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Is there an association between calcium level and preeclampsia in pregnant women? A systemic review

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Abstract

Background: Pregnancy-induced hypertension is a diagnosis used to describe a wide spectrum of patients who may have only mild elevations in blood pressure or severe hypertension with various organ dysfunctions. Preeclampsia is a form of pregnancy-induced hypertension which is defined as the new onset of hypertension and proteinuria after 20 weeks of gestation in a previously normotensive woman. Preeclampsia has been identified as the leading reason for maternal admission to the intensive care unit in the puerperal period. Trends of pregnancy-induced hypertension in low- and middle-income countries were increasing. The WHO recommend calcium supplementation as part of the antenatal care for the prevention of preeclampsia in pregnant women, particularly among those population where calcium intake low and at higher risk of developing hypertension.

Methods: The data were searched electronically From Pub Med, Google Scholar, Cochrane database reviews and Google. Case-control, retrospective and prospective cohort and clinical trial and papers published in the English language was included. Out of 460 pieces of literature searched electronically, only 23 pieces of literature were used in this study. The other 435 references were not reviewed based on exclusion criteria. In this review 14 case-control studies, 2 cross-sectional studies, 1 longitudinal study, 2 clinical trials, and 4 reviews were included.

Results: The age of the study participant's ranges from 18-41, all study participant's gestational age was greater than 12 wk. All studies used a diagnostic criteria for preeclampsia based on the following criteria: Blood pressure (BP) more than 140/90 and proteinuria >300 mg/do in 24 hr or 1+ in dipstick urine sample. Low levels of calcium have a significant association to preeclampsia as indicated in most studies.

Conclusion: Most studies explored that calcium level was low among preeclampsia women. Inconsistencies of recruitment (for example some researcher recruit at 20 weeks of gestational age others in 28 weeks of gestational age) of participant's leads to inconclusive and biased findings in this review. For future researcher should focus on pathophysiology calcium and hypertension. And also it is better the country should give special attention to improve the dietary calcium intake of pregnant women. In the future scientists should better assess calcium level through multiple methods like dietary, clinical and biochemical method and also the impact of calcium on neonatal and maternal should be assessed

Key Words Calcium, Preeclampsia, Pregnancy

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BACKGROUND

Preeclampsia defined as the new onset of hypertension and proteinuria after 20 weeks of gestation in a previously normotensive woman. Pre-eclampsia is a pregnancy-specific, multi-organ disorder.[1] The criteria for diagnosis is mainly dependent upon blood pressure and proteinuria.

Preeclampsia is diagnosed if a patient exhibits a systolic blood pressure ≥140 mm Hg or diastolic ≥ 90 mm Hg on two occasions at least 4 hours apart after 20 weeks of gestation in a woman with a previously normal blood pressure. Another diagnosis criteria for preeclampsia is having diastolic blood pressure greater than or equal to 160 mm Hg or systolic blood pressure greater than or equal to 110 mm Hg diastolic and having proteinuria dipstick test 1+.[2]
Trends of pregnancy-induced hypertension in low- and middle-income countries was increasing; the cost to manage hypertension and its consequences are huge in Africa and it hampered the continental economic, political and social development.[3]

The prevalence of preeclampsia in women from Kuwait is (35%), in Ethiopian women is 64.7%.[4,5] In one case study, it is reported that primary hyperparathyroidism is a cause for preeclampsia since it decreases the serum concentration of calcium by increasing bone resorption, decreasing urinary calcium excretion and through increasing intestinal calcium absorption.[6] 49.2 % of pregnant women in Deyang, China didn't fulfill the daily requirement of calcium which is developed by required nutrient intake (RNI) that is 1200 mg/day.[7] A dietary survey conducted in Ethiopia shows that average calcium intake of women childbearing age is estimated at 317.32mg per day, which is below the estimated average requirement and women living in the rural area have higher calcium consumption than urban.[8]

Hypertensive disorders of pregnancy contribute significantly to maternal mortality, prematurity, intrauterine growth retardation, perinatal mortality and a risk factor cardiovascular and metabolic disease for women; even if the etiology is uncertain.[2]

According to the World Health Organization (WHO) 2013 report, hypertensive disorders of pregnancy complicate approximately 2-8% of all pregnancies, which is associated with preterm and low birth weight and maternal mortality.[9]

In general, dietary intake and behavioral factors like eating habit of calcium source food are associated factors for the occurrence of preeclampsia.[3] During the time of pregnancy and lactation, the deterioration of calcium is high, so increasing intake of calcium-rich source food is a better approach as compared to calcium supplementation and fortification. WHO recommend populations, where calcium intake is low, calcium supplementation as part of the antenatal care, is recommended for the prevention of preeclampsia in pregnant women, particularly among those at higher risk of developing hypertension [WHO, 2013 #11182].

