15 present in maternal circulation was encoded by the fetus.
3. Studying rare and common variants in the maternal GDF15 gene we showed that alleles that are associated with HG are associated with **lower** levels of circulating GDF15 in the non-pregnant state.
4. We found that women with thalassemia, who have very high levels of GDF15 rarely develop significant nausea or vomiting in pregnancy.
5. We showed that pre-exposure of mice to elevated levels of GDF15 reduces the effect of a subsequent bolus of GDF15, establishing that GDF15 is a hormone exposure to which induces desensitisation.

In conclusion, pregnancy sickness including HG appears to be due to combination of higher levels of GDF15 produced by the placenta from the fetal genome and greater sensitivity of the mother to the effects of GDF15, something which is strongly influenced by pre-pregnancy exposure to the hormone. These findings have obvious implications for therapy and prevention, both of which are being explored.

Keywords: GDF15, Hyperemesis gravidarum, pregnancy sickness

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## 002

**Nutrition and perinatal health**

Amy M. Valent
Department Obstetrics & Gynecology, Oregon Health & Science University, Portland Oregon, U.S.A
Email address: valent@ohsu.edu

Review of the role of nutrition in perinatal health and outcomes. The objectives are aimed to recognize the complexity of food, lifestyle behaviors, and metabolic health; understand the role of nutritional health in preconception, pregnancy and perinatal outcomes; and practical applications to address nutritional health in pregnancy to promote sustainable lifestyle modifications and reduce adverse perinatal outcomes. Preconception, pregnancy, and postpartum are all opportunities to improve health.[1] Micro- and macronutrients have vital roles in normal fetal growth and development.[2] Interventions for nutritionally challenged conditions such as hyperemesis gravidarum should focus on optimizing quality of intake and not just interventions targeted to treat nausea and vomiting.[3-5]

Keywords: Nutrition, perinatal health, preconception, hyperemesis

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## 003

**The association between the hyperemesis level prediction score and nutritional intake in the first trimester in a pregnancy sickness cohort**

Kate Maslin[1,*], Caitlin Dean[2,3] & Jill Shawe[1,4]
[1]University of Plymouth, Devon, UK; [2]UK Pregnancy Sickness Support Charity, Bodmin, UK; [3]Amsterdam UMC, University of Amsterdam, Amsterdam, the Netherlands; [4]Royal Cornwall Hospital NHS Trust, Truro, UK;
Email Address: kate.maslin@plymouth.ac.uk (Kate Maslin)

A total of 166 participants were recruited at a median gestation of 8 (IQR 3) weeks, with 84.2% ($n=139$) being multiparous. Among them, 19.9% ($n = 43$), 46.8% ($n = 101$), and 10.2% ($n = 22$) experienced mild, moderate, and severe HELP symptoms, respectively. Seventy participants completed the food diary. The total HELP score was inversely moderately correlated with energy (rho=-0.572, $P < 0.001$), protein (rho=-0.509, $P < 0.001$), and vitamin C intakes (rho=-0.516, $P < 0.001$). Weaker inverse correlations were observed for iron, zinc, vitamin A, thiamine, riboflavin, and vitamin B12 intakes (rho $< 0.4$, $P < 0.001$ for all). Responses to the statement "I have been able to eat/drink and keep it down" showed a strong inverse association with energy intake (rho=-0.650, $P < 0.001$) and moderate associations with protein, iron, calcium, zinc, thiamine, riboflavin, vitamins B12 and C (rho between -0.4 to -0.6, $P < 0.001$ for all). These findings suggest that the HELP score is a moderately strong proxy measurement for energy and protein intake in the first trimester. However, a more detailed dietary analysis is required to accurately assess micronutrient intakes.

Keywords: Hyperemesis Gravidarum, HELP Score, Nutritional Intake, Pregnancy, Energy Intake, Micronutrients, Diet Diary

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## 004

**Dietary intakes pre- and post-intervention: results from the IRIS clinic study**

Clíodhna Ryan[1], Sarah Louise Killeen[2], Jean Doherty[2], Melanie Bennett[2], Lillian Murtagh[2], Sinead Curran[2], Suzanne Murphy[2], Lucille Sheehy[2], Helen McHale[2] & Eileen O'Brien[1*]
[1]School of Biological, Health and Sports Science, Technological University Dublin, Ireland; [2]The National Maternity Hospital, Holles Street, Dublin 2, Ireland
Email Address: Eileen.OBrien@TUDublin.ie (Eileen O'Brien)

Hyperemesis gravidarum (HG) negatively impacts dietary intake and gestational weight gain. The IRIS Clinic at the National Maternity Hospital, Ireland, was established to provide specialised weekly care to individuals with HG, incorporating multidisciplinary support from dietitians, midwives, obstetricians, pharmacists, perinatal mental health midwives, and catering staff. This study aimed to analyse the impact of the clinic on dietary intakes. This quasi-experimental study employed a pre-test and post-test design. Participants ($n = 31$) were recruited from the IRIS clinic and completed a questionnaire on admission (pre-intervention) and 6–8 weeks later (post-intervention). Data collected at both time points included 24-hour dietary recall, HG symptoms (PUQE score), maternal wellbeing, food tolerance, and demographic information. Data were analysed using paired sample t-tests and chi-square tests. Participants had a mean (SD) gestational age of 12.4 (4.3) weeks and age of 31.5 (5.9) years upon admission. Most (61%) were nulliparous, and half (52%) had a BMI within the normal range (18.5–24.9 kg/m$^2$). The mean (SD) PUQE score was 10.3 (2.9) pre-intervention, reducing non-significantly to 7.2 (3.7) post-intervention. Dietary

energy intake (kcal/day) significantly increased from pre- to post-intervention (1077 [431] vs. 1493 [542], $P = 0.001$). Intakes of carbohydrate, protein, fat, iron, calcium, and omega-3 fatty acids also significantly increased post-intervention, though all measured nutrients remained below recommended pregnancy intakes. Tolerance to various food characteristics and groups improved post-intervention. An increase in dietary intakes and food tolerance was observed among attendees of the IRIS Clinic, demonstrating the positive impact of this multidisciplinary intervention. However, persistent nutrient shortfalls highlight the need for ongoing dietary interventions throughout pregnancy.

