

# Comparison of Serum Calcium and Magnesium Between Preeclamptic and Normotensive Pregnant Nigerian Women in Abakaliki, Nigeria

Ugwuja EI, Famurewa AC<sup>1</sup>, Ikaraoha CI

Department of Chemical Pathology, Faculty of Clinical Medicine, Ebonyi State University, <sup>1</sup>Department of Medical Biochemistry, Faculty of Basic Medical Sciences, Federal University Ndufu-Alike Ikwo, Abakaliki, Ebonyi, Nigeria

## Address for correspondence:

Dr. Famurewa AC,  
Department of Medical Biochemistry,  
Faculty of Basic Medical Sciences,  
Federal University Ndufu-Alike Ikwo,  
P.M.B. 1010 Abakaliki,  
Ebonyi, Nigeria.  
E-mail: clementademola@yahoo.com

## Abstract

**Background:** Evidence suggests the involvement of calcium and magnesium metabolism in the pathophysiology of preeclampsia. However, findings from studies are heterogenous and inconsistent. **Aim:** The study aimed to compare the total serum calcium and magnesium levels in preeclamptic women with that of normotensive pregnant women. **Subjects and Methods:** A cross-sectional subjects of eighty pregnant women living in Abakaliki, Ebonyi state, South-East Nigeria, were recruited into the study. The present study compared serum calcium and magnesium in forty preeclamptic (cases) and forty normotensive (control) pregnant women matched for age, parity, and socioeconomic status. Serum calcium and magnesium levels were measured using atomic absorption spectrophotometer. Statistical analysis was done using SPSS Version 20 statistical software. Differences between means were compared using Student's *t*-test with  $P < 0.05$  considered as statistically significant. **Results:** While the mean serum calcium was comparable between preeclamptic and normotensive pregnant women (13.99 [3.29] vs. 14.02 [5.68]  $\mu\text{g/dl}$ ), the preeclamptic pregnant women have significantly ( $P < 0.001$ ) lower serum magnesium in comparison to their normotensive counterparts (3.22 [1.05] vs. 4.15 [0.78]). **Conclusion:** It may be concluded that serum magnesium seems to play a crucial role in the pathophysiology of preeclampsia in this environment.

**Keywords:** Calcium, Hypertension, Magnesium supplementation, Preeclampsia

## Introduction

Pregnancy is both desired and demanding for every woman of reproductive age. It is essentially a period that a woman's body undergoes adaptive physiological changes to accommodate fetal growth. One of the potential complications during this period is the emergence of pregnancy-induced hypertension and preeclampsia, commonly associated with increased maternal and infant mortality and morbidity.<sup>[1]</sup> Preeclampsia is a progressive, multi-systemic disorder characterized by triad of high blood pressure (BP) ( $\geq 140/90$  mmHg), edema,

and proteinuria ( $>300$  mg/day), developing after 20 weeks of gestation.<sup>[1]</sup> Incidence of preeclampsia has been estimated at 5–14% pregnancies worldwide, 4–18% in developing countries with increasing trend.<sup>[2,3]</sup> It has been found that preeclampsia has more impact in developing countries where pregnant women have been reported to consume diets with lesser amounts of essential minerals and vitamins.<sup>[1]</sup> During pregnancy, inadequate nutrition might be harmful not only to the mother but also to the growing fetus.<sup>[1]</sup> The pathophysiology of preeclampsia likely involves maternal-fetal physiological perturbations.

This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

**For reprints contact:** reprints@medknow.com

**How to cite this article:** Ugwuja EI, Famurewa AC, Ikaraoha CI. Comparison of serum calcium and magnesium between preeclamptic and normotensive pregnant Nigerian women in Abakaliki, Nigeria. *Ann Med Health Sci Res* 2016;6:33-7.

## Access this article online

### Quick Response Code:



Website: [www.amhsr.org](http://www.amhsr.org)

DOI:  
10.4103/2141-9248.180269

Although the exact etiology is unknown, the pathophysiological mechanism is characterized with the failure of the trophoblastic invasion of the spiral arteries, leading to mal-adaptation of maternal spiral arterioles, which may be associated with an increased vascular resistance of the uterine artery and a decreased perfusion of the placenta.<sup>[4,5]</sup> The implicated vascular resistance and under-perfusion of the placenta, according to a study,<sup>[6]</sup> may lead to the release of antiangiogenic factors into the maternal circulation and alter maternal systemic endothelial function to cause hypertension and other manifestations of the disease. Other contributory factors include obesity, diabetes, calcium deficiency, maternal age, and job stress.<sup>[7,8]</sup> Consequently, much research has focused on elucidating the pathophysiological events that regulate BP in pregnancy.

