

Comparison of Mean Serum Calcium Levels in Pregnancy with and without Pregnancy Induced Hypertension

RAKSHANDA BANO, SHAZIA TAHSEEN, FATIMA IMRAN BUTT, USMAN MASOOD BUTT, IMRAN MASOOD BUTT, AYESHA IMRAN BUTT

Department of Obstetrics and Gynaecology, Sir Ganga Ram Hospital, Lahore

Correspondence to Associate Professor, Dr Shazia Tahseen. Email: drshaziaimran2013@gmail.com Cell; 0300-4454797

ABSTRACT

Aim: To compare mean serum calcium levels in pregnancy, with and without pregnancy induced hypertension.

Study design: A Cohort study was done.

Place and duration of study: Department of Obstetrics and Gynaecology, Sir Ganga Ram Hospital, Lahore Unit III, from 1st January 2021 to 30th June 2021.

Methodology: Two hundred patients with gestational age between 28 to 40 weeks, were included in the present study, 100 patients in group A (hypertension) and 100 in group B (normotensive).

Results: The mean age of patients in group-A and group-B was 28.87 ± 4.32 years and 27.49 ± 4.80 years respectively. The mean gestational age in group-A was 35.86 ± 1.86 weeks and in group B was 35.90 ± 1.36 weeks. The mean serum calcium level was 7.26 ± 0.80 mg in group A and 8.94 ± 0.53 mg in group B which is statistically significant ($p < 0.001$).

Conclusion: It is concluded that serum calcium levels in women with pregnancy induced hypertension (PIH) are lower than in normal pregnant women. The calcium supplementation appears to reduce the risk of pregnancy induced hypertension. Therefore, calcium consumption in pregnancy should be encouraged, especially during the second and third trimester of pregnancy.

Keywords: Hypocalcemia, pregnancy induced hypertension, Normotensive patients.

INTRODUCTION

The abnormality of hypocalcemia is directly related to many clinical symptoms that may be mild to severe depending on level of hypocalcemia. So hypocalcemia management is related to symptoms severity¹. Hypoparathyroidism & chronic renal failure are associated with hypocalcemia to some extent. Normal level of calcium in plasma is 8.5mg/dl and below this level it is hypocalcemia². Hypocalcemia is also directly correlated with calcium intake in diet and excretion of calcium in urine of pregnant women and also its prevalence was noted as 66.4%. This pregnancy induced hypertension can be either primary or secondary depending on the fact whether it pre-existed in past or not. Pregnancy induced hypertension may also be gestational hypertension if it is found after 20 weeks of pregnancy or pre-eclampsia if it is a component of multisystem³.

Hypertension in pregnancy usually occurs after 20th week in a patient who is previously normotensive. When systolic BP > 140mmHg or diastolic BP > 90mmHg at interval of 4 hours then it is termed as pregnancy induced hypertension. Theories also suggest impaired trophoblastic invasion of spiral arterioles, uterine vascular changes, circulating oxidative radicals, endothelial dysfunction, and cytokine disturbances. Other risk factors include young age (66%), low socioeconomic class (75%), primigravida (62%) and irregular regular calcium supplementation (70%)^{4,5}. Pregnancy induced hypertension occurs in about 7% of all pregnancies and has hazardous effects on both mother and baby³. A local study reported that perinatal mortality as 13% & maternal death rate as 0.4% in females diagnosed with pregnancy induced hypertension⁶.

Approximately 50 to 330 mg of calcium dose is supplied by body to support the development of fetal skeleton⁷. This high demand of fetus calcium is met by supplies from the mother's plasma⁸. It was reported by Mohieldein et al⁹ that calcium level in study group and control group was 8.38 ± 1.04 mg/dl and 9.04 ± 1.13 mg/dl respectively in pregnancy induced hypertension. The calcium level of plasma in mother is directly related to baby's development as those women who have high calcium intake their babies have better bone development. When a comparison is done in pre-eclampsia and normotensive women then researchers report women of former group have lower calcium level. So calcium level should be an important component to be considered

in balanced diet^{9,10}. The rationale of this study was to compare mean serum calcium levels in pregnancy with and without pregnancy induced hypertension. Recommendations can be made regarding the calcium supplement for women who live in places of low socioeconomic status as for those who preferred to skip milk and milk products. Women should be sensitized regarding role of calcium during pregnancy to avoid its related complications and ensure healthy fetomaternal outcomes.

