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Review Article

Adverse Neonatal Outcomes in Pregnant Women with Severe Vomiting: A Meta-Analysis

Yuliu Huang [1], ****Shuixia Chen*** [2]

1. *Gynaecology Department, Zhejiang Hospital Sandun District, Hangzhou, 310030, China*
2. *Obstetrical Department. Zhejiang Hospital Sandun District, Hangzhou, 310030, China*

***Corresponding Author:** Email: ChenSX123123@126.com

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Abstract

Background: We aimed to systematically evaluate the risk of negative effect for newborns born to expectant mothers with severe vomiting in terms of birth weight, premature delivery, low Apgar score, and NICU hospitalization.

Methods: We conducted a systematically search for relevant studies on PubMed, Embase, Cochrane Library, and CNKI databases, using Newcastle-Ottawa Scale to evaluate research quality, and RevMan 5.3 software for meta-analysis from 2009 to 2022. The main outcome measures were: Low-birth weight, preterm delivery, low Apgar score and growth restriction.

Results: In 9 studies, the risk of Low birth weight in hyperemesis pregnant women was increased, and the random effect model was OR 2.38 (95% CI 0.43 to 13.13). The heterogeneity of the study was high (I^2=100%). Four studies showed an increased risk of low Apgar scores, with an OR of 2.69 (95% CI 0.30 to 24.48), and high heterogeneity (I^2=95%). The risk of premature birth in 5 papers is equivalent, with an OR of 0.93 (95% CI 0.71 to 1.22) and low heterogeneity (I^2=6%). The risk of growth restriction was higher in 7 papers, with an OR of 1.31 (95% CI 0.93 to 1.85) and lower heterogeneity (I^2=29%). Subgroup analysis showed that heterogeneity mainly stemmed from differences in the definition of hyperemesis.

Conclusion: Pregnant women with severe vomiting have a higher risk of giving birth to babies with low birth weight and low Apgar scores, and a higher risk of giving birth to babies with growth restriction, but the risk of premature birth is comparable.

Keywords: Dramatic vomiting; Pregnant and parturient women; Newborns; Adverse outcomes

Introduction

In recent years, with the deepening understanding of the importance of nutrition and metabolism during pregnancy, the international attention to hyperemesis and its complications has gradually increased (1). Excessive vomiting during pregnancy is a phenomenon of refractory vomiting when pregnant, which can lead to fluid and electrolyte imbalance, nutritional deficiency and Weight loss (2).

About 0.3%-10.8% pregnant women have experienced nausea and vomiting in the 1st three months of pregnancy (3). It is related to the incidence rate of mother and infant (4). Currently, severe vomiting during pregnancy is closely related to some perinatal outcomes. Women with se-

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vere vomiting have an increasing risk of preeclampsia, and low birth weight (LBW) (5). It is not related to Apgar score, congenital malformations, or perinatal death (6). Hyperemesis gravidarum usually relieves itself after 12 wk of pregnancy, and changes in maternal nutritional status and dehydration in early pregnancy will have an impact on placental development and neonatal growth, which will be alleviated with the cessation of hyperemesis (7). Hyperemesis gravidarum can also increase the risk of miscarriage and premature delivery, and cause intrauterine growth retardation, threatening the life of the fetus (8). In addition, hyperemesis gravidarum may lead to LBW and newborns with low Apgar score (LAS) (9), increasing the difficulty of neonatal care.

Therefore, hyperemesis gravidarum may rise the threats of various adverse neonatal outcomes (ANO) such as premature delivery, LBW, LAS and growth restriction. We aimed to carry out this analysis to systematically evaluate the impact of Hyperemesis gravidarum on neonatal outcomes, so as to provide reference.

