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Review Article/Meta Analyses

Perinatal risk factors for infantile hypertrophic pyloric stenosis: A meta-analysis☆

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ABSTRACT

Background: Infantile hypertrophic pyloric stenosis (IHPS) is the most common surgical cause of nonbilious vomiting in infancy. The etiology of IHPS is not completely understood. Hence, we performed a meta-analysis to investigate the association between perinatal factors and IHPS onset.
Methods: The MEDLINE, EMBASE, PubMed and Cochrane Library databases were searched for studies published in English before December 2016. The combined odd ratios (ORs) and 95% confidence intervals (CIs) were calculated using random-effects models.
Results: Fifteen studies were included. Several perinatal factors, including first-born (OR 1.19, 95% CI: 1.07–1.33), cesarean section delivery (OR 1.63, 95% CI: 1.53–1.73), preterm birth (OR 1.37, 95% CI: 1.12–1.67), and bottle-feed (OR 2.46, 95% CI: 1.76–3.43), were significantly associated with the IHPS onset. Among these, bottle-feed was the most significantly risk factor for IHPS onset. Although few studies have evaluated the relationship between perinatal factors and IHPS, they have major limitations including retrospective collection of data on perinatal events and testing of multiple hypotheses without appropriate statistical corrections.
Conclusions: First-born, cesarean section delivery, preterm birth, and bottle-feed are associated with the development of IHPS. Well-designed future studies are needed to help understand the etiology of IHPS.
Type of study: Systematic reviews and meta-analyses.
Level of evidence: Level III.

Contents

☆ Author contributions: study conception and design: Jianghu Zhu, Tingting Zhu, and Dezhi Mu; data acquisition: Jianghu Zhu, Tingting Zhu, Zhenlang Lin, and Yi Qu; analysis and data interpretation: Jianghu Zhu, Tingting Zhu, Zhenlang Lin, Yi Qu; drafting of the manuscript: Jianghu Zhu, and Tingting Zhu; critical revision: Dezhi Mu.

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Infantile hypertrophic pyloric stenosis (IHPS) is the most common condition requiring surgery during early infancy, with a prevalence of approximately 2 per 1000 live births [1,2]. IHPS is an idiopathic hypertrophy of the pyloric muscle in early infants and results in partial obstruction of the gastric outlet. The typical clinical presentations and symptoms are well established; these include projectile, nonbilious vomiting occurring at the age of 2–8 weeks, a palpable olive-shaped mass in the mid-epigastrium, and occasionally, gastric peristaltic waves during feeding [3–6]. Ultrasound examination is used for confirming the diagnosis of IHPS [7,8]. Pyloromyotomy, a surgical procedure for splitting the hypertrophied pyloric muscle through a periumbilical incision or laparoscopically, has become the first choice of treatment with curative outcomes and minimal complications [9]. Despite the well-known presentation and advances in diagnostic methods and therapy, the exact cause of IHPS remains unknown.

Male sex and a family history of IHPS are consistently reported as risk factors for IHPS. A 4–5-fold higher risk of the disease exists in boys than in girls as observed by several studies worldwide [2,10–13]. Further, a clustering of cases has also been observed within families [11,14–17]. These epidemiologic features of skewed sex distribution and familial aggregation suggest a genetic component to the etiology of IHPS. However, several studies indicate that perinatal factors may play an important role in the pathogenesis of IHPS. The fact that IHPS is rarely observed beyond the age of 3 months also suggests that the perinatal period is of clinical importance in the development of IHPS. Studies have investigated the association of delivery factors (such as birth order, labor mode, and plurality) and neonatal factors (such as gestational age, birth weight, birth weight for gestational age, and bottle-feed) with the onset of IHPS during perinatal period. However, the analysis of these studies has revealed inconsistent results.

To our knowledge, currently there are no meta-analyses focusing on this issue. Therefore, we performed a meta-analysis to investigate the association between perinatal factors and IHPS.

1. Materials and methods

1.1. Search strategy

We searched the MEDLINE, EMBASE, PubMed, and Cochrane Library databases for relevant studies that investigated the association between perinatal risk factors and IHPS using terms specific to IHPS and keywords such as, pregnancy, prenatal, perinatal, birth, neonatal and infant. The selected articles in English were limited to studies on human subjects published before November 2016. The medical subject heading (MeSH) terms and text words used for the search were the following: ("infantile hypertrophic pyloric stenosis" or "IHPS" or "pyloric stenosis" or "pyloric stricture") and ("risk" or "hazard" or "association" or "odds ratio" or "relative ratio") and ("neonatal" or "infant" or "birth" or "perinatal" or "prenatal" or "pregnancy").

1.2. Study selection

Two reviewers screened the titles and abstracts independently. Case-reports, commentary articles, review articles, editorials, and animal studies were excluded. Any study in which the abstract or title suggested the evaluation of perinatal risk factors along with the development of IHPS was selected for a further full-text review. Disagreements were resolved by discussion between the two reviewers. Studies were considered eligible for data extraction if they met the following criteria: (1) studies on specific factors in the perinatal period, (2) evaluation of their association with the development of IHPS, (3) an original study with published full-text of the article available, and (4) the odds risk (OR) or relative risk (RR) along with the corresponding 95% confidence intervals (CI) (or data to calculate them) were reported. Studies investigating other risk factors beyond the identified perinatal factors were excluded.

1.3. Data extraction

The following information was extracted onto piloted forms: first author name; year of publication, study location, study period, number of cases and controls, perinatal factors involved, study design, study results, and adjustment for covariates. Two reviewers independently extracted the data from studies. Differences were resolved by discussions among the reviewers and consultants.

1.4. Statistical analyses

The odds ratio (OR) was used as a common measure of the association between perinatal factors and IHPS. The relative ratios (RRs) and hazard ratios (HRs) were directly considered as OR. We calculated the crude OR for studies in which only the original data were reported.

The meta-analysis was performed using the Cochrane Collaboration's Review Manager (RevMan 5.3, The Cochrane Collaboration, United Kingdom). Heterogeneity of studies was tested by I^2 (significance level, >50%) [18] and $P < 0.1$ indicated statistical significance. Random-effects model was employed for computing the combined risk estimates owing to the small number of heterogeneity studies in this meta-analysis. We performed a sensitivity analysis to determine the impact of every single study on the overall risk estimate by omitting the respective study in each round of calculation. The publication bias was assessed by a visual inspection of the funnel plots.

2. Results

2.1. Literature search

We initially retrieved 324 unique citations from MEDLINE, EMBASE, PubMed, and the Cochrane Library. After the first screening based on titles and abstracts, most of the articles were excluded mainly because they were either reviews, case-reports, commentary articles, or not relevant to our analysis. Further, 57 potential articles were selected for full-text review. After reading through the selected 57 studies, we identified seven perinatal risk factors (birth order, plurality, labor, gestational age, birth weight, birth weight for the gestational age, and feeding practice) which were investigated in more than three studies with respect to their association with the onset of IHPS. Subsequently, 42 studies were excluded. Among these, 30 studies did not investigate the seven identified perinatal risk factors, six were reviews, three did not have available OR/RRs, two were case series and one was a commentary. Finally, 15