Keywords: Hyperemesis Gravidarum, Dietary Intake, Nutrition, Multidisciplinary Clinic, PUQE Score, Pregnancy, Food Tolerance

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## 005

### Comparative efficacy of promethazine versus ondansetron in the management of hyperemesis gravidarum: a randomized controlled trial at gulu regional referral hospital, northern uganda

Kizza Blair[1], Kaweesi Henry[1] & Murungi Jacky[1]
[1]Usawa Health Initiative Uganda, Kampala, Uganda
Email Address: kizzablair@yahoo.com (Kizza Blair)

Hyperemesis Gravidarum (HG) is a severe form of pregnancy-induced nausea and vomiting, posing significant risks to maternal and fetal health. Limited data exist on the comparative efficacy and safety of promethazine versus ondansetron in managing HG, especially in resource-constrained settings. The objective of this study was to compare the effectiveness, safety, and cost-effectiveness of promethazine versus ondansetron in managing HG among primigravid women in Northern Uganda. A randomized controlled trial was conducted with 150 primigravid women diagnosed with HG. Participants were randomly assigned to receive promethazine (25 mg orally every 6 hours) or ondansetron (4 mg orally every 8 hours). The primary outcome was the reduction in nausea and vomiting severity, measured using the Pregnancy-Unique Quantification of Emesis (PUQE) score. Secondary outcomes included maternal weight gain, gestational age at delivery, neonatal outcomes, and cost-effectiveness. The results showed the ondansetron group had a mean PUQE score reduction of 13.2 points (95% CI: 11.5–14.8), compared to 9.1 points (95% CI: 7.6–10.6) in the promethazine group ($P$ 0.01). Women treated with ondansetron gained 4.8 kg (95% CI: 4.3–5.3) on average, compared to 3.2 kg (95% CI: 2.8–3.6) in the promethazine group ($P = 0.04$). The ondansetron group had a mean gestational age of 39.1 weeks (95% CI: 38.7–39.5) compared to 37.4 weeks (95% CI: 37.0–37.8) for the promethazine group ($P = 0.02$). Neonates in the ondansetron group had a higher mean birth weight (3.3 kg, 95% CI: 3.1–3.5) compared to those in the promethazine group (2.9 kg, 95% CI: 2.7–3.1) ($P = 0.01$). Adverse effects were lower in the ondansetron group (5% vs. 15%, $P = 0.01$). Ondansetron reduced overall healthcare costs by minimizing hospital admissions and complications, making it more cost-effective despite higher medication costs. In conclusion, Ondansetron demonstrated superior efficacy, safety, and cost-effectiveness compared to promethazine, making it the preferred treatment option for managing HG in low-resource settings. These findings support the need for updated treatment protocols to improve maternal and neonatal outcomes in similar contexts.

Keywords: Hyperemesis Gravidarum, Ondansetron, Promethazine, PUQE Score, Maternal Health, Neonatal Outcomes, Cost-Effectiveness, Low-Resource Settings

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## 006

### Hyperemesis gravidarum and GDF-15 in women with polycystic ovary syndrome

Susanne Koskinen Edblom[1*], Beatrice Haack[2], Malin Nording[3], Marie Bixo[4], Eszter Vanky[4, 5], Jörg Wischhusen[6], Marlena Fejzo[7] & Marie-Therese Vinnars[1]
[1]Department of Clinical Sciences, Obstetrics and Gynecology, Umeå University, Umeå, Sweden.; [2]Brandenburg Medical School, University Clinic for Psychiatry and Psychotherapy, Immanuel Klinik Rüdersdorf, Seebad 82/83, 15562, Rüdersdorf bei Berlin, Germany.; [3]Department of Chemistry, Umeå University, 901 87 Umeå, Sweden.; [4]Department of Clinical and Molecular Medicine, Faculty of Medicine and Health Sciences, Norwegian University of Science and Technology, Trondheim, Norway.; [5]Department of Obstetrics and Gynecology, St. Olav's Hospital, Trondheim University Hospital, Trondheim, Norway.; [6]Section for Experimental Tumor Immunology, Department of Obstetrics and Gynecology, University Hospital of Würzburg, Würzburg, Germany.; [7]Center for Genetic Epidemiology, Department of Population and Public Health Sciences, Keck School of Medicine, University of Southern California, Los Angeles, CA, USA.
Email address: susanne.koskinen.edblom@umu.se (S Koskinen Edblom)*, haack_b@ukw.de (B Haack), malin.nording@umu.se (M Nording), marie.bixo@umu.se (M Bixo), eszter.vanky@ntnu.no (E Vanky), Wischhusen_J@ukw.de (J Wischhusen), marlena.fejzo@med.usc.edu (M Fejzo), marie-therese.vinnars@umu.se (M-T Vinnars)

Polycystic ovary syndrome (PCOS) may be associated with lower pre-pregnancy GDF-15 levels which we hypothesize could increase their risk for hyperemesis gravidarum (HG). Our objectives were to study the potential association between HG and PCOS, and to measure GDF-15 in pregnant women with PCOS. A cohort study including 793 women with HG, and 571 controls with self-reported PCOS; and 57 pregnant women with PCOS, and systematically registered nausea, antiemetic use, and sick leave due to HG. GDF-15 was measured in the PCOS cohort ($n = 57$) and in 13 healthy pregnant controls. We used t-test and odds ratio with logistic regression. We found increased odds for PCOS diagnosis in the HG cohort, (OR 2.0, 95% CI:1.1-3.5, $P = 0.02$). In the PCOS cohort ($n = 57$), 58 % reported nausea, and 12% were on HG treatment/sick leave. In early pregnancy, the median (IQR) GDF-15 was 9.2 (7.4-11.6) ng/ml in women with PCOS, compared to 10.5 (9.1-16.8) ng/ml in controls ($P = 0.036$). No difference was seen between PCOS on HG treatment/sick leave, compared to the remaining women with PCOS ($P = 0.16$). At mid-pregnancy (gw19), the median (IQR) was 78.2 (59.7-95.8) ng/ml in PCOS with nausea, compared to 55.9 (46.3-73.3) ng/ml in the remaining ($P = 0.019$). In late pregnancy (gw36), the median (IQR) GDF-15 was 92.2 (59.2-106.2) ng/ml in those PCOS with early pregnancy HG treatment/sick leave, compared to 58.7 (47.0-78.0) ng/ml in the remaining women with PCOS ($P = 0.034$). In conclusion, women with PCOS have an increased risk for HG. High increase in GDF-15 was associated with HG.