PATIENT AND METHODS

This cohort study was conducted in the Department of Obstetrics and Gynaecology, Sir Ganga Ram Hospital, Lahore Unit III, from 1st January 2021 to 30th June 2021 after IRB permission. Non probability purposive sampling was done. Sample size is 200 patients (100 in each group) is calculated with 95% confidence interval, 80% power of test and taking mean \pm SD of serum calcium level in both group i.e. 8.35 ± 1.04 mg/dl in group with PIH and 9.04 ± 1.13 mg/dl in group without PIH in patients after 20th week of pregnancy.

Inclusion Criteria

Group A

PIH (as per operational definitions)
Any parity
Child bearing age
Gestational age between 28-40 weeks

Group B

Normotensive
Any parity
Child bearing age
Gestational age between 28-40 weeks

Exclusion Criteria

- Pre-eclampsia (PIH plus proteinuria $\geq + 1$ on dipstick test)
- Twin pregnancy on USG
- Chronic hypertension on history

Data Collection Procedure: The study was conducted after permission from the ethical review committee of the hospital. Two hundred patients were admitted through Accident & Emergency and Out-patients Department of Obstetrics and Gynecology at Sir Ganga Ram Hospital, Lahore. They were divided in two groups; group A (hypertensive) and group B (normotensive). An informed consent was taken from the patient or the attendant. Their demographic details like age, parity and address were noted.

Received on 19-04-2022

Accepted on 25-08-2022

Gestational hypertension or pregnancy induced hypertension is the development of new arterial hypertension ($\geq 140\text{mmHg}/\geq 90\text{mmHg}$) in a pregnant after 20 weeks of gestation. Serum calcium level was done of each patient in both groups from the hospital laboratory. Normal serum calcium level is 8.5mg to 10.5mg/dl. The investigations, complete blood count and blood group, were done on routine basis. Data was analyzed by using SPSS version 22. The quantitative variables like age, systolic blood pressure, diastolic blood pressure and serum calcium level were calculated as mean and standard deviation in both groups. The variable like parity was calculated as frequency. Mean serum calcium levels was compared in both groups by using t test and p value of <0.5 was considered as significant.

RESULTS

Total of 200 patients were included in this study. Hundred patients were in group A (pregnancy induced hypertension) and also 100 patients in group B (normotensive). This study was carried out in the Department of Obstetrics and Gynecology at Sir Ganga Ram Hospital Lahore. The age range of patients was 18 to 40 years in both groups. Most of the patients in both groups were between 28 - 37 years of age. There were 36(36%) patients in group A and 47(47%) patients were between 18-27 years of age in group B. In group A, 62(62%) patients were between 28-37 years of age and in group B there was 50(50%) patients were between 28-37 years of age. Only 2(2%) patients in group A and 3(3%) patients in group B were > 37 years of age. The mean was 28.87 ± 4.32 in group A and 27.49 ± 4.80 years of age in group B. The gestational age range 32 to 39 weeks in both groups. Most of the patients in both groups were between 32-39 weeks of gestational age. In group A, 42(42%) patients, and in group B 31(31%) patients were between 32-35 weeks of gestational age. The mean gestational age was 35.86 ± 1.86 in group A, and mean gestational age was 35.90 ± 1.36 weeks in group B. There were 43(43%) patients who had parity 1 in group A, 14(14%) had parity 2, 6(6%) patients had parity 3, 18(18%) patients had parity 4, only 3(3%) patients had parity 5 and primigravida patients were 16(16%) in group A. In group B, 36(36%) patients had parity 1, 17(17%) of patients had parity 2, 8(8%) patients had parity 3, 8(8%) of patients had parity 4, only 1(1%) patient had parity 5 and 30(30%) pf the patients were primigravida.

