

Analysis of the effects on fetuses exposed to hyperemesis gravidarum during pregnancy

Análise dos efeitos em fetos expostos à hiperêmese gravídica durante a gravidez

Bianca Angerami de Souza Albero¹, Laís Rocha Afonso¹, Lizandra Catharine Perrett Martins¹, Maitê Ribeiro dos Santos¹, Bruna Marquez Rodrigues de Paula¹, Kamilla Martins Mayr¹, Gerson Aranha¹

ABSTRACT

Introduction: Hopelessness can be defined as the negative expectation about the future, associated with the lack of expectation of its change. This cognition may be found in the setting of disasters. **Objectives:** Evaluate the prevalence of hopelessness and its correlations with the quality of life and delineate the associated factors with its development in the population affected by the disaster of the Fundão dam at Mariana. **Methods:** 225 adults affected by the disaster were evaluated. The study explored the relationships between hopelessness and depression, quality of life, and its determinants. **Results:** 9% of the population were presented with a mild level of hopelessness. The correlation coefficient (CC) between hopelessness and depression was 0.220 ($p=0.001$) and between hopelessness and quality of life was -0.248 ($p<0.001$). This value remained significant, with the exclusion of individuals diagnosed with depression being -0.204 ($p=0.010$). Insomnia (OR: 5.92, $p=0.002$), being 60 years old or older (OR: 4.736, $p=0.009$) and risk of suicide (OR: 5.468, $p=0.005$) are predictors of hopelessness, while high resilience was a protective factor (OR: 0.115; $p=0.008$). **Conclusions:** A high degree of hopelessness was correlated with worsening quality of life even in individuals without depression. Thus, we suggest that interventions focused on reducing hopelessness should be included in assistance plans to minimize the impacts on those affected.

Keywords: Disasters; Quality of life; Mental health; Technological disasters; Depression; Suicide.

¹ Universidade Metropolitana de Santos. Santos, São Paulo, Brazil.

Responsible Editor:

Dr. Henrique Vitor Leite
Faculty of Medicine of the Federal University of Minas Gerais
Belo Horizonte/MG, Brazil

Corresponding Author:

Bruna Marquez Rodrigues de Paula
Email: bruna.maarquez@gmail.com

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RESUMO

Introdução: De etiologia desconhecida, a hiperêmese gravídica é um quadro caracterizado por vômitos persistentes, perda de 5% ou mais do peso, cetonúria, hipocalemia e desidratação. Acredita-se que a gonadotrofina coriônica humana (hCG) provoque aumento das náuseas e vômitos por meio de seu estímulo à produção de estrogênio pelo ovário, provocando a exacerbação dos sintomas do "enjoo matinal". **Objetivo:** Logo, essa revisão narrativa tem como objetivo analisar as repercussões fetais do quadro de hiperêmese gravídica. **Métodos:** Foram realizadas buscas em Sistema Online de Busca e Análise de Literatura Médica - MEDLINE®. Sendo utilizadas os Medical Subject Headings (MeSh terms) e seus sinônimos: "hyperemesis gravidarum", "fetal risks", sendo selecionados ao todo 13 artigos. **Resultados:** Os estudos demonstraram que a hiperêmese gravídica pode trazer malefícios para mãe e feto. A gestante pode apresentar distúrbios eletrolíticos, encefalopatia de Wernicke, fraqueza muscular, disfunções emocionais como depressão, ansiedade e estresse pós-traumático. **Discussão:** Os estudos revelaram que a patologia pode estar relacionada ao risco aumentado para desfechos adversos no nascimento, como baixo peso ao nascer, nascimento prematuro e pequena estatura para idade gestacional. Ademais, alguns estudos relataram os riscos prejudiciais no neurodesenvolvimento do recém-nascido, como problemas psicológicos e comportamentais na idade adulta, redução à sensibilidade à insulina, e comorbidades (obesidade e doenças cardiovasculares) além de distúrbios de desenvolvimento neuropsicomotor. **Conclusão:** Gestantes que apresentam o quadro de hiperêmese gravídica devem ser regularmente acompanhadas com consultas entre 1 a 2 semanas, conforme a gravidade do caso e o mais precocemente possível tratadas, a fim de evitar maiores complicações tanto maternas quanto fetais.