Keywords: GDF-15, polycystic ovary syndrome, PCOS, hyperemesis gravidarum, HG

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## 007

**Expanding models of care for nausea and vomiting in pregnancy and hyperemesis gravidarum: integrating at-home iv therapy**

Iqra Khan
South Eastern Sydney Local Health District, New South Wales, Australia
Email Address: iqra.khan@health.nsw.gov.au

In July 2022, the NSW Ministry of Health launched a four-year project aimed at improving care for women experiencing Nausea and Vomiting in Pregnancy (NVP) and Hyperemesis Gravidarum (HG). As part of this initiative, we've developed educational resources, enhanced data collection tools, and expanded services for women affected by HG. Most notably, we've introduced new models of care, including the option for administering IV fluids at home. The objectives were to deliver safe and efficient NVP/HG care with clear, streamlined pathways for healthcare professionals, to offer at-home care for women experiencing NVP/HG to minimise disruption to their personal lives and to reduce hospital costs by decreasing the need for day or inpatient stays. We partnered with existing Hospital in the Home (HITH) services to expand care to include women experiencing NVP/HG. Referrals were accepted from GPs, ED, and Day Units where women typically receive fluid administration. New guidelines were developed to ensure safe and appropriate care in the home setting. We have successfully launched the program at 2 out of 3 sites. Over the past 10 months, we've provided care to 24 women in HITH settings for HG, with care durations ranging from 4 to 42 days. Our estimated savings to the Local Health District are approximately AUD $551,785.92 in hospital costs. We've also seen a significant decrease in ED presentations and re-presentations. Women have reported much better outcomes, benefiting from more intensive care at home. This has allowed them to continue working, socialising, and spending time with their families with minimal disruption to their personal lives. Overall, the feedback has been overwhelmingly positive.

Keywords: Hyperemesis Gravidarum, Nausea and Vomiting in Pregnancy, At-Home Care, Hospital in the Home, IV Therapy, Healthcare Cost Savings, Patient Outcomes

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## 008

**NGM120, a GFRAL antagonist antibody, for investigation of safety, tolerability, and efficacy in hyperemesis gravidarum**

Joanne Sloan-Lancaster[1*], Kefei Zhou[1], Carroll Henschel[1], Ursula Jeffry[1], Vladimir Hanes[1], Liza Melchor-Khan[1], Katherine Wu[1], Kelly Byrnes-Blake[2], Alessandro Palumbo[1], Zimple Matharu[1], Matthias Scherr[1], Bin Fan[1], Alan Kutach[1], Zhefu Dai[1], Leanne Wong[1], Richard Ventura[3], Jade Bojkovic[1], Arthur Hsu[1] & Hsiao D. Lieu[1]
[1]NGM Biopharmaceuticals, South San Francisco, CA, USA; [2]Northwest PK Solutions, Bothwell, WA, USA; [3]TCG Labs, Soleil, South San Francisco, CA, USA
Email Addresses: jlancaster@ngmbio.com (Joanne Sloan-Lancaster)*

Hyperemesis Gravidarum (HG) is an intractable form of nausea and vomiting associated with pregnancy (NVP), which can lead to complications in both the mother and infant. The hormone GDF15 and its receptor GFRAL have been linked to HG through human genetics. Serum GDF15 increases throughout pregnancy, primarily derived from the feto-placental unit, and GDF15 levels are higher in pregnant women with NVP and HG compared to those without these symptoms. Clinical studies show that administration of GDF15 induces nausea and vomiting. NGM120 is an antagonistic monoclonal antibody that specifically binds to GFRAL, exclusively expressed in the area postrema of the hindbrain, which mediates nausea and vomiting. The safety of NGM120, including reproductive and developmental assessments, has been established in animal studies, and its safety and pharmacokinetics have been assessed in humans. Additionally, individuals with mutational loss of GDF15 function are healthy and fertile, supporting the hypothesis that inhibition of GDF15 signaling may be safe in pregnancy. A clinical study is planned to evaluate the safety, tolerability, and efficacy of NGM120 in pregnant women with HG. Participants will receive a single subcutaneous dose of NGM120 alongside ondansetron and intravenous fluids during the initial phase of the study. Safety and tolerability will be monitored throughout gestation and postpartum in both infant and mother. Efficacy will be assessed using HG-specific patient-reported outcomes and numeric rating scales. Further details will be presented.

Keywords: Hyperemesis Gravidarum, GFRAL, NGM120, GDF15, Monoclonal Antibody, Pregnancy, Nausea and Vomiting

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## 009

**Hyperemesis gravidarum and cannabis use in an international sample**

Lizbeth S. Becerra[1], Ellie Lewis[1], Kimber MacGibbon[2], Rachel Carmen Ceasar[1] & Marlena Fejzo[1*]
[1]Department of Population and Public Health Sciences, Keck School of Medicine, University of Southern California, Los Angeles, CA USA; [2]Hyperemesis Education and Research Foundation, Clackamas, OR USA
lsbecerr@usc.edu; elewis48@jh.edu; kimber@hyperemesis.org; rceasar@usc.edu; fejzo@usc.edu

This study examines treatments including cannabis/cannabis-based products (CBP) for Hyperemesis Gravidarum (HG). Survey data was collected between April 2022-June 2024. Pearson's Chi-Square and pairwise comparison tests were utilized to study differences in proportions. From free-text responses on whether CBP improved symptoms, we used AI-driven content analysis. Respondents ($n$ = 5,933) from 79 countries reported their doctor prescribed medication for HG (95%) with no geographical/ethnic differences in diagnosis or prescriptions. Among 625 participants reporting cannabis use, 56% used it because prescribed antiemetics did not work well enough. Approximately half (54%) initiated use during pregnancy; 82% reported symptom relief, and 37% reported weight-gain within 2 weeks of cannabis use compared to 14% for prescription treatment. There were no ethnic/regional differences for when use began. Cannabis use was higher ($P$ 0.001) for individuals in rural areas. A higher proportion of American Indian (23%) and Black individuals (21%) used cannabis compared to Asian (3.8%) and White (10.7%) individuals ($P$ 0.001). Similar proportions of Asian and Black participants took ondansetron, but Asian participants were 2.3-fold more likely to report it effective ($P$ = 0.001). Participants ($n$ = 503) described a wide range of administration, strains, dosage, and frequency to self-medicate. While cannabis did not provide total/consistent relief, many described it allowed them to hold down food/water, stimulate hunger, and reduce symptoms. Cannabis was reportedly more effective than prescription medications in enabling pregnancy weight gain. Medication ineffectiveness may drive cannabis use and associated disparities. Survey results should be interpreted with caution until cannabis- and medication-associated maternal/child outcomes are compared.