Recently, nutritional deficiency is gaining prominence in the pathogenesis of preeclampsia. Many clinical studies have shown the relationship between preeclampsia and perturbations in maternal biochemical macronutrients, including calcium and magnesium.<sup>[1,3,4,9,10]</sup> Currently, there is an increased interest in the management of preeclampsia with nutritional approach in relation to calcium and magnesium supplementation.<sup>[11,12]</sup> However, reports from clinical studies are inconsistent on the role of calcium and magnesium in preeclampsia development. Some studies have shown that decrease in serum calcium and/or magnesium may potentiate pathogenesis of preeclampsia,<sup>[7,12,13]</sup> whereas others have failed to show any association of blood levels of the elements and prevalence of preeclampsia.<sup>[5]</sup> Magnesium is a cofactor for enzymes and peripheral vasodilator for smooth muscles.<sup>[14]</sup> Calcium caused vasoconstriction by decreasing prostacyclin production and by increasing the vasoconstriction effect of angiotensin II and noradrenaline in the blood vessel wall.<sup>[15,16]</sup> Considering the physiological importance of calcium and magnesium, it appears that alterations in these nutrients during pregnancy may be risk and/or predisposing factors to preeclampsia. There is a need for further investigations on the role of calcium and magnesium in preeclampsia etiology. Thus, the present study was designed to investigate the possible role of calcium and magnesium in preeclampsia etiopathogenesis among pregnant Nigerians in Abakaliki metropolis.

## Subjects and Methods

The study was a case-control study carried out between January 2013 and June 2014 at the Department of Obstetrics and Gynecology of the Federal Teaching Hospital, Abakaliki, one of the referral tertiary health institutions in the South-Eastern part of Nigeria. The study included forty normotensive pregnant women (controls) and forty preeclamptic women (PW) (cases) who were not on calcium or other supplements attending antenatal clinic in the outpatient department of the hospital. The sample size determination for case-control studies was done according to Cochran's formula ( $z = 1.96$ , confidence interval = 95%), with a prevalence of preeclampsia in Nigerian population.<sup>[17]</sup> The selection followed simple random sampling;

they were matched for age, parity, and socioeconomic status and in their second or third trimester of pregnancy. Ethical approval for the study was granted by the Ethics and Research Committee of the Hospital. The approval was based on the provision of Helsinki Declaration (2000) and on the agreement that patient anonymity must be maintained, good laboratory practice/quality control ensured, and that every finding would be treated with utmost confidentiality and for the purpose of this research only. Written informed consent to participate in the study was obtained from the pregnant women. Sociodemographic and obstetric data were obtained with structured questionnaire reliable and validated. Following that, the BP was measured using mercury sphygmomanometer and stethoscopes (Kris-Alloy<sup>®</sup>, Wuxi Medical Instrument Factory, Wuxi city, Jiangsu, China), which was pretested on known nonhypertensives and known hypertensives and found to be precise. To ensure the accuracy of reading, appropriately sized cuff (cuff bladder encircling at least 80% of the arm) was used and the measurement done after the subject has been in a sitting resting state for 5 min. The subjects were said to be hypertensive according to the WHO/ISH criteria when their mean systolic BP (SBP) were  $\geq 140$  mmHg, and/or when their mean diastolic BP (DBP) was  $\geq 90$  mmHg.<sup>[18]</sup> Participants with SBP  $\geq 140$  mmHg and/or DBP  $\geq 90$  mmHg were measured again after at least 30 min interval for confirmatory purpose. Height and weight measurements were taken with the subjects in light clothing without shoes, caps or head tie on using a standard calibrated meter rule affixed to a wall perpendicular to a flat, smooth surface floor, whereas the body weight was measured using a digital weighing scale (Seca, Hamburg, Germany). The body mass index (BMI) was calculated as a ratio of the weight in kilogram (kg) and square of height in meter (m<sup>2</sup>).<sup>[19]</sup> BP was measured with patients in a restful position using a sphygmomanometer on at least two occasions.