Palavras-chave: Hiperêmese gravídica; Sofrimento fetal; Complicações na gravidez.

INTRODUCTION

"Morning sickness" is the popular name for a common gestational symptom that affects 70 to 80% of pregnant women. This condition is characterized by nausea and vomiting in early pregnancy, around the 4th to 7th week of gestation, and may peak during the 8th to 12th week. These symptoms are usually mild and self-limited, however, they can evolve to hyperemesis gravidarum, a more severe form of nausea and vomiting; affecting one in every 200 pregnant women¹. Hyperemesis gravidarum (GH) is a condition characterized by persistent vomiting, 5% or more weight loss, ketonuria, hypokalemia, and dehydration, and its etiology is still unknown, although there are signs that the stimulus is produced by the placenta. Evidence suggests that human chorionic gonadotropin (hCG) is responsible for the increase in nausea and vomiting through its stimulation of estrogen production by the ovary, causing the exacerbation of what are considered relatively normal symptoms of morning sickness¹.

Other theories propose genetic, physiological, and gastrointestinal factors, such as *Helicobacter pylori*. It presents a higher prevalence in groups with low education level and low income. It is the most common cause of hospital admission during early pregnancy and its incidence increases with multiple gestation, molar pregnancy, trisomies and fetal hydrops. Among the maternal complications resulting from the condition, we can list some milder ones, such as peripheral neuropathies due to vitamin B6 and B12 deficiencies, and more serious ones, such as Wernicke's encephalopathy^{1,2}.

In addition, studies have also shown that women in this situation have an increased risk for other conditions such as spontaneous premature birth³. Some research has shown that pregnant women who lost weight early in pregnancy conceived newborns with lower mean birth weights compared to those born to mothers whose weight increased or was maintained during this period¹.

A propensity for these infants to have birth weights less than the 10th percentile was also observed^{1,2}. Therefore, this review aims to analyze the fetal repercussions of hyperemesis gravidarum, being of extreme importance for obstetricians in prenatal care to avoid fetal complications.

METHODS

A search was made in the Online Medical Literature Analysis and Search System - MEDLINE[®]. The Medical Subject Headings (MeSh terms) and their synonyms were used: "hyperemesis gravidarum", "fetal risks".

In the search, 43 articles were found, being selected articles from 2005 to 2022, of English language, being the inclusion criteria articles in which the type of participants were pregnant women with hyperemesis gravidarum or intense nausea with confirmed clinical diagnosis and articles in which the fetal and neonatal outcomes and/or complications were caused by maternal hyperemesis gravidarum diagnosed according to clinical criteria during pregnancy and which had treatment and articles in which the fetal and neonatal outcomes and/or complications were caused by maternal hyperemesis gravidarum diagnosed according to clinical criteria during pregnancy and which had no treatment. The exclusion criteria were studies in which there was no relationship between motion sickness and pregnancy, studies in which the complications and/or neonatal and fetal outcomes had no correlation with hyperemesis gravidarum.

Thus, 13 articles were selected, among which there were narrative reviews and case reports, due to the scarcity of randomized clinical trials, meta-analysis and systematic reviews. And this selection was evaluated by all the authors of this article.

RESULTS

Studies have shown that Hyperemesis Gravidarum can harm both mother and fetus¹⁻⁴. The pregnant woman may present electrolyte disturbances, Wernicke's encephalopathy⁵, muscle weakness, emotional dysfunctions such as depression, anxiety, and post-traumatic stress⁴⁻⁶.

Furthermore, studies have also shown (Bolin et al) that placental disorders can occur, such as placental abruption. Low birth weight, preterm birth, small for gestational age, psychological gestational age, psychological, behavioral, and neurodevelopmental disorders were noted as predominant in the selected articles^{6,7}.

A study, involving 819 women with HG, showed that 16% of the babies were born prematurely, and that 8% of the parturient reported low birth weight of their children ($w < 2,500g$)⁴ and according to the cutoff study, pregnant women with HG were 1.2 times more likely to have low birth weights than the control group ($RR = 1.2$; $95\%CI = 1.0-1.5$)⁵.