Methods

Literature search

This study searched EMbase, Cochrane Library, PubMed and other database systems from 2009 to 2022 to compare the related researches on neonatal outcomes of pregnant women with Hyperemesis gravidarum and those without Hyperemesis gravidarum. The main search terms include "hyperemesis gravidarum", "pregnancy complication", "infant and newborn", "premature birth", "low birth weight", "hyperemesis", "HEG", etc. The language is limited to English or Chinese. Inclusion criteria: 1) The type of study was observational study or randomized controlled trial; 2) The neonatal outcomes of Hyperemesis gravidarum and normal pregnant women were compared; 3) Report relevant indicators of neonatal outcomes, including preterm birth, birth weight infants, or neonatal hospitalization rates; 4) Corresponding indicators can be calculated by providing effect indicator reports or raw data. Exclusion criteria for literature: 1) Commentary, review type studies or case reports; 2) Failure to report relevant neonatal outcome indicators; 3) Repeated publication or data duplication. Extract relevant research feature information, including research type, sample size, effect indicator classification, and data.

Statistical methods

The experimental data was statistically analyzed using Review Manager 5.3 software. Compare the differences in the detection results of different research methods using OR and its 95% CI as the effect measure indicators. $P<0.05$ indicates a statistically meaningful difference. To test for inter study heterogeneity, $I^2=0$ indicates no statistical heterogeneity, $I^2<50\%$ indicates moderate heterogeneity; $I^2>50\%$ means significant heterogeneity. If there was no statistical heterogeneity between the studies, a fixed effects model (FEM) was utilized for meta-analysis; otherwise, a random effects model (REM) was used for it.

Results

Characteristics of inclusion in the study

The literature search process and results are detailed in Fig. 1, and the characteristics of each study are shown in Table 1. Listed multiple studies from 2009 to 2022. It covers 9 countries including Türkiye, the Netherlands, Indonesia, Norway, Singapore, Japan, New Zealand, the United States and China. This includes multiple research designs, including retrospective cohort studies, prospective case-control studies, and prospective cohort studies. Most studies use ICD (International Classification of Diseases) coding to define hyperemesis, while others rely on medical records. The total number of cases of severe vomiting is 12063, and the total sample size of the study is 172160. The adverse pregnancy outcomes associated with hyperemesis mainly include low birth weight, low APGAR score (LAS), preterm birth, and growth restriction (Table 1).

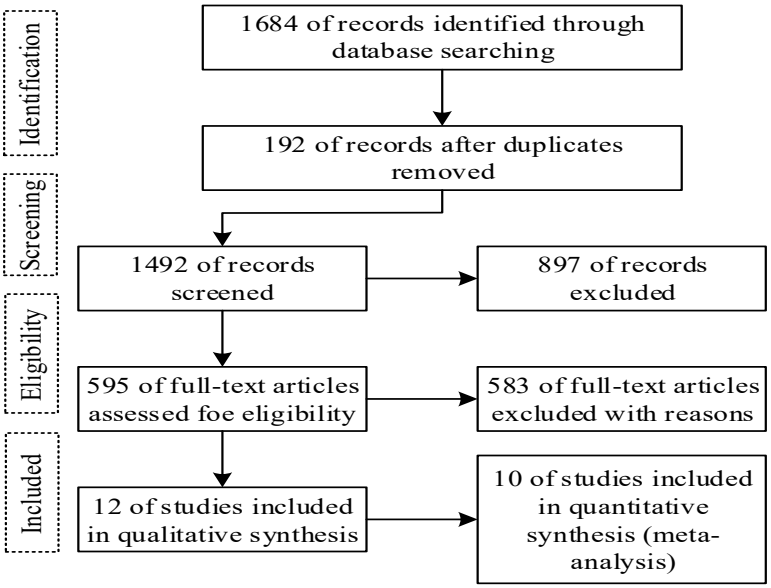

Fig. 1. Flow chart of the literature search

Table 1: Specific Characteristics of Each Study

Research (yr)	Area	Research design	Definition of severe vomiting	Severe vomiting/Total sample size	Adverse outcomes
Gunay (2020)(10)	Turkey	cohort study	ICD-9	186/386	①②③④
Grooten (2017) (11)	the Netherlands	Prospective case control	Medical records	601/5549	①③④
Buyukkayaci (2015) (12)	Turkey	Randomly sampled case control	ICD-8/ICD-10	50/100	①③④
Koudijs (2016) (13)	Indonesia	Prospective case control	Medical records	46/2233	①②③④
Vikanes (2013) (14)	Norway	Prospective cohort	Medical records	814/71468	①②
Ong (2021) (15)	Singapore	Prospective cohort	Medical records	67/486	①③④
Morisaki (2022) (16)	Japan	Prospective cohort	Medical records	9983/91313	①
Coetzee (2011) (17)	New Zealand	Cohort study	ICD-10	75/142	①②④
Mullin (2012) (18)	USA	Prospective cohort	Medical records	201/390	④
Song (2009) (19)	China	Prospective cohort	Medical records	40/93	

