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Original Article

The relationship between serum calcium level and women with pregnancy-induced hypertension in China: a meta-analysis

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Abstract: The aim of our study was to determine the relationship between serum calcium levels and PIH. In our study, we searched databases, including Wangfang, Chinese National Knowledge Infrastructure, and PubMed, to find literature regarding the relationship between PIH and calcium levels. The meta-analysis was performed using Review Manager 5.3 software. A total of 8 articles were included in our study. The results of the heterogeneity of PIH ($P<0.001$; $I^2 = 95\%$) showed heterogeneity among the included studies, and we used the random effect model for the meta-analysis. In the meta-analysis, significant differences was found between serum Ca and subjects with PIH (MD = -0.27; 95% CI, -0.40 to -0.30). Our research suggests that decreasing of serum calcium maybe a risk of PIH.

Keywords: Calcium, hypertension, case-control study

Introduction

Calcium (Ca) is also involved in many vital processes, such as neuronal excitability, release of neurotransmitters, muscle contraction, membrane integrity, and blood coagulation [1]. previous study documented that serum Ca has an influence on blood pressure in elderly male subjects [2].

Hypertensive disorders of pregnancy, such as pre-eclampsia (PE) and pregnancy-induced hypertension (PIH), are major causes of maternal morbidity [3, 4]. The results of a previous study revealed that 9.4% of pregnancies are affected by PIH [5]. Some studies suggested that deficiencies of trace elements, such as zinc (Zn), Ca, and Mg, occur in pregnant women [6-8], However, other study also indicated that no changes in Mg and ionized Ca homeostasis occur in the course of PIH [9]. We design this meta-analysis was to determine whether serum Ca levels are associated with PIH.

Materials and methods

Literature search

Potential studies were identified by a comprehensive literature searching, which covered the following computerized bibliographic databases until 1 January 2016: Wanfang; PubMed; and the Chinese National Knowledge Infrastructure. We searched the retrieved article using the following terms: “calcium”; “pre-eclampsia in pregnant women”; “pre-eclampsia pregnant women”; “hypertensive pregnancy”; “pregnancy-induced hypertension”; and “pregnancy hypertension”. Additionally, we searched related articles by reading the references lists of relevant studies selected. Studies published in Chinese and English were included in the present meta-analysis.

Inclusion and exclusion criteria

The retrieved articles met the following criteria: (1) study involved humans; (2) research focused on the association between PIH and Ca; (3) data needed was extracted from the article; (4) publication language was confined to English and Chinese.

Data extraction

To control the bias and improve the reliability, two reviewers independently extracted data from the relevant article that followed a standardized data-collection form. The following

Table 1. Characteristics of studies included

Author	Year	Number	Age (years)		Location
			Control	PIH	
Meiqing T [13]	2010	90	27.2	27.8	Shan Xi
Ying L [14]	2010	100	28.9	28.2	Liao Ning
Yanqing Z [15]	2008	160	25.9	26.5	Shan Dong
Siyong Y [16]	2009	142	28.7	29.0	He Bei
Yanhua H [17]	2005	89	28.6	28.2	Guang Dong
Lili G [18]	2013	118	24-33	24-33	He Bei
Yan L [19]	2013	139	22-32	22-32	Guang Dong
Baolan W [20]	2013	435	24.5	23.9	Shan Xi

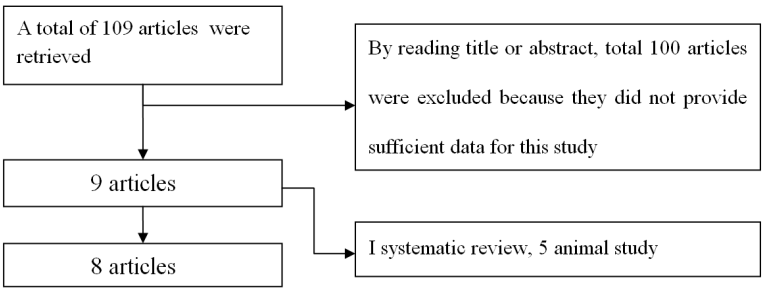

Figure 1. Flow diagram of screening article included.

information was gathered from each study: first author; year of publication; country of residence; age; number of cases and controls; and serum, plasma, or placental levels of Ca in patients with PIH and healthy pregnant women.

