INPLASY

The association between intrahepatic cholestasis of pregnancy and risk of small for gestational age in China: a meta-analysis

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Tan, X; Hu, YY; Chen, HQ.

Corresponding author:
Hongqin Chen

chenhongqin2022@163.com

Author Affiliation:
West China Second University Hospital, Sichuan University.

ADMINISTRATIVE INFORMATION

Support - None.

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 2 August 2026 and was last updated on 2 August 2026.

INTRODUCTION

Review question / Objective To identify the relationship of intrahepatic cholestasis of pregnancy (ICP) with the occurrence risk of small for gestational age (SGA) in China.

Condition being studied Small for gestational age (SGA) infants are quite common in clinical practice and are a focus of concern due to their potential to cause developmental issues across multiple systems in the fetus. The currently widely accepted definition of small for gestational age (SGA) infants is those born with a birth weight below the 10th percentile of the normal average weight for the same gestational age [1]. In 2001, the World SGA Development Conference announced that SGA refers to birth weight and/or length below two standard deviations of the mean for the same gestational age (≤ -2 SD), approximately equivalent to the 3rd percentile of birth weight and/or length for the same gestational age [2, 3]. Although its concept is controversial and its mechanisms are complex, given the short-term and long-term health effects of SGA on child development, it is increasingly attracting scholarly attention. With the development of modern perinatal medicine and the widespread promotion of neonatal resuscitation techniques in our country, the incidence of SGA has significantly decreased [3, 4]. However, due to the large population base in our country, it remains an important public health issue.

The occurrence of SGA can be influenced by various risk factors. Maternal factors are among the primary factors affecting fetal development. These factors include maternal malnutrition, smoking, alcohol consumption or drug use during pregnancy, gestational hypertension, diabetes, intrauterine infections, and so on [5]. The fetal health condition itself can also affect its growth and development [6, 7]. For instance, chromosomal abnormalities, genetic diseases, or other congenital defects may lead to restricted fetal growth [6, 7]. Additionally, certain pregnancy complications such as preeclampsia, placental abruption, etc., may affect the fetus's blood supply and nutrient delivery, thereby impacting fetal growth [8, 9].

Intrahepatic cholestasis of pregnancy (ICP) is a pregnancy-specific liver disorder characterized by elevated maternal serum bile acids and is associated with an increased risk of adverse perinatal outcomes, including preterm birth, fetal distress, and stillbirth. Increasing evidence suggests that excessive bile acids may impair placental function through oxidative stress, inflammation, vascular dysfunction, and altered nutrient transport, thereby compromising fetal growth. In addition, placental bile acid accumulation may reduce oxygen and nutrient delivery to the fetus, providing a biologically plausible link between ICP and fetal growth restriction [10, 11]. However, published studies investigating the association between ICP and small for SGA have yielded inconsistent findings, particularly among Chinese pregnant women. Therefore, we performed this meta-analysis to systematically evaluate the association between ICP and the risk of SGA in the Chinese population.
Therefore, this study aimed to further clarify the association between ICP and occurrence risk of SGA among Chinese population based on available evidence.

METHODS

Search strategy The CNKI, Medline and Web of Science databases were searched up to May 4, 2024 to identify studies conducted among Chinese pregnant women with the following searching key words: intrahepatic cholestasis of pregnancy, ICP, small for gestational age and SGA. Besides, the MeSH terms and free texts were used and references cited in included studies were reviewed.

Participant or population Cohort or case-control studies conducted in China involving pregnant women of Chinese populations, in which participants were divided into ICP and non-ICP group.

Intervention Cohort or case-control studies conducted in China involving pregnant women of Chinese populations, in which participants were divided into ICP and non-ICP group.

Comparator The number of SGA neonates in the ICP and non-ICP groups were reported.

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

Eligibility criteria Studies which met following criteria were included: 1) cohort or case-control studies conducted in China involving pregnant women of Chinese populations, in which participants were divided into ICP and non-ICP group; 2) the diagnosis of ICP was based on international or national guidelines; 3) the number of SGA neonates in the ICP and non-ICP groups were reported; 4) SGA was defined as a birth weight below the 10th percentile for gestational age in the absence of major congenital anomalies, according to nationally or internationally accepted diagnostic criteria and during data extraction, the definition of SGA was verified independently by two reviewers for each included study.
Studies which met following criteria were excluded: 1) duplicated, overlapped or insufficient data; 2) studies the type of meeting abstracts, animal trials, letters, editorials or case reports; 3) low-quality studies.

Information sources The CNKI, Medline and Web of Science databases were searched up to May 4, 2024.

Main outcome(s) Number of SGA patients in the ICP and non-ICP groups.

Additional outcome(s) None.

Quality assessment / Risk of bias analysis The quality was evaluated according to the Newcastle-Ottawa Scale (NOS) score and studies with NOS scores ≥6 were considered to have acceptable methodological quality and were included in the meta-analysis.

Strategy of data synthesis All analysis was conducted by STATA version 15.0 software. The heterogeneity between studies was assessed by I2 statistics and Q test. When significant heterogeneity was observed representing as I2 > 50% and/or P < 0.1, the random effects model was used; or the fixed effects model was applied [14]. RRs with 95% CIs were combined to evaluate the association between ICP and risk of SGA. Subgroup analysis based on the combination of specific comorbidity was performed. Sensitivity analysis was conducted to assess the stability of pooled results. Begg's funnel plot and Egger's test were performed to identify publication bias, and obvious publication bias was defined as P < 0.05 [15, 16]. If obvious publication bias was detected, the trim-and-fill method was applied to identify potentially unpublished studies [17].

Subgroup analysis Subgroup analysis based on the combination of specific comorbidity was performed.

Sensitivity analysis Sensitivity analysis was conducted to assess the stability of pooled results.

Language restriction None.

Country(ies) involved China - West China Second University Hospital, Sichuan University.

Keywords Intrahepatic cholestasis of pregnancy; small for gestational age; occurrence; meta-analysis.

Contributions of each author

Author 1 - Xi Tan.
Email: tanxi@scu.edu.cn
Author 2 - Yayi Hu.
Email: 81420435@qq.com
Author 3 - Hongqin Chen.
Email: chenhongqin2022@163.com