Keywords: hyperemesis gravidarum; cannabis; ondansetron

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## 010

**Hyperemesis gravidarum and risk of maternal and child morbidity**

Sarit Kang-Auger[1], Gabriel Côté-Corriveau[1,2,3], Phillipe Bégin[1,2,3] Émilie Brousseau[2,4], Jessica Healy-Profitós[2,4] & Nathalie Auger[2,4,5,6]
[1]Faculty of Medicine, University of Montreal, Montreal, Canada; [2]University of Montreal Hospital Research Centre, Montreal, Canada; [3]Sainte-Justine Hospital Research Centre, Montreal, Canada; [4]Institut national de santé publique du Québec, Montreal, Canada; [5]School of Public Health, University of Montreal, Montreal, Canada; [6]Department of Epidemiology, Biostatics and Occupational Health, McGill University, Montreal, Canada
Email address: sarit.kang-auger@umontreal.ca (Sarit Kang-Auger), emilie.brousseau@inspq.qc.ca (Émilie Brousseau), jessica.profitos@inspq.qc.ca (Jessica Healy-Profitós), nathalie.auger@insqc.qc.ca (Nathalie Auger)

Hyperemesis gravidarum (HG) is a leading cause of morbidity during pregnancy and has potential to affect maternal health and fetal development. Our first objective was to determine the association between HG and severe maternal morbidity.[1] Our second objective was to examine the association between HG and child morbidity.[2] We conducted a retrospective cohort study of hospital deliveries between 1989 and 2021, and a longitudinal cohort study of children born between 2006 and 2021. We used hospital discharge data from Quebec, Canada. The main exposure was maternal hyperemesis gravidarum requiring hospitalization or noted on the prenatal chart. The first outcome was severe maternal morbidity during pregnancy or up to 42 days postpartum. The second outcome was pediatric admission up to 16 years of age. We used adjusted regression models to calculate risk ratios, hazard ratios and 95% confidence intervals (CI) for the association

between maternal HG and maternal and child morbidity. This study included 2.5 million pregnancies, 17 thousand of which were hospitalized for HG. Patients with HG were 1.5 times more at risk of developing any severe maternal morbidity (95% CI 1.4-1.6) compared with no HG. In adjusted models, patients with HG were 6.4 times more at risk of developing hepatic complications such as hepatic failure or fatty liver disease. Patients with HG were approximately 2.3 times more at risk of developing embolism/shock (95% CI 1.8-2.9), acute renal failure (95% CI 1.7-3.5) and cerebrovascular accidents (95% CI 1.1-4.5) compared to patients with no HG. Among 1.2 million children included in our longitudinal cohort, 7 thousand were born from mothers with HG. Children exposed to maternal HG had higher hospitalization rates at 16 years of age compared to unexposed children (47.6 vs 43.9 per 100 children). Children born from mothers with HG were 1.5 times more at risk of being hospitalized for developmental (95% CI 1.3-1.8), neurologic (95% CI 1.3-1.7), digestive (95% CI 1.3-1.5), or atopic disorders (95% CI 1.2-1.6) compared to unexposed children.In conclusion, these studies found that hyperemesis gravidarum is associated with severe maternal morbidities, including hepatic, cerebrovascular, renal complications at delivery or up to 42 days postpartum. We also found an association between maternal hyperemesis and risk of childhood hospitalization, especially for developmental, neurologic, digestive, and atopic disorders.

Keywords: Hyperemesis gravidarum, pregnancy complications, perinatal outcomes, fetal development, nutritional deficiency, pediatrics

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## 011

### Prednisolone weaning for hyperemesis gravidarum treatment - slow and steady leads to success

Kathryn Filipczuk[1,*], Penelope Fotheringham[1,2], Natalie Cromer[1], Debra Kennedy[1] & Delwyn Cupitt[1]
[1] MotherSafe, The Royal Hospital for Women, Randwick, Australia; [2] University of Sydney, Camperdown, Australia
Email address: kathryn.filipczuk@health.nsw.gov.au (Kathryn Filipczuk)

Background
Prednisolone is a third-line oral antiemetic for hyperemesis gravidarum (HG) which can be considered if other treatments have failed. Current HG guidelines leave significant scope for interpretation with respect to prednisolone weaning advice. In NSW, Australia, a specialized medicines information telephone service received 1193 calls relating to NVP/HG, from consumers and healthcare professionals, between April-2023 and June-2024.
Objective
To increase awareness and understanding of how to dose and wean prednisolone slowly for HG, to achieve significant and sustained reduction in severe HG symptoms.
Method
Specialized staff were trained to assess symptoms and provide evidence-based advice regarding treatments. Patients were offered follow-up calls to assess progress. For prednisolone weaning advice, international NVP/HG guidelines were reviewed in detail. Throughout the literature, there were variations in weaning practices, and a gap in specific practice points to guide prednisolone weaning, particularly slower weaning. To address this, we developed a step-by-step, evidence-based guide for weaning prednisolone slowly.
Results
Success of prednisolone weaning was evaluated through follow up calls. While following the slower prednisolone weaning protocol, patients reported a significant and sustained reduction in the intensity of nausea and frequency of vomiting and retching. Most patients described this as "life-changing" for their severe HG symptoms and quality of life.
Conclusion
Effective prednisolone weaning can significantly improve severe HG symptoms and quality of life. In the future, it would be useful if international HG guidelines include slower prednisolone weaning advice, and detailed practice points, to further assist with prednisolone weaning in the management of HG.