Preeclamptic women were selected based on the following inclusion criteria:

- New onset of hypertension after 20 weeks of gestation with BP  $\geq 140/90$  mmHg or rise in SBP  $>30$  mmHg and DBP  $>15$  mmHg in at least two occasions, above booking BP
- Proteinuria  $>300$  mg/day as detected by dipsticks.

Pregnant women with kidney disease, diabetes, endocrine disorder, or any other systemic disease/secondary causes of hypertension was excluded from the study. Pregnant women on calcium supplement, food characterized with high calcium or minerals were screened out of the study. Pregnant women without hypertension (normotensives) were selected if BP  $< 140/90$  mmHg with no increase in SBP up to 30 mmHg and DBP up to 15 mmHg due to pregnancy and without evidence of proteinuria.

### Sample collection

Between 8:00 am and 10:00 am, fasting venous blood (5 ml) was collected from antecubital vein without stasis and

dispensed into plain plastic bottle (3 ml) while 2 ml was dispensed into ethylenediaminetetraacetic acid bottles for packed cell volume (PCV) analysis. The serum was separated after clotting and stored at  $-20^{\circ}\text{C}$  until total calcium and magnesium were determined.

### Laboratory analysis

Calcium and magnesium were determined using Atomic Absorption Spectrophotometer (Buck Scientific, Model AVG 210),<sup>[20]</sup> whereas PCV was estimated according to a standard method.<sup>[21]</sup>

### Statistical analysis

Statistical analysis was performed using SPSS Version 20 (Chicago IL, USA). Differences between mean values were determined using the Student's *t*-test, at  $P < 0.05$  for statistical significant difference.

## Results

Table 1 depicts the mean age, gestational age, and BMI values for normotensive pregnant women and PW. The mean age 27.55 (4.23) for normotensive pregnant women was not significantly different ( $P = 0.08$ ) from the mean age 29.45 (3.70) for PW. There were statistically significant differences ( $P < 0.001$ ) between the weight, height, and BMI for normotensive pregnant women and PW.

In Table 2, mean serum calcium 14.02 (5.68) for normotensive pregnant women was statistically comparable ( $P = 0.98$ ) to the PW 13.99 (3.29). However, the magnesium level was significantly ( $P < 0.001$ ) lower in preeclamptic pregnant women than in their normotensive counterparts (3.22 [1.05] vs. 4.15 [0.78]). The mean PCV for normotensive and preeclamptic pregnant women showed no statistically significant difference ( $P = 0.54$ ) (41.07 [5.11] vs. 41.80 [4.24]).

**Table 1: Comparison of age and body mass index between normotensive and preeclamptic women<sup>a</sup>**

Parameters	NW (n=40)	PW (n=40)	P
Age (years)	27.6 (4.23)	29.5 (3.70)	0.08
Gestational age (weeks)	21.5 (3.73)	21.4 (3.22)	0.87
Weight (kg)	71.5 (4.38)	66.4 (5.60)	<0.001*
Height (m)	1.66 (0.14)	1.83 (0.16)	<0.001*
BMI (kg/m <sup>2</sup> )	27.2 (5.39)	20.3 (3.90)	<0.001*

\* $P < 0.05$  (significantly different), <sup>a</sup>Values are mean (SD). NW: Normotensive women; PW: Preeclamptic women, SD: Standard deviation

**Table 2: Comparison of calcium, magnesium, packed cell volume between normotensive and preeclamptic women<sup>a</sup>**

Parameters	NW (n=40)	PW (n=40)	P
Calcium (mg/dl)	14.0 (5.70)	13.9 (3.30)	0.98
Magnesium (mg/dl)	4.2 (0.78)	3.2 (1.10)	<0.001*
PCV (%)	41.1 (5.11)	41.8 (4.24)	0.54

\* $P < 0.05$  (significantly different), <sup>a</sup>Values are mean (SD). NW: Normotensive women, PW: Preeclamptic women, PCV: Packed cell volume

## Discussion

Hypertension in pregnancy is an important public health challenge, and the research efforts are yet to unravel the etiologic cause. Imbalance of physiologically important nutrients may progress to deleterious health effects and much more in pregnancy state. Studies in Nigeria have reported etiologic association of dietary calcium and magnesium with preeclampsia, but evidence to support this association is weak, inconsistent, and conflicting.<sup>[5,7,12,13,22,23]</sup>