Calcium supplementation as part of the prenatal care is recommended from 20 weeks of gestation until the end of pregnancy for those at higher risk of developing hypertension to prevent pre-eclampsia and to improve fetal health outcome.[9,11] What is unrecognized is that the recommended dietary allowance of calcium is much less than from demand for pregnant women (Figure 1). Even if WHO recommends calcium supplementation program during pregnancy both developing and developed countries didn't apply the program and the population habitual intake of calcium were not known [Omotayo, 2016 #11183]. This review is intended to explain the association between preeclampsia and serum calcium level.

Research Question: Does blood calcium level associated with preeclampsia?
Objective: The objective of this study is to compare the calcium level among preeclampsia and normotensive women.

METHODS

Inclusion Criteria

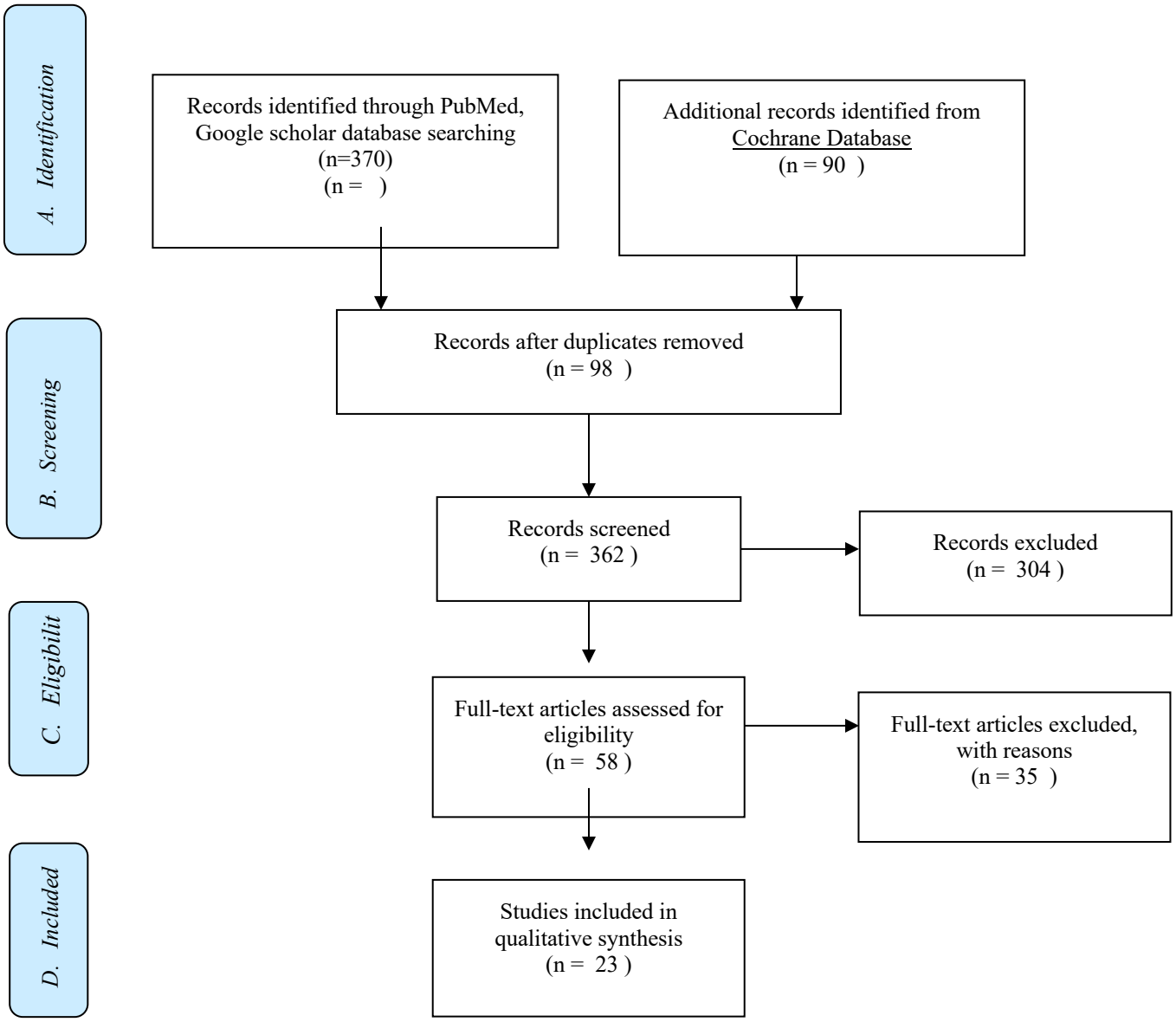
All observational studies (case-control, cross-sectional and cohort) and interventional studies included. Regarding to exclusion criteria case reports, case series, and proceedings were not included in the study.