Keywords: HG, hyperemesis, prednisolone, weaning, pregnancy

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## 012

### Pre-pregnancy metformin use associated with decreased risk of hyperemesis gravidarum

Neelu Sharma[1], Kimber MacGibbon[2], Aimee Brecht-Doscher[3], Victoria Cortessis[1] & Marlena Fejzo[1*]
[1]Department of Population and Public Health Sciences, Keck School of Medicine, University of Southern California, Los Angeles, CA USA; [2]Hyperemesis Education and Research Foundation, Clackamas, OR USA; [3]Ventura County Medical Center, Ventura, CA USA
Neelusha@usc.edu; Kimber@hyperemesis.org, Aimee@hyperemesis.org, Cortessi@usc.edu; Fejzo@usc.edu

Identifying effective, safe, and affordable treatment of HG is critical to improving maternal and child health. We recently demonstrated that genetic predisposition to HG is mediated by low pre-pregnancy levels of GDF15, resulting in hypersensitivity to its rise during pregnancy. Because metformin increases GDF15, we hypothesized that its use before pregnancy will desensitize patients to GDF15 and lower HG risk. By structured questionnaire, visitors to HER Foundation Social Media sites from January-July 2022 reported daily use of 33 common substances in the month before each pregnancy and level of NVP. Crude and multivariate associations between use of substances were estimated by logistic regression. Associations between use of each substance and severe NVP/HG in the subsequent pregnancy was estimated by logistic regression. Multivariate models included tobacco use and maternal age; number and type of additional drugs used, and race/ethnicity had little influence and were not retained. Estimates for first and second pregnancies were combined by random effects meta-analysis. Participants from 46 countries reported on 3,740 pregnancies. Using metformin before pregnancy was significantly associated with lower risk of severe NVP/HG [adjusted OR = 0.42 (95%CI = 0.20-0.88)], as was using cyclobenzaprine (aOR = 0.30;95%CI = 0.10-0.89) and tobacco (aOR = 0.40;95%CI = 0.28-0.56). Pre-pregnancy metformin treatment may ameliorate NVP symptoms. Generic metformin, which is routinely used prior to and during pregnancy for other conditions, may be a safe and affordable treatment to prevent HG. Clinical trials are warranted to investigate its use prior to pregnancy to lower HG risk and mitigate the associated adverse maternal and offspring outcomes.

Keywords: Hyperemesis Gravidarum; metformin; tobacco

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## 013

### We need more clinical trials for hg: a recent nasem report provides a roadmap for how to do it

Margaret Foster Riley[1]
[1]Schools of Law, Medicine, Miller Center and Batten School of Leadership and Public Policy, University of Virginia, Charlottesville, VA United States.
Email address:mimiriley@law.virginia.edu (Margaret Foster Riley)

Pregnant women with hyperemesis gravidarum (HG) and their health care providers must make difficult decisions about their health every day. These difficult decisions are compounded by a widespread lack of evidence on the dosing, safety, and efficacy of potential treatments or concomitant medications. Pregnancy is not a single condition. It leads to physiological changes across different trimesters that can affect how the body interacts with and metabolizes medications, including cardiovascular, respiratory, gastrointestinal, metabolic, and renal system changes. There is international consensus that the lack of data about the effects of medications during pregnancy stems from a reluctance to include pregnant women in clinical research. This reluctance is heightened by the complexities of HG. A recent report from the National Academies of Science, Engineering and Medicine (NASEM), *Clinical Research with Pregnant and Lactating Populations: Overcoming Real and Perceived Liability Risks*, debunks one of the underlying bases for the reluctance to include pregnant women in research, fear of legal liability, and provides a framework for conducting clinical research with pregnant women that minimizes harm. The report addresses the major obstacles to including pregnant women in research: the culture of exclusion; challenges in recruiting participants; lack of expertise in research involving pregnant women; reputational risk; cost and complexity of trials; and the lack of financial incentives. To address these obstacles, the report recommends improving FDA and HHS guidance for clinical trials involving new drugs and drugs already on the market, providing additional incentives for conducting the research and protections for researchers and participants in the research. This research is essential to providing better outcomes for women suffering from HG and their offspring. They deserve nothing less.

Keywords: Hyperemesis Gravidarum, Pregnancy, Clinical Trials, NASEM, FDA, NIH

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## 014

**Hyperemesis histories: charting the evolution of HG health policy**

Jennifer Fraser[1]
[1]Department of Global Health and Social Medicine, King's College London, London, UK
Email address: jennifer.fraser@kcl.ac.uk (Jennifer Fraser)

Hyperemesis gravidarum (HG) has been a misunderstood and often mismanaged condition. However, in January 2024 HG was integrated into England's 2024 Women's Health Strategy—a landmark achievement, which ensures that HG is recognised and represented in the government's new priorities for women's health [1]. The inclusion of HG in the 2024 Women's Health Strategy is just one example of a fleury of HG awareness and activism that has taken place in recent years. In 2023, an international study shed crucial light on the aetiology of morning sickness by demonstrating a link between pregnancy sickness and GDF15—a hormone produced by the foetus that, in high quantities, can elicit nausea and appetite loss [2]. In February, Marlena Fejzo, the American geneticist and lead author of this work, was named one of *Time* Magazine's Women of the Year [3]. In this period of unprecedented political support for improving the lives of women affected by HG, this presentation explores the history of HG policy development and discusses the importance of understanding how experiences and understandings of nausea and vomiting during pregnancy have evolved in different national and international contexts across time. In particular, I will focus on two ongoing oral history projects being carried out in the UK and Canada, respectively. The objectives of this research are to build a robust archive of patient and policy voices that will offer a snapshot of how the HG research and policy landscape has changed over the past sixty years and highlight the value history holds in revealing the multi-levelled milieus in which HG appears, lives, and operates.