Table-1: Descriptive statistics of age (years), gestational age (weeks), BP and calcium level

		Mean	S.D	p-value
Age (years)	Group-A	28.87	4.32	> 0.05
	Group-B	27.49	4.80	
Gestational age (weeks)	Group-A	35.86	1.86	> 0.05
	Group-B	35.90	1.36	
Systolic blood pressure	Group-A	152.00	08.87	< 0.05
	Group-B	116.10	6.34	
diastolic blood pressure	Group-A	96.90	5.80	< 0.05
	Group-B	74.10	5.33	
Calcium level	Group-A	7.26	0.80	< 0.05
	Group-B	8.94	0.53	

Table-2: Frequency distribution of age groups and parity

		Group-A	Group-B
Age groups(years)	18-27	36(36%)	47(47%)
	28-37	62(62%)	50(50%)
	>37	2(2%)	3(3%)
	32-35	42(42%)	31(31)
	36-39	58(58%)	69(69%)

In group A, 6(6%) patients had 100-130 systolic blood pressure and in group B there was 95 (95%) had 100-130mmHg systolic blood pressure. There were 94 (94%) patients had 131-170mmHg blood pressure in group A and 5 (5%) patients had 131-170mmHg blood pressure in group B. Four (4%) patients had 60-80mmHg diastolic pressure in group A and 94(94%) patients had 60-80mmHg diastolic pressure in group B. The mean systolic blood pressure was $152.0\pm 8.87\text{mmHg}$ systolic blood pressure in group A and $116.0\pm 6.34\text{mmHg}$ in group B which is statistically significant ($p<0.001$). The mean of diastolic blood pressure was $96.90\pm 5.89\text{mmHg}$ in group A and $74.10\pm 5.55\text{mmHg}$ in group B which is statistically significant ($p<0.05$). The comparison of serum calcium level was presented in both groups. There were most of the patients 57(57%) in group A between 6.0-7.0mg serum calcium level and in group B there was only 1(1.0%) patient. Twenty-five (25%) patients in group A and 8(8%) patients in group B had serum calcium level of 7.1-8.0mg. Sixteen (16%) patients in group A and 39 (39%) patients in group B had 8.1-9.0mg serum calcium levels. only 2 (2%) patients had 8.1-10.0mg serum calcium level in group A and 53 (53%) patients had 9.1-10.0mg in group B. The mean serum calcium level was $7.26\pm 0.80\text{mg}$ in group A and $8.94\pm 0.53\text{mg}$ in group B which is statistically significant ($p<0.001$).

Table-3: comparison of BP and calcium level in study groups.

		Group-A	Group-B	p-value
Systolic blood pressure	100-130	6(6%)	95(95%)	<0.001
	131-170	94(94%)	5(5%)	
Diastolic blood pressure	60-80	4(%)	94(94%)	<0.001
	81-110	96(96%)	6(6%)	
Calcium level	6.0-7.0mg	57(57%)	1(1%)	<0.001
	7.1-8.0mg	25(25%)	8(8%)	
	8.1-9.0mg	16(16%)	38(38%)	
	9.1-10.0mg	2(2%)	53(%)	

DISCUSSION

Hypertension in pregnancy usually occurs after 20th week of gestation in women who was previously normotensive. In developing countries pregnant women are usually suffering from low calcium level so they can face problems during the time of expecting first child, at end of reproductive years, diastolic notch, especially if they have family history of preeclampsia (PE). The fetus has elevated requirements for calcium due to its function in bone development¹¹. Baulon carried out a study with sample of mean maternal age at time of delivery as 25.8 years¹². Mohieldein⁹ study reported the average age of women in study group as 27.4 ± 6.1 years; and for control group as 24.4 ± 6.6 years. Akmal⁵ reported in his study that group 1 involved 100 pregnant women with normal BP & gestational age was almost 30-40 weeks; while group 2 involved patients with diastolic BP 100mmHg & gestational age as 30-40 weeks. Other hypertensive pregnant women with factors other than PIH were excluded. Malas reports the average age as 23.40 ± 2.94 years in that of control group & 25.04 ± 5.10 years in that of study group¹³. The average \pm SD age in our research was approximately 28.87 ± 4.32 in group A & 27.49 ± 4.80 years in that of group B and is comparable to several national & international studies. Baulon reported the average \pm SD gestational age at time of delivery as 39.30 ± 1.55 weeks, with a relatively less gestational age for cases of severe preeclampsia. There were all women who gave birth to baby at hospital (99.8%)¹⁴.