In the present study, we have analyzed for serum total calcium and magnesium for the purpose of comparison between normal pregnant women and PW. The BMI of normotensive pregnant women was significantly higher than the PW [Table 1]. The normotensive pregnant women were overweight, whereas PW had normal BMI. However, maternal obesity predisposes a woman to developing preeclampsia, and a relationship between increasing BMI and the risk of developing preeclampsia is well established. Although maternal high BMI is related to adverse maternal pregnancy outcomes such as preeclampsia, eclampsia, pre- and post-term delivery,<sup>[23,24]</sup> the reason for the higher BMI in the normotensives is obscure. However, genetic factors have been associated with the development of hypertension.<sup>[25]</sup> There was no significant difference in the mean serum calcium in both pregnant women in this study. This is in contrast with several studies<sup>[4,15,26]</sup> suggesting hypocalcemia as a possible cause for preeclampsia. For instance, Guhan *et al.*<sup>[15]</sup> and Indumati *et al.*<sup>[26]</sup> reported significantly lower calcium levels in preeclamptic patients and pregnancy-induced hypertension, respectively. Moreover, study among pregnant women in Bangkok Metropolis reported significantly lower calcium levels for severely PW, but no statistical difference was found for calcium in mildly preeclamptic group when compared with normal pregnancy group.<sup>[4]</sup> However, in corroboration with our current finding, other studies<sup>[3,23,27]</sup> have refuted the suggestion of the involvement of low calcium in the pathogenesis of preeclampsia. Earlier studies of Golmohammad *et al.*<sup>[23]</sup> and Vahidrodsari *et al.*<sup>[27]</sup> also concluded that serum calcium may not be involved in the pathogenesis of preeclampsia. In Nigeria, Adewolu<sup>[3]</sup> reported no association between serum calcium and preeclampsia and concluded that calcium may not play a vital role in preeclampsia among the Nigerian population. On the basis of the physiological role of dietary calcium,<sup>[14]</sup> epidemiologic studies have shown that restricted dietary calcium is associated with increased BP. Such finding led to dietary calcium supplementation trials in normotensive and hypertensive populations. However, the results from such trials have been disappointing. For example, Levine *et al.*<sup>[16]</sup> in a prospective study in American population showed that calcium supplementation during pregnancy did not prevent preeclampsia in healthy nulliparous women, although Crowther *et al.*<sup>[28]</sup> and Herrera *et al.*<sup>[29]</sup> reported otherwise.

Magnesium is an essential intracellular cation that contributes to neurotransmission and peripheral vasodilation. At the

subcellular level, magnesium regulates contractile protein, modulates transmembrane transport of calcium, sodium, and potassium, act as an essential cofactor in the activation of ATPase, controls metabolic regulation of energy-dependent cytoplasmic and mitochondrial pathways; regulate oxidative-phosphorylation processes, and influences DNA and protein synthesis.<sup>[30]</sup> The present study showed that serum magnesium level in preeclamptic women was significantly lower compared to normotensive pregnant women. Various studies have suggested the influence of magnesium on fetal and maternal morbidity both prepartum and postpartum.<sup>[1]</sup> Previous studies have established inverse association between serum magnesium and occurrence of preeclampsia<sup>[7,14,15,31,32]</sup> similar to our report in this study. Both clinical and experimental data suggest that alterations in magnesium status not only influence vascular contractility, but also vascular smooth muscle cell growth, cardiac excitability, an important factor associated with vascular structural changes in hypertension.<sup>[30]</sup> MacDonald *et al.*<sup>[33]</sup> have shown experimentally that magnesium has a vasoprotective effect. However, conflicting data from extensive investigations have been reported. Golmohammad *et al.*<sup>[23]</sup> in India and Adewolu<sup>[3]</sup> in Nigeria reported no significant difference in magnesium levels among normal pregnancy, pregnancy-induced hypertension, and preeclampsia. Nonetheless, the evidence for causal association between magnesium supplementation and BP reduction was weak in a meta-analysis of 12 randomized trials with follow-up ranging from 8 to 26 weeks.<sup>[34]</sup> A dose-response pattern was found in another meta-analysis with twenty studies; however, magnesium intake only resulted in a small overall reduction in BP, a mean of  $-0.6$  mmHg for SBP and  $-0.8$  mmHg for DBP.<sup>[35]</sup> On the basis of these data, the authors concluded that the relationship between magnesium and hypertension seems inconsistent and not convincing.