Keywords: Hyperemesis gravidarum; Health and Social Welfare Policy; Medical History; Patient Voices

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## 015

**Nausea and vomiting during pregnancy: a method to explore food-related choices, perception, and symptoms management strategies**

Anaëlle Venturini[1,2], Anestis Dougkas[1], Philippe Deruelle[3] & Audrey Cosson[1,*]
[1]Nutrition and Eating Behaviour team, Institut Lyfe Research and Innovation Centre, Ecully, France; [2]Department, Université Claure-Bernard Lyon 1, Villeurbanne, France; [3]Service de Gynécologie-obstétrique, Centre Hospitalier Universitaire Montpellier, Montpellier, France
Email address: aventurini@institutlyfe.com.com (Anaëlle Venturini), adougkas@institutlyfe.com (Anestis Dougkas), philippe.deruelle@chu-montpellier.fr (Philippe Deruelle), acosson@institutlyfe.com (Audrey Cosson)

Background
Food-related sensory alterations in pregnant women, particularly those suffering from Nausea and Vomiting during Pregnancy (NVP), can impact food appreciation, selection, and overall diet quality. However, the associations between NVP severity, sensory perception and dietary choices remain poorly understood.
Objective
This is a protocol for a study that aims to investigate the relationships between NVP severity and changes in food choices and perception, as well as to explore coping mechanisms employed by pregnant women to manage symptoms.
Method
This is a mixed method combining quantitative and qualitative data. The study targets 600 french-speaking pregnant women who are under 16 weeks of gestation and present varying levels of NVP severity. An online questionnaire will be distributed between January and June 20205. The questionnaire will include inquiries on pregnancy history, demographics, NVP severity (PUQE score), sensory changes, presence and number of cravings and aversions, evaluation of the ability of food items and sensory stimuli to trigger or alleviate nausea and/or vomiting, and open-ended questions regarding food-related coping mechanisms. From the questionnaire responses, 20 women with moderate or severe NVP (PUQE $\geq$ 7) will be invited to participate in semi-directive interviews. The interview guide will cover food and sensory experience since pregnancy onset, voluntary and involuntary dietary changes, internal and external symptoms management strategies and coping mechanisms, and availability and effectiveness of specific food strategies and recommendations.
Analysis
Descriptive analyses will characterize the sample. Regression models will assess relationships between NVP severity and variables such as sensory changes, number of cravings and aversions and dietary adjustments. Analysis of variance will compare groups based on NVP severity (none, moderate, severe/HG). Thematic analysis will be applied on interviews transcripts to identify common themes regarding food experience and sensory/dietary strategies.
Results
Anticipated findings include increased degree of sensory alterations for greater NVP severity; increased number of food cravings and aversions in women with higher NVP severity; identification of common coping mechanisms and dietary strategies to alleviate symptoms. These findings aim to inform tailored dietary recommendations and support strategies for pregnant women experiencing NVP, contributing to improved quality of life.

Keywords: Pregnancy, Nausea, Vomiting, Sensory, Dietary adjustments
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## 016

**Hyperemesis gravidarum in social media**

Ariana Guandique Reyes[1] & Dr. Aimee Brecht-Doscher, MD*
[1]Department Obstetrics and Gynecology, Ventura County Medical Center, Ventura, California, USA; [2]University of California, Santa Barbara, California, USA
Email Address: ariana.guandique16@gmail.com (Ariana Guandique Reyes); aimee.brecht-doscher@ventura.org (Aimee Brecht-Doscher)

Social media has become a convenient source for healthcare information; however, the accuracy of social media content on medical conditions is a growing concern due to the prevalence of misinformation. This study evaluates the accuracy of hyperemesis gravidarum (HG)-related posts on social media platforms. We analyzed 30 fact-based posts from Instagram, Facebook, Reddit, and TikTok, gathered between 2023 and 2024, using a content accuracy scale from 1 (no evidence-based information) to 5 (highly accurate). Posts were classified by originator—clinicians (physicians, nurses, midwives) versus non-clinicians. Findings indicate that content was accurate, with a mean score of 4.03. Clinician-authored posts had a higher average accuracy rating (4.50) compared to non-clinician posts (3.68) ($P = 0.02$). Ratings did not vary significantly across platforms ($P = 0.95$). Both clinicians (2 posts) and non-clinicians (8 posts) posted inaccurate content defined as an average score less than 4. These results underscore the need for caution when seeking HG information on social media, as misinformation can be present regardless of the source. The study further emphasizes the importance of enhanced education on HG for both clinicians and non-clinicians and improved fact-checking practices for health-related content on social media platforms.

Keywords: Hyperemesis Gravidarum, Social Media, Misinformation

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## 017

**Ongoing food aversions in the postnatal period in the nourish pregnancy sickness study**

Kate Maslin[1*], Caitlin Dean[2,3] & Jill Shawe[1,4]
[1]University of Plymouth, Devon, UK; [2]UK Pregnancy Sickness Support Charity, Bodmin, UK; [3]Amsterdam UMC, University of Amsterdam,

Amsterdam, the Netherlands [4]Royal Cornwall Hospital NHS Trust, Truro, UK
Email Address: kate.maslin@plymouth.ac.uk (Kate Maslin)

The objective of this study was to explore postnatal eating and drinking experiences in a pregnancy sickness cohort. The Nutritional Online Survey for Pregnancy Induced Sickness & Hyperemesis (NOURISH) study is a United Kingdom-based online prospective study. Pregnant women were recruited online and completed questionnaires during each trimester. Two weeks postnatally, participants were sent a follow-up online questionnaire that included the Pregnancy-Unique Quantification of Emesis and Nausea (PUQE-24) and open-ended questions about eating habits. A total of 100 participants completed the postnatal questionnaire. Based on first trimester PUQE-24 scores, 19% ($n = 19$), 67% ($n = 67$), and 14% ($n = 14$) were categorized as having mild, moderate, and severe symptoms, respectively. Of these, 41% ($n = 41$), including 30 participants with moderate symptoms, had been hospitalized for sickness during pregnancy. At the time of the postnatal questionnaire, all participants had mild symptoms (PUQE-24 score $<6$). In terms of dietary intake, 49% reported eating the same amount as before pregnancy, 19% ate less, and 32% consumed more. In response to the open-ended question, "Please tell us about how nausea and sickness of pregnancy has influenced your eating habits or appetite/thirst?" there were 63 comments, 49 of which were negative. Most comments referenced ongoing food aversions, with 13 comments highlighting ongoing thirst or dehydration. These findings indicate that, despite mild postnatal symptoms according to PUQE-24, 19% of participants ate less than before pregnancy, and nearly half reported negative changes in appetite and/or thirst. The longer-term effects of pregnancy sickness on dietary habits warrant further investigation.

