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Systematic Review

The Relationship between Serum Calcium Level and Risk Factor of Pregnancy-Induced Hypertension: A Meta-Analysis

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Abstract

Background: The relationship between serum calcium levels and pregnancy-induced hypertension is controversial. This work aimed to evaluate the relationship between serum calcium levels and the risk of pregnancy-induced hypertension. **Methods**: The following database: Chinese National Knowledge Infrastructure and PubMed, were searched to identify articles on the relationship between serum calcium levels and pregnancy-induced hypertension. The meta-analysis was conducted by using Review Manager (RevMan) [Computer program]. **Results**: A total of twenty one articles included in the present study. The meta-analysis revealed that patients with pregnancy-induced hypertension (PIH) had lower calcium levels (standardized weighted mean difference (SMD) = –0.68; 95% (–0.79, –0.56); $p <$ 0.05). **Conclusions**: Our study suggests that serum calcium levels may be associated with the risk of pregnancy-induced hypertension.

Keywords: calcium; hypertension; case-control study; meta-analysis

1. Introduction

Pregnancy-induced hypertension (PIH) is a significant cause of maternal morbidity [1,2]. A previous study disclosed that 5.1% of pregnancies are affected by PIH [3]. Furthermore, approximately 15% of global maternal deaths (~30,000 deaths per year) are attributed to hypertensive disorders of pregnancy [4]. Consequently, the prevention and treatment of PIH in urgent in the present study.

Calcium plays a critical role in many vital processes, such as neuronal excitability, the release of neurotransmitters, muscle contraction, membrane integrity, and blood coagulation [5]. In addition, blood pressure is regulated by intracellular calcium in the vascular smooth muscle cell via vasoconstriction and variations in the vascular volume. Therefore, appropriate calcium intake for pregnant women can prevent future osteoporosis and reduces the risk of PIH [6]. However, results reported in previous studies were inconsistent for the relationship between serum calcium level and PIH [7]. Thus, this meta-analysis must confirm the relationship between serum calcium level and PIH.

Our meta-analysis aimed to determine whether or not serum calcium level levels are associated with the risk of PIH, which will offer the basis for the prevention and treatment of PIH.

2. Methods

This study protocol was followed PRISMA guidelines.

2.1 Literature Search

We searched related articles from the Chinese National Knowledge Infrastructure and PubMed databases until July 12, 2022. The following terms: “calcium”; and “pregnancy hypertension”, was used for articles published. In addition, we also searched the references list of relevant studies selected from the electronic databases manually to find additional articles. The language of papers published is restricted to Chinese and English.

2.2 Inclusion and Exclusion Criteria

The retrieved articles met the following criteria: (1) the study involved humans; (2) the study focused on the relationship between PIH and serum calcium level; (3) data needed was easily extracted directly or indirectly from the article; (4) publication language was confined to English and Chinese.

2.3 Quality Assessment

Two authors evaluated the independently using Newcastle-Ottawa Scale (NOS) [8]. We used NOS to assess non- randomized controlled trial (RCT) studies. It includes three main domains (1) selection (cases and control definition, cases and controls selection) maximum of four stars, (2) comparability (are cases and controls comparable or not) maximum of two stars, (3) exposure (for what degree we are confident that our population exposed to the exposure) maximum three stars.

2.4 Statistical Analysis

The meta-analysis was performed using Review Manager (RevMan) [Computer program] (Version 5.4. The

Table 1. Characteristics of studies included.

First author	year	Total	Sample types	Country	NOS
Tong M [11]	2010	90	serum	China	9
Wei J [12]	2008	187	serum	China	9
Li Y [13]	2010	100	serum	China	8
Zhao Y [14]	2008	160	serum	China	9
Yu S [15]	2009	142	serum	China	8
Hao Y [16]	2005	89	serum	China	9
Guo L [17]	2013	118	serum	China	9
Zhao, F [18]	1989	212	serum	China	9
Kumar N [19]	2019	220	serum	India	5
Li YZ [20]	2022	511	serum	China	9
Li XJ [21]	2020	166	serum	China	9
Zhu SY [22]	2019	290	serum	China	9
Liu SQ [23]	2012	80	serum	China	9
Wu MZ [24]	2006	218	serum	China	9
Xu J [25]	2011	120	serum	China	8
Liang YB [26]	2009	133	serum	China	9
Gu LJ [27]	2014	110	serum	China	9
Wang LP [28]	2008	100	serum	China	7
Zheng Q [29]	2015	220	serum	China	7
Wen XG [30]	2015	143	serum	China	9
Xie F [31]	2020	160	serum	China	9

Note: NOS, Newcastle-Ottawa Scale.