Quality assessment

Risk of bias was assessed independently by two authors using the Cochrane Collaboration's tool for assessing risk of bias, which includes judgments of "low", "high", or "unclear" stemming from the following seven domains [10]: (1) random sequence generation; (2) allocation concealment; (3) blinding of participants and personnel; (4) blinding of outcome assessor; (5) incomplete outcome data; (6) selective reporting; and (7) other sources of bias. The risk of bias among randomized trials and the risk can be classified into 'low' (high risk of bias), 'high' (low risk of bias), or unclear [11].

Statistical analysis

The meta-analysis was performed using Review Manager 5.3 (Cochrane Collaboration). Heterogeneity among effect sizes was tested using a Q statistic and an I^2 index. The Q statistic tests. The funnel plot was applied to detect potential publication bias [12].

Results

A total of 95 potential articles were identified. Scanning identified 63 unsuitable articles because the articles did not provide sufficient data for this study. Of the remaining 9 articles, one was a systematic review. Finally, there were 8 studies that satisfied our criteria for the meta-analysis (**Table 1** and **Figure 1**).

The results of the heterogeneity of PIH ($P<0.001$; $I^2 = 95\%$) showed heterogeneity among the included studies, and we used the random effect model for the meta-analysis. In the meta-analysis, significant differences was found between serum Ca and subjects with PIH (MD = -0.27; 95% CI, -0.40 to -0.30), as shown in **Figure 2**.

Publication bias and sensitivity analysis

Publication bias was determined by visualization of funnel plots. There was no evidence of publication bias (**Figure 3**). Low risk of bias was found in present study (**Figure 4**).

Discussion

In this meta-analysis, significant differences was found between serum Ca and PIH, Which inconsistent with a previous study [1, 8]. Sikorski *et al.* [21] proposed that Zn is the most important element related to maternal and fetal metabolism during pregnancy [1, 22].

In recent years, studies involving Ca metabolism during pregnancy have been conducted. PIH is a pregnancy-specific condition that augments maternal and infant mortality and morbidity [23]. PIH is caused by many factors, including heredity and immunodeficiency, and

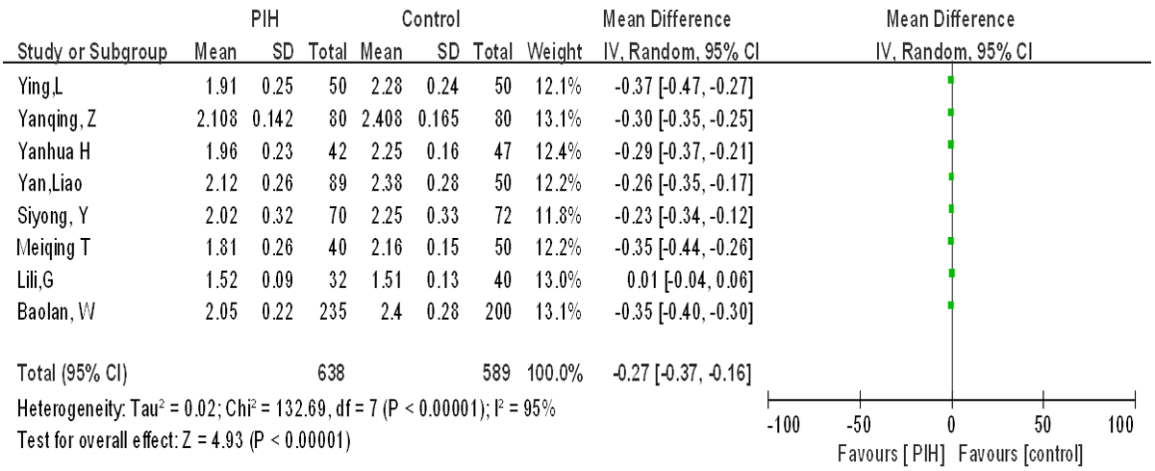

Figure 2. Forest plot of serum Ca levels for subjects with PIH versus healthy controls. The combined MD and 95% CI were calculated using the random-effects model.