Furthermore, in a retrospective study involving 259 adults, psychological and behavioral disorders (such as depression, anxiety, autism) were reported in subjects exposed to intrauterine HG³, as well as an increased risk of cardiovascular comorbidities in the fetus⁴.

Children exposed in utero to HG had a 3-fold increase in the odds of neurodevelopmental disorders including attention and anxiety disorders. An increased incidence of risk for autistic spectrum disorder has been reported in 8% of exposed children compared to children whose mothers had and had not had hyperemesis gravidarum^{7,8}.

It is also noted that HG, by causing maternal nutritional deficiency, can lead to vitamin deficits such as vitamin K causing bleeding disorders that can result in damage to the fetus as a possible, although rare, fetal intracranial hemorrhage⁹. Moreover, the lower intake and absorption of nutrients and proteins can adversely affect intrauterine fetal growth¹⁰.

Other disorders have been found to be present in the studies reviewed, such as considerable reduction in insulin sensitivity, and comorbidities manifested during adulthood such as obesity and cardiovascular diseases, in addition to neuropsychomotor development disorders. Studies have shown that maternal malnutrition during the first trimester, besides the possible resulting oxidative stress, may act teratologically on the fetus, negatively affecting its development, such as the cerebral development (CNS), thus increasing the risk of neurological disorders during childhood and/or adult life^{6,11,12,1}.

DISCUSSION

The results of the studies evaluated suggest that the current findings are conflicting findings regarding the association between hyperemesis gravidarum and its effects on the fetus. This is due to the degree of heterogeneity among the studies, different definitions regarding the clinic of HG, and lack of homogeneous samples.

The following effects on the baby were noted predominantly in the selected articles: low birth weight, preterm birth, small stature for gestational age, psychological, behavioral, and neurodevelopmental disorders. The pregnant woman may present electrolyte disturbances, Wernicke's encephalopathy, muscle weakness, emotional dysfunctions such as depression, anxiety, and post-traumatic stress. Furthermore, the possible occurrence of placental disorders, such as premature placental abruption, is also observed^{5,7,9,11,13}.

Women with hyperemesis gravidarum were more likely to have spontaneous preterm birth when compared to women who did not have HG. Moreover, in women who had weight gain lower than 7kg and hyperemesis gravidarum during pregnancy, an increased risk of prematurity was found compared to cases of HG with weight gain. No associations were found with Apgar scores, congenital anomalies, or perinatal death³⁻⁵.

Maternal characteristics partially determine the outcome of pregnancy in patients with hyperemesis gravidarum. However, other factors may be associated, such as insufficient weight gain during pregnancy, maternal stress situations, or *H. pylori* infection involving the placenta. All of these events can contribute to the adverse birth outcomes associated with HG^{5,9}.

As for the treatment, about 10% of pregnant women who present nausea and vomiting will need medication, being the first line treatment the association of oral vitamin B6 and doxylamine, which is recommended by the American College of Obstetricians and Gynecologists (ACOG). According to randomized studies, this combination reduces symptoms by up to 70%, and therefore (between commas) reduces fetal complications caused by hyperemesis gravidarum¹.

CONCLUSION

Hyperemesis gravidarum may be associated with increased risk of adverse outcomes at birth and neurodevelopmental disorders, and may cause harm to both mother and fetus. Therefore, this condition should be treated during prenatal care, as early as possible, and the pregnant woman should be monitored regularly by her obstetrician in order to avoid further complications for both mother and fetus.

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AUTHORS' CONTRIBUTION:

Conceptualization, Investigation, Methodology, Visualization & Writing - Review & Editing: Bianca Angerami de Souza Albero, Laís Rocha Afonso, Lizandra Catherine Perret Martins, Maitê Ribeiro dos Santos and Bruna Marquez Rodrigues de Paula. Project administration, Supervision & Writing - Original Draft: Bianca Angerami de Souza Albero, Laís Rocha Afonso, Lizandra Catherine Perret Martins, Maitê Ribeiro dos Santos, Bruna Marquez Rodrigues de Paula and Gerson Aranha. Data Curation & Formal Analysis: Kamilla Martins Mayr.

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