Cochrane Collaboration, 2020, London, UK). The standardized weighted mean difference (SMD) with a corresponding 95% confidence interval (CI) was used to compare the mean serum calcium level between the two groups. Heterogeneity among effect sizes was tested using a Q statistic and an I^2 index. The Q statistic tests the null hypothesis that effect sizes are homogeneous in the analysis (Q = 0) [9]. The random effect model was used when the I^2 index was over 50%. The funnel plot was applied to detect possible publication bias [10].

3. Results

A total of 21 potential articles were identified in this study (Table 1, Ref. [11–31] and Fig. 1). NOS was used to assess non-RCT studies (Table 1).

The heterogeneity test found heterogeneity exists (I^2 index = 95%). Then, a random effect model was used to compare the mean serum calcium level between the two groups. The results indicated that the mean serum calcium level in the PIH group was lower than in the control group ($p < 0.05$, Fig. 2, Ref. [11–31]).

Publication Bias and Sensitivity Analysis

Funnel plots determined publication bias. There was no evidence of publication bias (Fig. 3).

4. Discussion

In this meta-analysis, we discovered that the mean serum calcium level in the PIH group was lower than in the control group. The results are consistent with previous results of meta-analysis [32]. Specifically, the serum calcium levels decreased in patients with PIH according to random effects, consistent with an earlier study [5,33]. A recent study also confirmed that calcium supplementation could effectively reduce the risk of PIH [34,35].

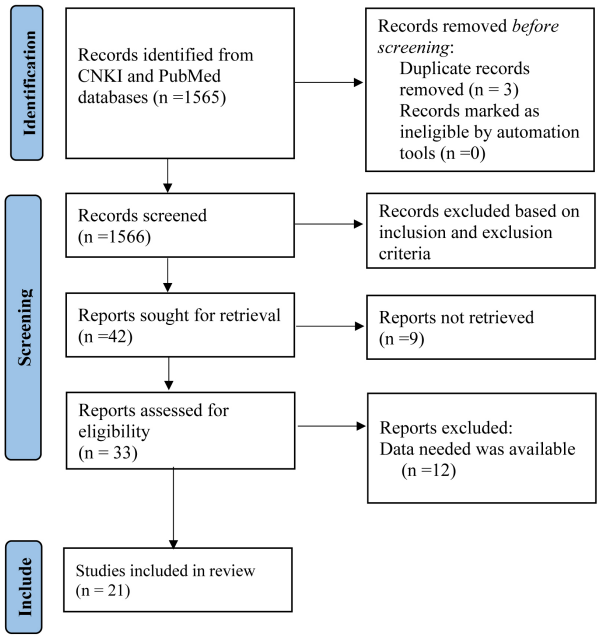

Fig. 1. PRISMA diagram of the search strategy.

In recent years, studies have been carried out on serum trace elements levels during pregnancy. PIH is a pregnancy-specific condition that augments maternal and infant mortality and morbidity [36]. Vitamin D can facilitate the absorption of calcium. Thus, vitamin D supplementation also reduces the risk of PIH. Furthermore, a meta-analysis suggested that vitamin D supplementation also works well in preventing PIH [37]. Therefore, measuring serum calcium levels may be a novel way to monitor the risk of PIH.

5. Strengths and Limitations

The strengths of this study include a comprehensive literature search for all relevant No-RCTs, including the content of ordinary pregnant women and pregnancy hypertension women. In addition, we considered effect moderation by trial location and maternal and intervention characteristics. Finally, we reported a broad range of outcomes and considered core outcomes for pregnancy hypertension.