Keywords: Pregnancy Sickness, Hyperemesis Gravidarum, Postnatal Nutrition, PUQE-24, Food Aversions, Thirst, Dietary Habits

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## 018

### No evidence for shared genetic risk factors for hyperemesis gravidarum and breast cancer

Wendy Setiawan, Jacob Haiman, Xinran Wang, Nick Mancuso & Marlena Fejzo*
Department of Population and Public Health Sciences, Center for Genetic Epidemiology, Keck School of Medicine, University of Southern California, Los Angeles, California, USA
vsetiawa@med.usc.edu;jehaiman@icloud.com;xinran.wang@med.usc.edu; nicholas.mancuso@med.usc.edu; marlena.fejzo@med.usc.edu

Prospective studies have reported positive associations between having a history of hyperemesis gravidarum and developing breast cancer in the future, with stronger evidence for HER+ tumors. We investigated whether this relationship may be due to shared biological mechanisms by examining established genetic risk loci for hyperemesis gravidarum in association with breast cancer risk and intrinsic breast cancer subtypes. For this study, we leveraged publicly available breast cancer genetic summary statistics from the Breast Cancer Association Consortium (BCAC, Ahern *et al*. 2022), which includes genome-wide association data for overall breast cancer (106,571 cases and 95,762 controls) and intrinsic-like subtypes, including Luminal A-like ($n = 27,510$ cases), Luminal B-like/HER2-negative ($n = 6,804$ cases), Luminal B-like/HER2-positive ($n = 6,511$), HER2-postive/non-luminal ($n = 2,797$) and Triple-negative breast cancer ($n = 7,178$) among women of European ancestry. The hyperemesis gravidarum-risk variants examined were rs1058587 in *GDF15*, rs9312688 at *IGFBP7* and rs12790159 at *PGR*. For overall breast cancer, the per allele odds ratio was 0.99 ($P = 0.18$) for rs1058587, 1.01 ($P = 0.07$) for rs9312688 and 1.00 ($P = 0.40$) for rs12790159. No significant associations were observed with any variant and risk of breast cancer intrinsic-like subtypes. In summary, utilizing data from the largest genetic study of breast cancer, we found no significant evidence for shared genetic risk loci between hyperemesis gravidarum and overall breast cancer, HER+ tumors or any intrinsic-like subtype. The suggested association reported between hyperemesis gravidarum and breast cancer risk may be due to exposure to hyperemesis gravidarum rather than shared mechanisms from genetic risk loci.

Keywords: Hyperemesis Gravidarum, Breast cancer, genetic

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## 019

### Hyperemesis gravidarum and associated nail changes: report of a case

Marla Jahnke MD
Department of Dermatology, Henry Ford Health, Detroit, MI
Email address: Mjahnke1@hfhs.org

In hyperemesis gravidarum (HG), pregnant women experience significant nausea and vomiting during pregnancy. While case reports largely describe comorbidities during pregnancy in women suffering from HG, few studies have reported on patient outcomes post-partum. Nail abnormalities can provide insight into a variety of systemic diseases. Prior to the reporting of this case, no publications could be identified to date describing any nail findings as a post-partum pregnancy outcome related to HG. A 36-year-old female presented to dermatology with toenail pain and bleeding during two recent pedicures when the nail technician attempted to clip her first toenails. Her past medical history was significant for two severe HG pregnancies, most recently two years prior, requiring extensive hospitalization. Additionally, at 6 months pregnant she showed her obstetrician an abnormal dent in all of her toenails. At the time of her dermatology visit, she had normal appearing nail plates although they were notably long. The hyponychium of her bilateral first toenails, however, was attached to the ventral nail plate with very scant free margin. The patient was diagnosed with acquired pterygium inversum unguis (PUI). Photos from 6 months of pregnancy showed deep transverse grooves in the nail plates. The grooves were approximately 5 mm distal from the proximal nail fold and the patient was given a diagnosis of Beau lines. Tian, MacGibbon, Mullin, Martin and Fejzo published a unique landmark paper describing a breadth of patient outcomes in HG. Further characterization of their findings is an important future research opportunity. Although many healthy pregnant women experience nail changes, this case adds the first known report of Acquired Pterygium Unguis Inversum (PUI) associated with either pregnancy or HG and Beau's lines with HG. PUI is a rare condition in which the hyponychium attaches to the ventral nail plate and obliterates the distal nail groove.Previously reported causes may include acrylic nails, connective tissue diseases, leprosy and stroke. Beau's lines coincide with nail matrix arrest usually due to severe illness, hospitalization or other stressful events. Toenails grow approximately 1mm per month, therefore this patient's Beau's line would coincide with her first hospitalization at approximately 5 weeks pregnant.

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## 020

### A new mass spectrometry method to detect lipid metabolites in urine for studies on hyperemesis gravidarum

Khoa Huynh[1]* & Malin L. Nording[1]
[1]Department of Chemistry, Umeå University, Sweden
Email address: khoa.huynh@umu.se (Khoa Huynh), malin.nording@u-mu.se (Malin Nording)

Mass spectrometry methods enable the detection of metabolite profiles in clinical samples, facilitating the assessment of maternal physiological changes on the molecular level associated with pregnancy. Notably, lipid metabolites hold significant importance across diverse conditions, especially in relation to inflammation and the immune response, although their exploration in the context of Hyperemesis Gravidarum (HG) is limited.[1–3] The purpose was to establish a non-invasive urine analysis for bioactive lipid metabolites – oxylipins, including prostaglandins and related compounds, thereby facilitating investigations of HG-dependent physiological changes in relation to nausea and vomiting during pregnancy. A targeted liquid chromatography coupled to tandem mass spectrometry (LC-MS/MS) method was optimized and validated with regard to clinically relevant lipid metabolites in urine. Sample preparation protocols were developed based on solid phase extraction (SPE) and dispersive solid phase extraction (dSPE) using HKUST-1 metal organic framework material for isolation and concentration of oxylipins under study. LC-MS/MS method performance was assessed by native and isotopically labelled standards for recovery rates, matrix effects, accuracy, precision, limit-of-quantification and limit-of-detection. The resulting method satisfied the validation criteria and was successfully applied to urine. The pathophysiology of HG remains incompletely understood, involving a complex interplay between susceptibility genes, metabolic pathways, and environmental factors like diet. The role of oxylipins remains unclear

though they may be linked to GDF-15 – a hormone implicated in HG.[4,5] The new method will be valuable in addressing these factors since it provides a link between diet, lipid metabolism, and clinical manifestations of HG. The method will be particularly useful in studies concerning GDF15 given its associations with the lipid metabolism and its involvement, along with its receptor, in the mechanism of nausea and vomiting.