Note: ① is LBW, ② is LAS, ③ is preterm birth, ④ is growth restriction.

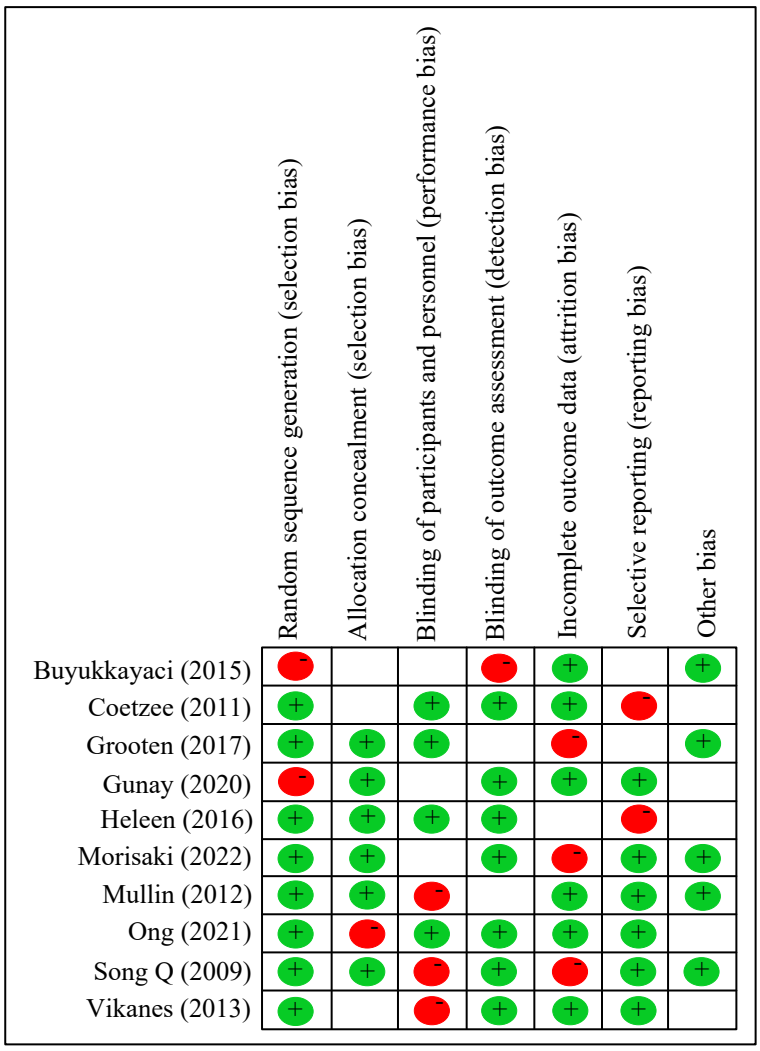

Fig. 2: Summary Results of Literature Bias Risk

Inclusion in literature quality evaluation

As Fig. 2, most of the 10 articles are low-risk, high-quality, and meet the requirements for further experiments.

Comparison of methodological results

Comparison of LBW、LAS Results

From Fig. 3A, I^2=100% indicates high literature heterogeneity. Using a REM for meta-analysis, the combined OR (95% CI) was 2.38 (0.43, 13.13). In Fig. 3B, I^2=95% indicates high heterogeneity in the literature, and the combined OR (95% CI) was 2.69 (0.30, 24.48) using a REM for meta-analysis.