Search strategy

The data were searched electronically from Pub Med, Google Scholar, Cochrane database reviews and Google. Searching was done by using the keywords "calcium and pregnancy or preeclampsia". Only the English language was used for searching.

Procedural Selection, screening, and excursions of articles from 3 search engines shown in the following diagrams.

PRISMA Flow Diagram



RESULTS

Out of 460 pieces of literature searched electronically, only 23 pieces of literature were used in this study. The other 435 references were not reviewed based on the exclusion criteria. Those papers included in the review were published from the year 1997 to 2016 from 26 countries.

In this review 14 case-control studies, 2 cross-sectional studies, 1 longitudinal study, 2 clinical trials, and 4 reviews were included. The age of the study participants ranges from 18-41. All study participant's gestational age was greater than 12 weeks. All studies use a diagnostic criterion for preeclampsia are blood pressure (BP) more than 140/90 and proteinuria >300 mg/dL in 24 hr or 1+ in a dipstick urine sample.

Blood calcium level than 2.1 ***mmol/l*** have significant association to preeclampsia as explored in Ghana,[12] Vadodara,[13] Dab hade Pune,[14] Nigeria,[15] in Babylon province,[16] and India.[17,18] But other findings from Nigeriaand Iran confirmed that no difference in serum calcium level among non-pregnant, normotensive and preeclampsia women.[19,20] They also describe serum calcium level have no role in the occurrence of preeclampsia. (Table 1)

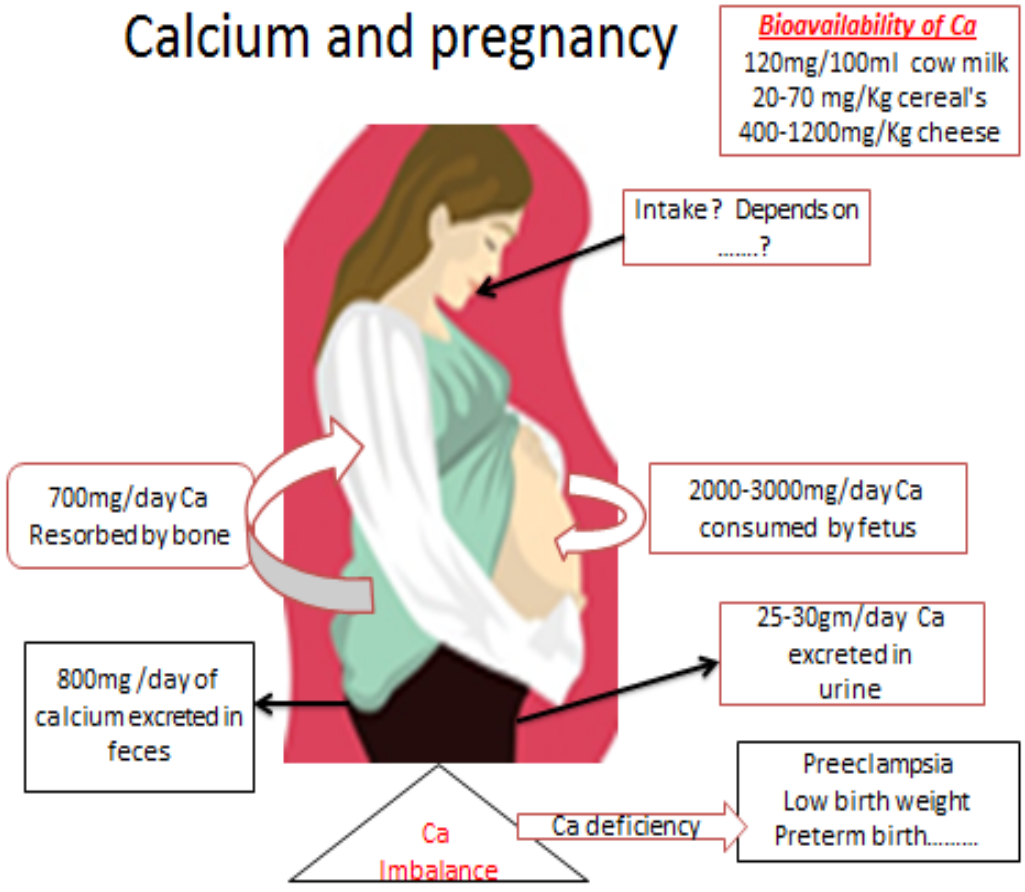


Figure 1. Calcium demand and reccomendation among pregnant women.