One study reports the mean age as 37.00 ± 2.69 week for that in control group and 36.76 ± 3.15 weeks for that in study group¹³. Another interesting study by Job stress reports that reducing job stress can directly lessen chance of developing pre-eclampsia¹⁵. Gestational hypertension occurred more frequently in women that had increased stress of job¹⁶. But still some researchers object advising complete bed rest to patients with gestational hypertension¹⁷. Still there are no consistent opinions¹⁸. Aqs

relation of bed rest to gestational hypertension is not still completely understood¹⁹. Herrea reported the average±SD gestational age as 38.8±2.2 in that of group A & 38.6 ± 1.6 weeks in that of group B²⁰. Bucher in his study provided a pooled analysis giving statement of a reduction in systolic BP of -5.40mmHg (with 95% confidence interval (p-value<.001) and in diastolic BP of 3.44mmHg. Giving the conclusion that appropriate calcium supplementation can prevent gestational hypertension and pre-eclampsia²¹.

Herrera reported the systolic BP as 116.0±9.6mmHg in that of group A & 122.2±21.2 in that of group B & diastolic BP as 76.3±7.8mmHg in that of group A & 84.3±10.9 considered statistically significant (p0.005)²⁰. Wagner study on preeclampsia reported high BP as 140mmHg or higher systolic BP or 90mmHg or higher diastolic BP after interval of 20 weeks of gestation in pregnant women with previously normal BP. Proteinuria, that is 0.3g or can be more protein in urine collection after interval of 24-hour (that usually gives 1+ or greater on dipstick test). BP in case of severe PE was 160mmHg or as higher systolic or as 110mmHg or as higher diastolic BP, two times in at least 6 hours interval, in a pregnant woman on bed rest²². Our study shows 100-170 mmHg as systolic BP & as 60-110mmHg diastolic BP in pregnant women being comparable with national and international studies.

Sibai reports that an antihypertensive treatment should be carried out in women with BP as 160 to 180mmHg or higher²³. One other study reports diastolic BP of 105 to 110mmHg or higher²⁴. 140 to 155mmHg systolic BP and diastolic BP as 90 to 105mmHg should be the treatment goal. There should be a gradual lowering of BP for such cases²⁵. Sibai also reports that many drugs usage should be avoided in pregnant hypertensive women because of adverse reaction that may occur²⁶. For PE hypertensive women, Hydralazine (Apresoline) & labetalol (Normodyne, Trandate) are considered most useful. Nifedipine (Procardia) & sodium nitroprusside (Nitropress) can be used as alternatives in spite of potential associated risks. For labetalol, it should be kept in mind that it is contraindicated for women with asthma or chronic heart failure²⁵. ACE inhibitors are also contraindicated in pregnant women. Complete treatment of PE requires bed rest and also it is resolved after delivery. Patient should be immediately hospitalized as to avoid any convulsions and any harm to fetus. It must also be kept in mind that costs for taking care of pre-eclampsia is less than that of taking care of pre mature baby. According to Reynolds management goals for severe preeclampsia should be (1) Avoiding convulsions, (2) maternal BP control, & (3) delivery. If pre-eclampsia develops after 26 week interval then fetus lungs may suffer and fetal jeopardy may occur. If preterm delivery occurs then maternal transfer to some tertiary center should be advised to do carry out neonatal intensive care²⁷. Managing patients with preeclampsia of severe level occurring early in pregnancy is a challenge to handle. To ensure proper lung development of fetus some institutions carry out antihypertensive treatment for mother. Corticosteroids can also be used to achieve this goal²⁷.

One study reports serum calcium level for that of control group as 9.50±0.16mg and for that of study group 8.22± 0.12mg considered statistically significant (p<9.995)¹³. Mohieldein⁹ reported mean serum calcium level in study group as (8.38±1.04mg%), and the average serum calcium level in that of control group as (9.04±1.13mg%) that was statistically significant. Flynn reported serum calcium as a significant balanced diet component as it is required for bone and teeth development and all other needs of life²⁸. Emily reported that during a full term pregnancy, 30g of mother's calcium is taken by fetus, by mother's bones if level is low in serum. Contrarily if serum level is high in plasma then there will more calcium in breast milk making baby's bones strong²⁹.