Comparison of preterm birth, growth restriction Results

In Fig. 3C, I^2=6%, the literature has low heterogeneity, and the FEM was taken for meta-analysis with a combined OR (95% CI) of 0.93 (0.71, 1.22). From Fig. 3D, I^2=29%, and the literature has low heterogeneity. Using a FEM for meta-analysis, the combined OR (95% CI) was 1.31 (0.93, 1.85).

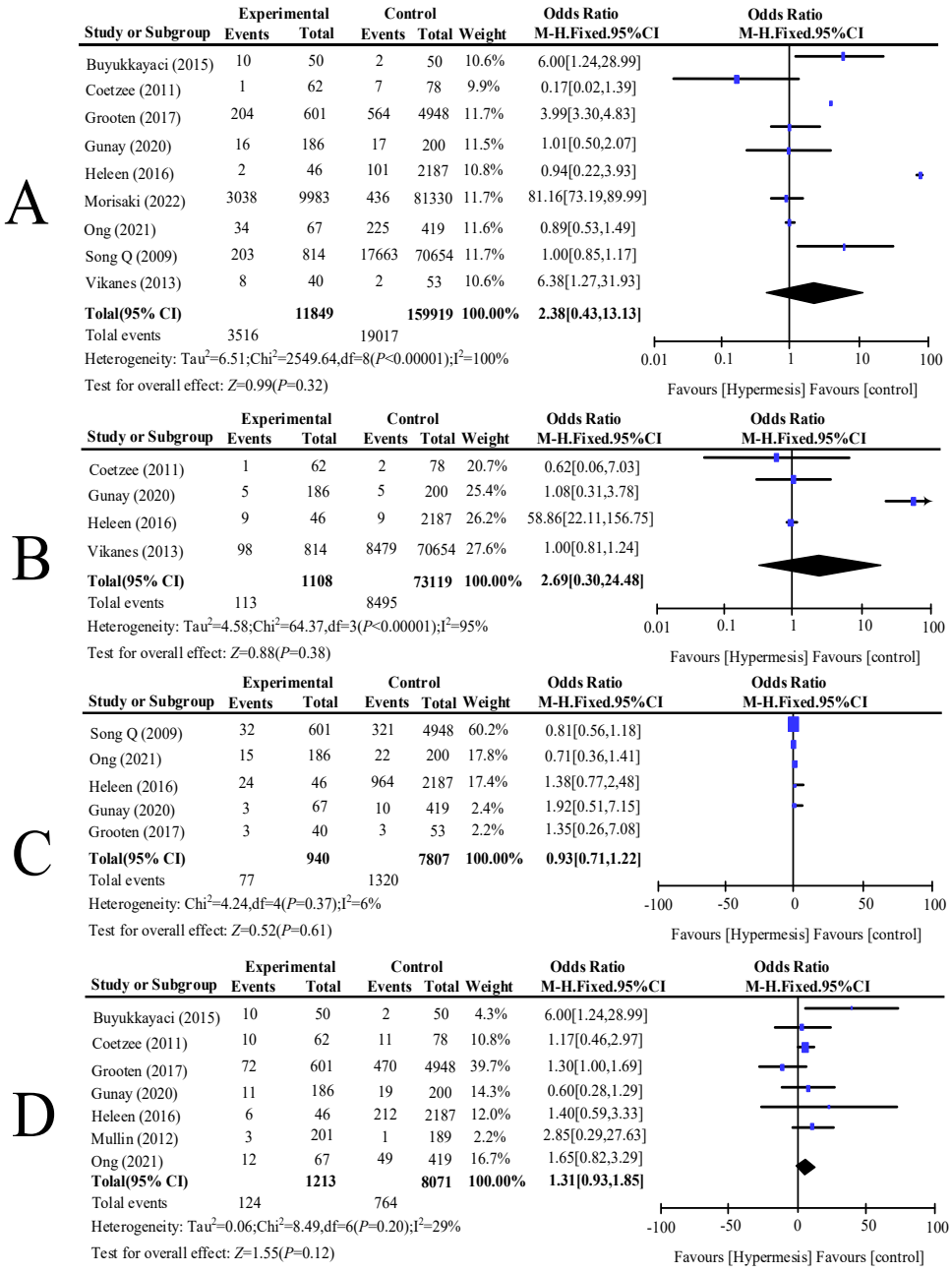

Fig. 3: Forest plot of maternal emesis and neonatal outcome indicators

A: Forest map of the occurrence of LBW in newborns of pregnant women with and without severe vomiting. **B**: Forest map of the occurrence of LASs in newborns of pregnant women with and without severe vomiting. **C:** Forest map of the incidence of premature birth in newborns of pregnant women with and without hyperemesis. **D:** Forest map of the occurrence of neonatal growth restriction in pregnant women with and without severe vomiting