TABLE I. SUMMARIZATION OF ARTICLES ON CALCIUM LEVEL AMONG STUDY PARTICIPANTS

References	Study Population	Sample size	Calcium level (mg/dL)	Country
[14]	Preeclampsia	40	7.4 ± 0.55*	India.
	Normal healthy	40	9.61 ± 0.95	
	Normotensive pregnant	40	8.68 ± 2.5	
[13]	Preeclampsia	80	9.61 ± 0.95**	Vadodara
	Normotensive	80	7.0937+0.37798	
[17]	Preeclampsia	50	7.9113+0.91181**	India
	Normotensive pregnant	40	9.357 +0.837	
[31]	Normotensive pregnant	50	4.02±0.54 **	Karnataka
	Non-pregnant*	50	4.85±0.31	
	PIH	50	3.43±0.52	
[20]	Severe preeclampsia	20	5.05±0.35***	Iran
	Mild preeclampsia	20	4.89±0.34	
	Normotensive Pregnant	40	4.96±0.62	
[15]	Preeclampsia	60	1.91 ± 0.28*	Nigeria

	Normotensive pregnant	60	2.32 ± 0.2	
[18]	Preeclampsia	60	7.84 ± 0.87 **	India
	Normotensive pregnant	60	8.97± 0.69	
[16]	Severe preeclampsia	30	6.854±0.28**	Babylon
	Mild preeclampsia	35	7.81±0.24	
	Normotensive pregnant	50	8.16±0.34	
[32]	Preeclampsia	48	2.05±0.4**	Nigeria
	Normotensive pregnant	78	2.6±0.4	
	Eclampsia	30	1.9±0.2	
[33]	Severe preeclampsia	36	8.7 + 0.59*	
	Normotensive pregnant	33	8.99+ 0.31	Bangkok
	Mild preeclampsia	35	9.05 + 0.52	
[12]	Preeclampsia =	100	1.168 **	Ghana
	PIH*	120	1.248	

	Normotensive pregnant *	160	2.385	
[34]	Preeclampsia	50	4.0—9.6*	Sudan
	Normotensive	50	10.6—14.2	
[19]	Preeclampsia	20	2.18 ± 0.2 ***	Nigeria
	Normotensive	20	2.12 ±0.3	
	Non-pregnant	20	2.33 ± 0.3	
[35]	Preeclampsia	60	8.19± 0.71 **	Bangladesh
	Normotensive	30	9.08± 0.83	
[10]	Preeclampsia	30	8.510±1.454 **	Assam
	Normotensive	30	9.903 ±0.6866	
[36]	Preeclampsia	11	9.2 ± 1.02*	Nigeria
	Normotensive	23	0.87	

* = P-value <0.05

** = P-value <0.001

*** = p-value>0.05

PIH = pregnancy-induced hypertension

DISCUSSION

A longitudinal study conducted among Iranian pregnant women shows that there is no correlation between serum calcium levels within the first three trimesters of pregnancy.[21]

A clinical trial completed in the United States among 4489 (2295 had received calcium and 2294 had received a placebo) found that there were no significant differences in relative risk of preeclampsia and pregnancy-associated hypertension, obstetric and perinatal complication among calcium receiver and placebo group. In general, calcium supplementation had no significance in the prevention of pregnancy hypertension disorder as well as an obstetric and perinatal complication in this trial.[22] A systemic review concluded that blended polypill (aspirin, calcium, vitamin D, vitaminB12, and folic acid) is an effective treatment for pregnancy-induced hypertension disorder and its complication.[23] A meta-analysis done in

the developing country shows that calcium supplementation during pregnancy is used to prevent pregnancy-induced hypertension disorder and its complication.[24] Another systemic review evidenced that low dose calcium supplementation is confirmed to reduce the risk of preeclampsia.[25] A comparative study revealed that low level of calcidiol recorded in the Ethiopian population as compared to Norwegian even if much abundance of ultraviolet light in the region.[26] A statistically significant reduction in systolic blood pressure among calcium supplemented adult but not diastolic blood pressure as evidenced from Cochrane review.[27] Supplementing pregnant women with vitamin D in a single or continued dose may reduce the risk of pre-eclampsia, low birth weight, and preterm birth. However, when vitamin D and calcium are combined, the risk of preterm birth is increased, even if the pathophysiology well not explored yet.[28] As birth interval increases the likelihood of developing of preeclampsia is also increases as evidenced from A meta-analysis done in the developed country.[29] An increase in calcium intake slightly reduces both systolic and diastolic blood pressure in normotensive people, particularly in younger than 35 years old, suggesting the role of in the prevention of hypertension.[30]

CONCLUSION

Most studies explored that calcium level was low among preeclampsia women. Inconsistencies of recruitment (for example some researcher recruit at 20 weeks of gestational age others in 28 weeks of gestational age) of participants lead to inconclusive and biased findings in this review. In future instances, researchers should focus on pathophysiology calcium and hypertension. Countries and government agencies should strive to give special attention to improve the dietary calcium intake of pregnant women. Scientists will be able to better to assess calcium levels in pregnant women through dietary, clinical, and biochemical methods. Furthermore, the impact of calcium on neonatal and maternal should be assessed.

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