## Conclusion

This study has reported a possible role for magnesium but not calcium in the pathogenesis of preeclampsia, with overweight BMI in normal pregnant women. Early detection and treatment of hypomagnesemia may give beneficial health effect in pregnancy-induced hypertension and preeclampsia. However, the current conflicting evidence for calcium and magnesium role in hypertensive disorders, including preeclampsia, is a major challenge confronting universal observation for the use of calcium and magnesium supplementation in preeclampsia management.

## Financial support and sponsorship

Nil.

## Conflicts of interest

There are no conflicts of interest.

## References

- Jain S, Sharma P, Kulshreshtha S, Mohan G, Singh S. The role of calcium, magnesium, and zinc in pre-eclampsia. *Biol Trace Elem Res* 2010;133:162-70.
- Villar J, Betran AP, Gulmezoglu M. Epidemiological basis for the planning of maternal health services. London: WHO/RHR; 2001.
- Adewolu OF. Serum sodium, potassium, calcium and magnesium in women with pregnancy-induced hypertension and preeclampsia in Oredo local government, Benin metropolis: A pilot study. *Afr J Med Health Sci* 2013;12:1-5.
- Punthumapol C, Kittichotpanich B. Serum calcium, magnesium and uric acid in preeclampsia and normal pregnancy. *J Med Assoc Thai* 2008;91:968-73.
- Cunningham FG. Hypertensive disorder in pregnancy. In: Cunningham FG, Leveno KJ, Bloom SL, Hauth JC, Gilstrap PL, Wenstrom KD, editors. *Textbook of Williams Obstetrics*. 22<sup>nd</sup> ed. New York: McGraw-Hill; 2005. p. 761-808.
- Roberts JM, Cooper DW. Pathogenesis and genetics of pre-eclampsia. *Lancet* 2001;357:53-6.
- Chaurasia PP, Jadav PA, Jasani JH. Changes in serum calcium and serum magnesium level in preeclampsia vs normal pregnancy. *Int J Biomed Adv Res* 2012;3:511-3.
- Sibai BM. Prevention of preeclampsia: A big disappointment. *Am J Obstet Gynecol* 1998;179:1275-8.
- Tavana Z, Hosseinmirzaei S. Comparison of maternal serum magnesium level in pre-eclampsia and normal pregnant women. *Iran Red Crescent Med J* 2013;15:e10394.
- Hanisch CG, Pfeiffer KA, Schlebusch H, Schmolling J. Adhesion molecules, activin and inhibin - Candidates for the biochemical prediction of hypertensive diseases in pregnancy? *Arch Gynecol Obstet* 2004;270:110-5.
- Fawcett WJ, Haxby EJ, Male DA. Magnesium: Physiology and pharmacology. *Br J Anaesth* 1999;83:302-20.
- Onyegbule OA, Meludu SC, Dioka CE, Udigwe GO, Udo JN, Ezidighoh AN, *et al.* Comparison of serum levels of calcium and magnesium among preeclamptics and normotensive pregnant women at Nnamdi Azikiwe University Teaching Hospital, Nnewi, Nigeria. *Int J Res Med Sci* 2014;2:404-8.
- Enaruna NO, Ande A, Okpere EE. Clinical significance of low serum magnesium in pregnant women attending the University of Benin Teaching Hospital. *Niger J Clin Pract* 2013;16:448-53.
- Sandip S, Asha K, Paulin G, Hiren S, Gagandeep S, Amit V. A comparative study of serum uric acid, calcium and magnesium in preeclampsia and normal pregnancy. *J Adv Res Biol Sci* 2013;5:55-8.
- Guhan VN, Jeyakumar M, Prabhakara RK, Daniel M, Sivaa R, Priyadharshini S. Serum calcium and magnesium levels in preeclamptic patients - A case control study. *Int J Pharm Sci Rev Res* 2014;26:149-51.
- Levine RJ, Hauth JC, Curet LB, Sibai BM, Catalano PM, Morris CD, *et al.* Trial of calcium to prevent preeclampsia. *N Engl J Med* 1997;337:69-76.
- Kooffreh ME, Ekott M, Ekpoudom DO. The prevalence of pre-eclampsia among pregnant women in the University of Calabar Teaching Hospital, Calabar. *Saudi J Health Sci* 2014;3:133-6.

