

INPLASY PROTOCOL

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None declared.

Assisted reproductive technology and the risk of cerebral palsy in the offspring: a systematic review and meta-analysis

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Review question / Objective: To assess the association between the use of assisted reproductive technology (ART) and the risk of cerebral palsy (CP) in offspring.

Condition being studied: Growing evidence have shown that ART is associated with an increased risk of adverse perinatal sequel, such as preterm birth, low birth weight, multiple birth, birth defects, and intrauterine growth restriction, which may account for the development of CP. As a consequence, a number of studies have assessed the risk of CP in offspring born after ART. However, the results were inconsistent. Some studies reported that children born after ART were at an increased risk of CP compared with those born after naturally conceived, while others found no risk, or even a protective effect. Although a previous meta-analysis reported a significant association between ART and CP risk in offspring, evidence was limited because only 3 cohort studies were available at that time and all enrolled studies were from Scandinavian countries.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 18 March 2021 and was last updated on 18 March 2021 (registration number INPLASY202130060).

INTRODUCTION

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account for the development of CP. As a consequence, a number of studies have assessed the risk of CP in offspring born after ART. However, the results were inconsistent. Some studies reported that children born after ART were at an increased risk of CP compared with those born after naturally conceived, while others found no risk, or even a protective effect. Although a previous meta-analysis reported a significant association between ART and CP risk in offspring, evidence was limited because only 3 cohort studies were available at that time and all enrolled studies were from Scandinavian countries.

METHODS

Participant or population: All living births conceived via assisted reproductive technology.

Intervention: None.

Comparator: All living births conceived naturally.

Study designs to be included: Cohort or case-control studies

Eligibility criteria: The inclusion criteria for the study were as follows: (1) cohort or case-control studies, (2) the exposure of interest was ART, (3) the outcome of interest was CP, and (4) the effect estimates (odds ratios, risk ratios, and hazard ratios) could be extracted or calculated. The exclusion criteria were as follows: (1) reviews, case reports, conference abstracts, comments, letters, or animal studies, and (2) studies with insufficient information. If data from the same population had been published repeatedly, then the most recent and comprehensive study was selected.

Information sources: A systematic search of PubMed, Embase, the Cochrane Library, and Web of Science was conducted to identify relevant studies regarding the association between ART and risk of CP in offspring. The reference lists of the relevant articles were hand searched for potentially

eligible studies. We did not attempt to locate unpublished studies.

Main outcome(s): The main outcome measure was the incidence of CP in children born after ART and natural conception.

Quality assessment / Risk of bias analysis: The Newcastle-Ottawa Scale (NOS)

Strategy of data synthesis: Heterogeneity among studies was assessed using the I² inconsistency test and Cochran's Q test. We apply a fixed effects (Mantel-Haenszel) model to obtain summary OR when there is no obvious heterogeneity across studies ($P > 0.10$ for the Q-test and $I^2 < 50\%$), otherwise, we use a random effects (DerSimonian-Laird) model.

Subgroup analysis: Subgroup analysis were performed based on study location, study design, study quality, and whether they were adjusted for confounding variables to examine the source of potential heterogeneity.

Sensitivity analysis: Sensitivity analysis was conducted to assess whether a single study significantly affected pooled estimates by removing one study at a time.

Country(ies) involved: China.

Keywords: cerebral palsy; assisted reproductive technology; meta-analysis.

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