Subgroup analysis

From Fig. 4A, LBW is the main grouping criterion, and the sample size is used as the grouping basis. The grouping boundary points with significant changes in sample size are set at 200 and 500. According to the results of subgroup grouping, when the sample size >200 and >500, their I^2 values were 100%, and there was still high heterogeneity. The combined OR (95% CI) were 12.14 (11.43, 12.90) and 13.27 (12.48, 14.10). The

results of subgroup grouping were defined based on the drama theory. According to medical records, its I^2 was 100%, indicating high heterogeneity. The I^2 of the literature defining severe vomiting combined with ICD-8/9/10 was 73%, indicating a decrease in heterogeneity. This may be related to the significant gap in the definition of heterogeneity and hyperactivity in this study. The combined OR (95% CI) were 12.47 (11.73, 13.25) and 1.14 (0.65, 2.00), respectively, as shown in Fig. 4B.

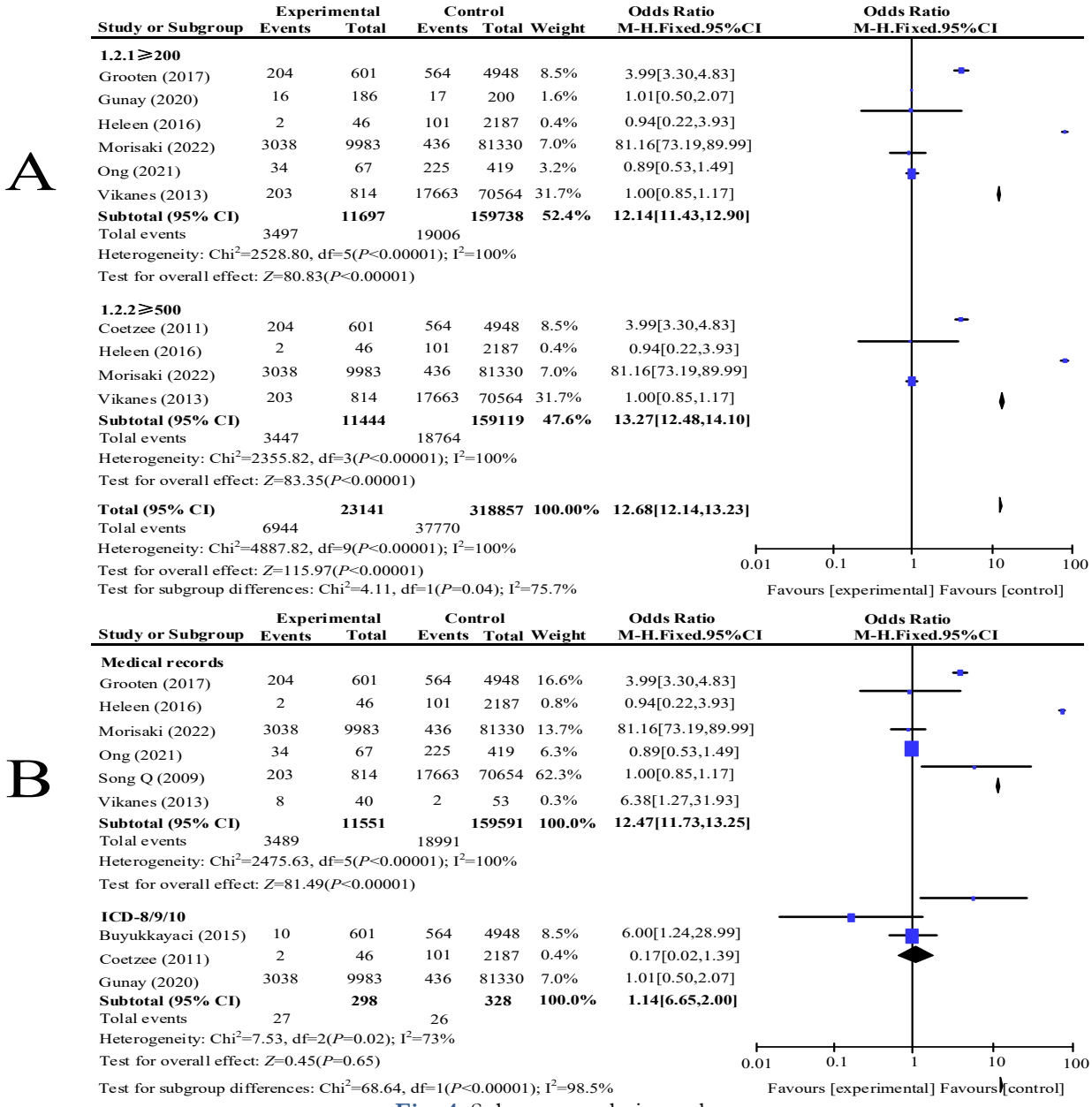

Fig. 4: Subgroup analysis results

A: Subgroup analysis of the incidence of LBW in newborns of pregnant women with and without hyperemesis. **B:** Specific definition subgroup analysis of the incidence of low birth weight in newborns of pregnant women with and without severe vomiting

Discussion

The increased risk of LBW and LAS infants indicates that vomiting symptoms are related to the poor condition of newborns in the early postnatal period and the increased risk of asphyxia and Anoxic event events (20). Neonatal underweight and neonatal asphyxia can cause delayed neural development and abnormal development of various systems, increasing the risk of neonatal mortality (21). Therefore, the results of this study validate the strengthening of prenatal monitoring for pregnant women with severe vomiting to improve the fetal environment and avoid underweight newborns; strengthen the monitoring and care of newborns after birth, prevent and promptly detect serious complications such as asphyxia. The risk of premature birth did not increase and the risk of growth restriction only slightly increased, indicating that the association between severe vomiting during pregnancy and these two outcomes may be weak. This may be because the formation of premature birth and growth restriction is related to multiple issues, and hyperemesis is only one aspect of many factors (22), or the accuracy of meta-analysis results may be limited due to the influence of heterogeneity in research.