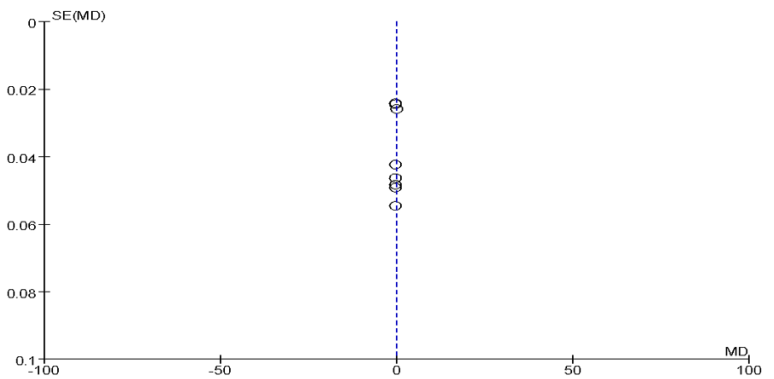

Figure 3. Funnel plot of serum Ca levels for subjects with PIH versus healthy controls.

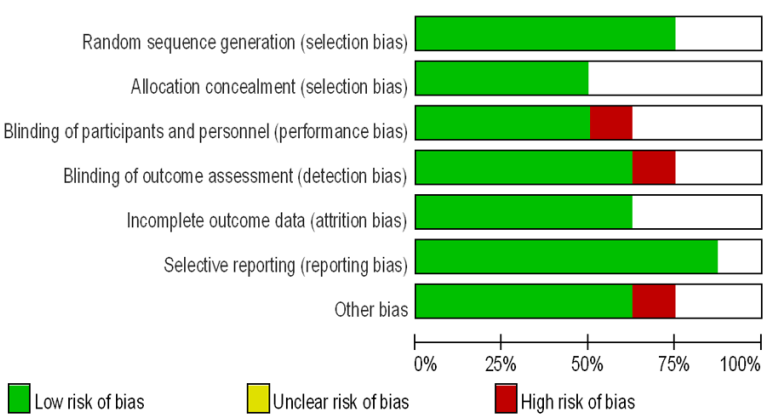

Figure 4. Risk of bias graph.

deficiencies in trace elements are thought to play a vital role in the development of PIH.

Some limitations also should be addressed in our study. Publication bias may have lower estimated because only article published in English and Chinese were included in present study.

Conclusion

Our findings suggest that the decrease in Ca were associated with PIH. Thus, the serum calcium levels should be measured for PIH patients.

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Disclosure of conflict of interest

None.

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References

[1] Jain S, Sharma P, Kulshreshtha S, Mohan G and Singh S. The role of calcium, magnesium, and zinc in pre-eclampsia. Biol Trace Elem Res 2010; 133: 162-170.

[2] Yao Y, He L, Jin Y, Chen Y, Tang H, Song X, Ding L, Qi Q, Huang Z, Wang Q and Yu J. The relationship between serum calcium level, blood lipids, and blood pressure in hypertensive and normotensive subjects who come from a normal university in east of China. Biol Trace Elem Res 2013; 153: 35-40.

[3] Easterling TR. Pharmacological management of hypertension in pregnancy. Semin Perinatol 2014; 38: 487-495.

[4] Kosanovic M, Jokanovic M, Jevremovic M, Dobric S and Bokonjic D. Maternal and fetal cadmium and selenium status in normotensive and hypertensive pregnancy. Biol Trace Elem Res 2002; 89: 97-103.

[5] Hao Y. Clinical significance of serum calcium, magnesium in pregnant women and determination of uric acid in pregnancy induced hypertension syndrome. The Journal of Practical Medicine 2005; 21: 952-953.