Rasmusen reports that in almost 5% to 10% of pregnancies pre-eclampsia occurs. In addition to this pregnancy induced hypertension (PIH), proteinuria, and oedema is also present³⁰. Exact reason for pre-eclampsia is undetermined yet it is a supported theory that it originates from placenta and involves

reaction between mother and fetus serum^{31,32}. For study group mean serum level was reported as (8.38±1.04 mg/dl), and average serum calcium level in control group as (9.04±1.13mg/dl) that was statistically significant. All these results suggest an inverse relationship of calcium level and PIH³³. In our study the serum calcium level deficiency was assessed by measurement of calcium retention. The results of study showed that 82% of the patients in group A were calcium deficient compared with only 9% in group B who were calcium deficient, with mean±SD 7.26±0.80 in group A and 8.94±0.53 in group B (p<0.001) which is statistically significant and compared with other studies. Seely reports that women with preeclampsia had relatively lower serum ionized levels than those who were normotensive (1.20 2410.01 vs. 1.26 ± 0.01 mmol/L, (p-value < 0.02). Both groups had equivalent levels of 25(OH)D; but, preeclampsia observed to have much lower 1,25-dihydroxyvitamin D levels (172.1±18.5 vs. 219.6±12.7mmol/L, (p-value < 0.05). Hence, low levels of 1,25-(OH)2D can contribute to less intestinal calcium absorption during phase of increased calcium demand, leading to lower ionized calcium levels, hypocalciuria in preeclampsia, increased parathyroid hormone. Calcium sensitivity may also affect vascular resistance³⁴. Calcium metabolism may also be affected in pregnancy. Almost 30-50gm calcium should be stored during pregnancy, half of which that is 25gms is needed by fetus. In third trimester 80% of this is deposited in fetus. Ionized calcium is transferred at rate of 50 mg/day at 20 weeks from mother to fetus and 350 mg/day at 35 weeks. Reduced serum calcium levels cause increase of parathyroid hormone levels, elevating calcium level in cells increasing vascular smooth muscle contraction and hence BP. So, it is supported that intracellular increase of calcium indirectly affects BP. There is much supportive data for relationship of calcium level in serum to that of pre-eclampsia and gestational hypertension so if the levels increased it can reduce the harmful effects on both mother and fetus³⁵ If almost 2 g of calcium supplementation is provided per day, it eventually decreases BP reducing vascular smooth muscle contraction so pregnancy can be safe. There is a shift of ions from intracellular space to extracellular space that leads to reduction of BP. Bucher meta-analysis involving randomized controlled trials studying calcium supplementation effects on PIH & preeclampsia also supported above theories²¹.

CONCLUSION

It is concluded that serum calcium levels in pre-eclamptic pregnant women are lower than in normal pregnant women. There is a relationship between low calcium level and pregnancy induced hypertension. The calcium supplementation appears to reduce the risk of pregnancy induced hypertension, especially in populations living in poor sanitary conditions associated with risk factors for pregnancy induced hypertension. It may play a beneficial role in the prevention of pregnancy induced hypertension by maintaining serum calcium levels. Therefore, calcium consumption in pregnancy should be encouraged, especially during the second and third trimester of pregnancy.

Conflict of interest: Nil

REFERENCES

1. Adams ME, Atkinson MH, Lussier AJ, Schulz JI, Siminovitch KA, Wade JP, et al. The role of viscosupplementation with hylan GF 20 (Synvisc®) in the treatment of osteoarthritis of the knee: a Canadian multicenter trial comparing hylan GF 20 alone, hylan GF 20 with non-steroidal anti-inflammatory drugs (NSAIDs) and NSAIDs alone. *Osteoarthritis and cartilage* 1995;3(4):213-25.
2. Athakker R. Hypocalcemia: Pathogenesis, differential diagnosis, and management. A primer on the metabolic bone diseases and disorders of mineral metabolism. *Am Soc Bone and Miner Res* 2006;6:213.
3. Shennan A, Gupta M, de Swiet M, Halligan A, Taylor D. Lack of reproducibility in pregnancy of Korotkoff phase IV as measured by mercury sphygmomanometry. *The Lancet* 1996;347(8995):139-42.
4. Buchbinder A, Sibai BM, Caritis S, MacPherson C, Hauth J, Lindheimer MD, et al. Adverse perinatal outcomes are significantly