There are some limitations in our meta-analysis. First, this study included only published articles, and some unpublished articles may need to recruit in the present study. Second, this meta-analysis only searched the articles published in Chinese and English. Therefore, language bias also is not avoided. Third, a subanalysis of different phenotypes of hypertensive disorders of pregnancy should be

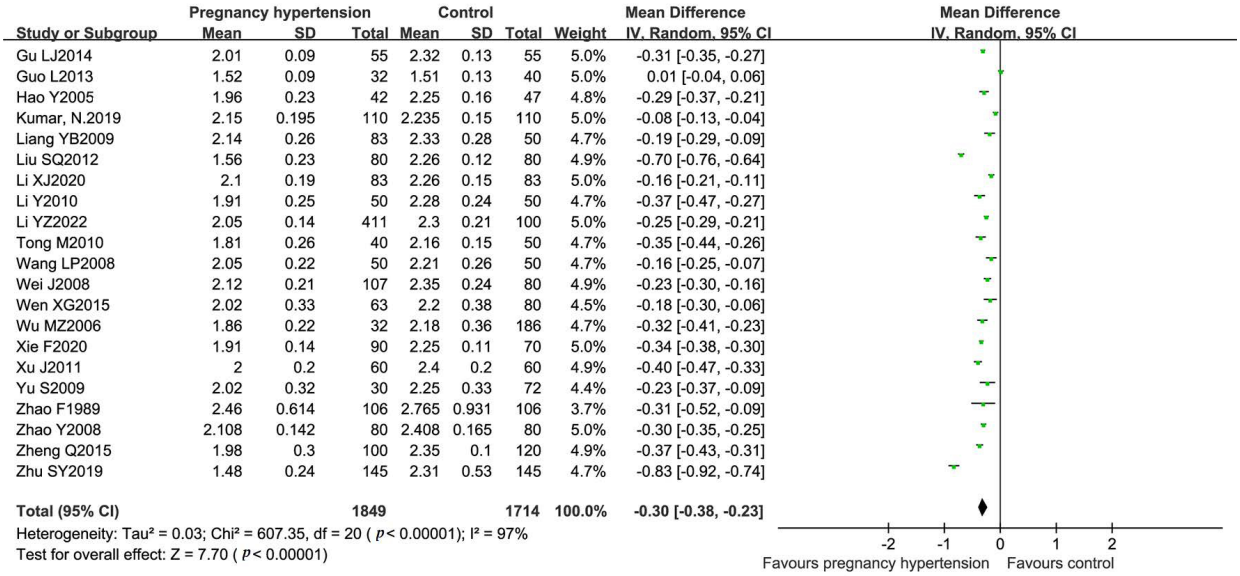

Fig. 2. Forest plot and the risk of bias among studies included.

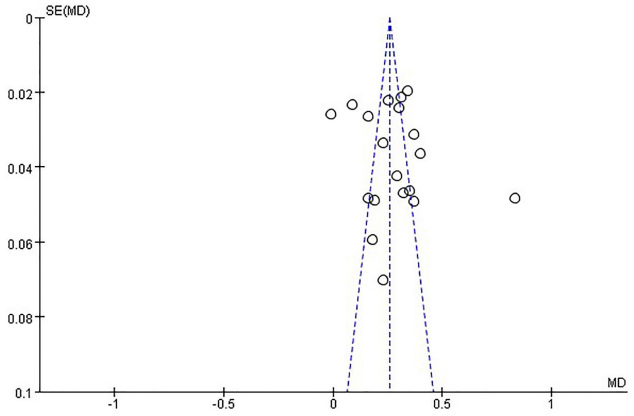

Fig. 3. Funnel plot and the risk of bias among studies included.

performed [38]. However, this subanalysis is not possible due to a lack of data.

6. Conclusions

Our research suggests that the reduction in serum calcium concentration may be closely related to PIH. Pregnancy can easily lead to maternal calcium deficiency, increasing blood pressure. Future research should focus on ensuring calcium supplements maintain serum calcium balance and target women with low serum calcium for personalized PIH prevention.

Author Contributions

CPL and LPH made contributions to study conception and design; YXS and LPH participated in data collection; LPH and YXS dedicated to data analysis and interpretation; CPL and YXS involved in the drafting of the manuscript. All authors read and approved the final manuscript.

Ethics Approval and Consent to Participate

Not applicable.

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Conflict of Interest

The authors declare no conflict of interest.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.31083/j.ceog5003066.

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