18. Whitworth JA; World Health Organization, International Society of Hypertension Writing Group. 2003 World Health Organization (WHO)/International Society of Hypertension (ISH) statement on management of hypertension. *J Hypertens* 2003;21:1983-92.
19. Ulasi II, Ijoma CK, Onodugo OD. A community-based study of hypertension and cardio-metabolic syndrome in semi-urban and rural communities in Nigeria. *BMC Health Serv Res* 2010;10:71.
20. Endres DB, Rude RK. Mineral and bone metabolism. In: Carel AB, Edward RA, editors. *Tietz Textbook of Clinical Chemistry*. 3<sup>rd</sup> ed. Philadelphia: Saunders Company; 1999. p. 1395-412.
21. Dacie JV, Lewis SM. *Practical Hematology*. 8<sup>th</sup> ed. Edinburgh: Churchill Livingstone; 1995. p. 49-59.
22. Nguyen H, Odelola OA, Rangaswami J, Amanullah A. A review of nutritional factors in hypertension management. *Int J Hypertens* 2013;2013:698940.
23. Golmohammad S, Amirabi A, Yazdian M, Pashapour N. Evaluation of serum calcium, magnesium, copper, and zinc levels in women with preeclampsia. *Iran J Med Sci* 2008;33:231-4.
24. Yazdani S, Yosofniyapasha Y, Nasab BH, Mojaveri MH, Bouzari Z. Effect of maternal body mass index on pregnancy outcome and newborn weight. *BMC Res Notes* 2012;5:34.
25. Ehret GB, Caulfield MJ. Genes for blood pressure: An opportunity to understand hypertension. *Eur Heart J* 2013;34:951-61.
26. Indumati V, Kodliwadmatu MV, Sheela MK. The role of serum electrolyte in pregnancy-induced hypertension. *J Clin Diagn Res* 2011;5:66-9.
27. Vahidrodsari F, Ayaty S, Tourabizadeh A, Ayat-Allahi H, Esmaeli H, Shahabian M. Serum calcium, magnesium in preeclampsia and normal pregnancies: A comparative study. *J Reprod Infertil* 2008;9:256-62.
28. Crowther CA, Hiller JE, Pridmore B, Bryce R, Duggan P, Hague WM, *et al.* Calcium supplementation in nulliparous women for the prevention of pregnancy-induced hypertension, preeclampsia and preterm birth: An Australian randomized trial. FRACOG and the ACT Study Group. *Aust N Z J Obstet Gynaecol* 1999;39:12-8.
29. Herrera JA, Arevalo-Herrera M, Herrera S. Prevention of preeclampsia by linoleic acid and calcium supplementation: A randomized controlled trial. *Obstet Gynecol* 1998;91:585-90.
30. Touyz RM. Role of magnesium in the pathogenesis of hypertension. *Mol Aspects Med* 2003;24:107-36.
31. Takaya J, Yamato F, Kaneko K. Possible relationship between low birth weight and magnesium status: From the standpoint of "fetal origin" hypothesis. *Magnes Res* 2006;19:63-9.
32. Idogun ES, Imarengiaye CO, Momoh SM. Extracellular calcium and magnesium in preeclampsia and eclampsia. *Afr J Reprod Health* 2007;11:89-94.
33. Macdonald RL, Curry DJ, Aihara Y, Zhang ZD, Jahromi BS, Yassari R. Magnesium and experimental vasospasm. *J Neurosurg* 2004;100:106-10.
34. Dickinson HO, Nicolson DJ, Campbell F, Cook JV, Beyer FR, Ford GA, *et al.* Magnesium supplementation for the management of essential hypertension in adults. *Cochrane Database Syst Rev* 2006;19:CD004640.
35. Jee SH, Miller ER 3<sup>rd</sup>, Guallar E, Singh VK, Appel LJ, Klag MJ. The effect of magnesium supplementation on blood pressure: A meta-analysis of randomized clinical trials. *Am J Hypertens* 2002;15:691-6.