Compared with other meta-analysis studies, this study shows that the conclusion of increased risk of LBW in pregnant women with severe vomiting is consistent, but the conclusion of increased risk of premature birth is different. For example, the risk of LBW in hyperemesis pregnant women increased (OR=1.43, 95% CI: 1.02-1.99), but the risk of premature delivery did not increase (OR=2.81, 95% CI: 1.69-4.67) (23). Overall, 61 studies were included in this study, and there were some distinctions between the results and this study, the differences should be related to the differences in the included studies. Pregnant women with severe vomiting have a LAS (asphyxia event) and an increased risk of neonatal growth restriction (24). It also demonstrated an increased risk of asphyxia in pregnant women with severe vomiting (OR=1.05, 95% CI: 10.72-1.54) and an increased risk of neonatal growth restriction (OR=1.18, 95% CI: 0.96-1.44), which is consistent with the results of this study. The results of this study are consistent with other meta-analysis studies in terms of LBW and LAS risk in newborns; But in terms of the risk of premature birth, the results differ from other studies.

Conclusion

This study explores the neonatal outcomes of pregnant women with severe vomiting through meta-analysis. Pregnant women with severe vomiting may have an increased risk of low birth weight and low Apgar score infants, with a higher risk of growth restriction, but no increase in preterm birth risk. The study suggests enhanced antenatal monitoring of pregnant women with severe emesis and perinatal care of the newborn, which may improve neonatal outcomes.

Journalism Ethics considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

Consent to publication

Not applicable

Data availability statement

The original contributions presented in the study are included in the article

Funding

Not applicable

Conflict of interest

The authors declare that there is no conflict of interests.

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