[6] Pathak P and Kapil U. Role of trace elements zinc, copper and magnesium during pregnancy and its outcome. Indian J Pediatr 2004; 71: 1003-1005.

[7] Kiilholma P, Paul R, Pakarinen P and Gronroos M. Copper and zinc in pre-eclampsia. Acta Obstet Gynecol Scand 1984; 63: 629-631.

[8] Mahomed K, Williams MA, Woelk GB, Mudzamiri S, Madzime S, King IB and Bankson DD. Leukocyte selenium, zinc, and copper concentrations in preeclamptic and normotensive pregnant women. Biol Trace Elem Res 2000; 75: 107-118.

[9] Smolarczyk R, Romejko E, Wojcicka-Jagodzinska J, Czajkowski K, Teliga-Czajkowska J and Piekarski P. [Homeostasis of calcium-phosphorus-magnesium in women with pregnancy induced hypertension]. Ginekol Pol 1996; 67: 488-492.

[10] Kim CK, Kim DH, Lee MS, Kim JI, Wieland LS and Shin BC. Randomized controlled trials on complementary and traditional medicine in the korean literature. Evid Based Complement Alternat Med 2014; 2014: 194047.

[11] Higgins JP, Altman DG, Gøtzsche PC, Jüni P, Moher D, Oxman AD, Savovic J, Schulz KF, Weeks L, Sterne JA; Cochrane Bias Methods Group; Cochrane Statistical Methods Group. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ 2011; 343: d5928.

[12] Song F and Gilbody S. Bias in meta-analysis detected by a simple, graphical test. Increase in studies of publication bias coincided with increasing use of meta-analysis. BMJ 1998; 316: 471.

[13] Meirong T. Serum calcium, magnesium, of uric acid level and pregnancy induced hypertension syndrome relationship. Maternal and Child Health Care of China 2010; 25: 23-25.

[14] Ying L. Relationship between pregnancy induced hypertension and serum calcium and magnesium. Laboratory Medicine and Clinic 2010; 7: 546.

[15] Yanqing Z. Serum calcium, magnesium, nitrogen, creatinine and uric acid in pregnancy-induced hypertension syndrome. Journal of Community Medicine 2008; 6: 4-5.

[16] Siyong Y, Yongli C, Shujuan K and Hui G. The clinical significance of serum levels of zinc calcium and magnesium in pregnancy-induced hypertension. Chinese Journal of Difficult and Complicated Cases 2009; 8: 433-434.

[17] Yanhua H, Minggang C, Wenping C and Huilin Q. Clinical significance of serum calcium, magnesium in pregnant women and determination of uric acid in pregnancy induced hypertension syndrome. The Journal of Practical Medicine 2005; 21: 952-953.

[18] Lili G, Shengli G, Shouxia L, Shuyong Z, Haixin L, Lihui N, Peng Z and Leping W. The study on the relationship between trace elements content in whole blood and hypertensive disorder complicating pregnancy. Chinese Journal of Birth Health & Heredity 2013; 21: 60-62, 135.

[19] Yan L, Guan L and Lianqing P. Determination of calcium, uric acid and creatinine and fibrinogen in patients with pregnancy-induced hypertension syndrome. Jilin Medical Journal 2013; 34: 4029-4030.

[20] Baolan W, Qiuxia P, Hua L, Juan Z, Yindi L and Aiqin H. Correlation analysis between calcium content in Pregnant women and gestational hypertension. Progressin Modern Biomedicine 2013; 113: 5716-5718.

[21] Sikorski R, Juszkiewicz T and Paszkowski T. Zinc status in women with premature rupture of membranes at term. Obstet Gynecol 1990; 76: 675-677.

[22] Villanueva LA, Figueroa A and Villanueva S. [Blood concentrations of calcium and magnesium in women with severe pre-eclampsia]. Ginecol Obstet Mex 2001; 69: 277-281.

[23] Gupta S, Jain NP, Avasthi K and Wander GS. Plasma and erythrocyte zinc in pre-eclampsia and its correlation with foetal outcome. J Assoc Physicians India 2014; 62: 306-310.