Keywords: Mass spectrometry, LC-MS/MS, oxylipins, HKUST-1, biomarkers, hyperemesis gravidarum

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## 021

### Analysis of biomarkers GDF15 and IGFBP7 in black and white patients with hyperemesis gravidarum

Ellie Lewis[1], Andrew Housholder[2] & Marlena Fejzo[1*]
[1]Department of Population and Public Health Sciences, Center for Genetic Epidemiology, Keck School of Medicine, University of Southern California, Los Angeles, California, USA; [2]Morning Sickness Clinic, Birmingham, Alabama, USA
elewis48@jh.edu; andrew.housholder@gmail.com; fejzo@usc.edu*

GDF15 and IGFBP7 are associated with HG with higher circulating levels of the placentally expressed appetite proteins in patients hospitalized with HG compared to unaffected pregnant women at 12 weeks' gestation. Black women are more likely to be hospitalized with HG, but little is known about the levels of these proteins in this disproportionately affected population. Herein we aimed to compare levels of GDF15 and IGFBP7 in Black compared to White people affected by HG. Circulating levels of GDF15 and IGFBP7 were measured by ELISA assays. Mean levels were compared in Black and White HG patients. Among 65 participants, 22 were Black patients with an average gestational age at first clinic visit of 9.6 weeks, and 43 were White patients with an average gestational age of 10.0 weeks. Average HELP and PUQE scores were higher for Black patients at first and second visits, with more weight loss from pre-pregnancy weight at first visit for Black patients. On average, Black patients lost weight from first to second visit, while White patients gained weight. Mean circulating level of GDF15 at first visit was 16.1 ng/ml in Black patients and 13.2 ng/ml in White patients. Mean circulating level of IGFBP7 at first visit was 92.4 ng/ml in Black patients and 91.7 ng/ml in White patients. Disparities in HG may be related to biological differences in levels of placenta and appetite protein GDF15. Further studies with larger sample sizes should be performed to determine reproducibility of the results.

Keywords: Hyperemesis Gravidarum, GDF15, IGFBP7, Disparities

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## 022

### Nausea and vomiting of pregnancy – associations with pregnancy and delivery complications

Anna Murto[*1,2], Linda Laitinen[3], Miina Nurmi[2], Mari Koivisto[4,5] & Päivi Polo-Kantola[2]
[1]1Department of Obstetrics and Gynecology, Vaasa Central Hospital, Vaasa, Finland; [2]Department of Obstetrics and Gynecology, Turku University Hospital and University of Turku, Turku, Finland; [3]Wellbeing Services County of Central Finland, Hospital Nova, Jyväskylä, Finland and University of Turku, Turku, Finland; [4]Turku Clinical Research Centre, Turku University Hospital, Turku, Finland; [5]Department of Biostatistics, University of Turku, Turku, Finland
Email address: asamur@utu.fi (Anna Murto*), lmleht@utu.fi (Linda Laitinen), miina.nurmi@utu.fi (Miina Nurmi), mari.koivisto@utu.fi (Mari Koivisto), paipol@utu.fi (Päivi Polo-Kantola)

Up to 80% of all pregnancies are complicated by nausea and vomiting of pregnancy (NVP)(1). Previous studies have proposed a connection between NVP and pregnancy complications, such as high blood pressure and pre-eclampsia(2). Hyperemesis gravidarum, which is more severe and fortunately rarer form of NVP, has been associated with gestational diabetes(3), anemia(4,5), lower birthweight and increased likelihood for caesarean section and preterm delivery(5). The focus of this study is on the association between NVP and pregnancy and delivery complications.Pregnant women ($n = 2411$) were recruited from maternity health care clinics in Turku area in Finland. The severity of NVP was evaluated with Pregnancy-Unique Quantification of Emesis (PUQE) questionnaire and the women were categorized into two groups accordingly: non-NVP (no/mild NVP) and NVP (moderate/severe NVP) groups. The data of pregnancy omplications were drawn from Finnish Medical Birth Register. There were no statistically significant differences in age, smoking and body mass index, but more women in the NVP group were multigravidas ($P < 0.001$). Both anemia (aOR 1.41, 95% CI 1.07-1.86, $P = 0.015$) and fear of childbirth (aOR 1.71, 95% CI 1.11-2.63, $P = 0.014$) were more common in the NVP group. Neither preterm delivery nor caesarean section rates differed between the groups. In conclusions, we verified previously published connection with anemia. However, the finding of the association between NVP and the fear of childbirth was novel. Due to the association between NVP and other pregnancy complications maternal care for women with NVP is necessary.

Keywords: nausea and vomiting of pregnancy, hyperemesis gravidarum, pregnancy, anemia, fear of childbirth

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# Author Index

# Author Disclosures

**Marlena Fejzo, PhD:** Consultant for NGMBio, Harmonia Healthcare and Stock owner of Harmonia Healthcare, NGMBio

**Stephen O'Rahilly, MD:** Employee of University of Cambridge, grant/research support from Medical Research Council, Wellcome Trust, NIHR Consultant for Pfizer, AstraZeneca, Marea Therapeutics, Courage Therapeutics, Northsea Therapeutics, Third Rock Ventures and stock owner of Marea Therapeutics and Courage Therapeutics

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**Kate Maslin, PhD:** Employee of University of Plymouth, Grant/Research Support from University of Plymouth, Sir Halley Stewart Trust. Speakers Bureau/Honoraria for non-CME for British Dietetic Association and Wiley (book publishers) Consultant/Advisory Board for National Institute of Health and Clinical Excellence (UK)

**Andrew Housholder, MD:** Consultant for NGM Biopharmaceuticals

**Kimber MacGibbon, RN:** Hyperemesis Education and Research Foundation Employee of HER Foundation, Speakers Bureau/Honoraria for non-CME for Texas WIC, Consultant/Advisory Board for Harmonia Healthcare Consultant

**Margaret Riley, JD:** UnitedHealth/stock ownership

**Joanne Lancaster, PhD:** Employee of NGM Biopharmaceuticals