- higher in severe gestational hypertension than in mild preeclampsia. *Am J Obstet Gynecol* 2002;186(1):66-71.
5. Noreen A, Rana G. Women with pregnancy induced hypertension: epidemiological difference between normotensive pregnant women. *Professional Med J* 2006;13(2):310-2.
 6. Jehan A, Musarrat J, Nadra S. Perinatal outcome in pregnancy induced hypertensive mothers. *Pak Armed Forces Med J* 2004;54(8):76-8.25.
 7. Jarjou LM, Prentice A, Sawo Y, Laskey MA, Bennett J, Goldberg GR, et al. Randomized, placebo-controlled, calcium supplementation study in pregnant Gambian women: effects on breast-milk calcium concentrations and infant birth weight, growth, and bone mineral accretion in the first year of life-. *Am J Clin Nutr* 2006;83(3):657-66.
 8. Beinder E. Calcium-supplementation in pregnancy--is it a must? *Ther Umsch* 2007;64(5):243-7.
 9. Mohiudein AH, Dokem AA, Osman YHM, Idris H. Serum calcium level as a marker of pregnancy induced hypertension. *Sudan J Med Sci* 2007;2(4):245-8.
 10. Geraldo Lopes Ramos J, Brietzke E, Martins-Costa SH, Vettorazzi-Stuczynski J, Barros E, Carvalho C. Reported calcium intake is reduced in women with preeclampsia. *Hypertens Pregnancy* 2006;25(3):229-39.
 11. Pitkin RM. Calcium metabolism in pregnancy and the perinatal period: a review. *Am J Obstet Gynecol* 1985;151(1):99-109.
 12. Baulon E, Fraser WD, Piedboeuf B, Buekens P, Xiong X. Pregnancy-induced hypertension and infant growth at 28 and 42 days postpartum. *BMC Pregnancy and childbirth* 2005;5(1):5-10.
 13. Malas NO, Shurideh ZM. Does serum calcium in pre-eclampsia and normal pregnancy differ? *Saudi Med J* 2001;22(10):868-71.
 14. Baulon E, Fraser WD, Piedboeuf B, Buekens P, Xiong X. Pregnancy-induced hypertension and infant growth at 28 and 42 days postpartum. *BMC Pregnancy Childbirth* 2005;5(1):5-10.
 15. Wergeland E, Strand K. Work pace control and pregnancy health in a population-based sample of employed women in Norway. *Scand J Work Environ Health* 1998;24:206-12.
 16. Marcoux S, Bérubé S, Brisson C, Mondor M. Job strain and pregnancy-induced hypertension. *Epidemiology* 1999;376-82.
 17. Goldenberg RL, Cliver SP, Bronstein J, Cutter GR, Andrews WW, Mennemeyer ST. Bed rest in pregnancy. *Obstet Gynecol* 1994;84(1):131-6.
 18. Herrera J. Nutritional factors and rest reduce pregnancy-induced hypertension and pre-eclampsia in positive roll-over test primigravidas. *Int J Gynecol Obstet* 1993;41(1):31-5.
 19. Mathews D. A Randomized Controlled Trial Of Bed Rest And Sedation Or Normal Activity And Non-Sedation In The Management Of Non-Albuminuric Hypertension In Late Pregnancy. *Int J Obstet Gynaecol* 1977;84(2):108-14.
 20. Herrera J, Shahabuddin A, Ersheng G, Wei Y, Garcia R, López-Jaramillo P. Calcium plus linoleic acid therapy for pregnancy-induced hypertension. *Int J Gynecol Obstet* 2005;91(3):221-7.
 21. Bucher HC, Guyatt GH, Cook RJ, Hatala R, Cook DJ, Lang JD, et al. Effect of calcium supplementation on pregnancy-induced hypertension and preeclampsia: a meta-analysis of randomized controlled trials. *Jama* 1996;275(14):1113-7.
 22. Wagner LK. Diagnosis and management of preeclampsia. *Am Fam Physician* 2004;70(12):2317-24.
 23. Sibai BM. Diagnosis and management of gestational hypertension and preeclampsia. *Obstet Gynecol* 2003;102(1):181-92.
 24. Practice ACoO. ACOG practice bulletin. Diagnosis and management of preeclampsia and eclampsia. Number 33, January 2002. American College of Obstetricians and Gynecologists. *Int J Gynaecol Obstet* 2002;77(1):159-67.
 25. Gifford R. Report of the national high blood pressure education program working group on high blood pressure in pregnancy. *Am J Obstet Gynecol* 2000;183:S1-S15.
 26. Sibai BM. Chronic hypertension in pregnancy. *Obstet Gynecol* 2002;100(2):369-77.
 27. Reynolds C, Mabie W, Baha M. hypertension states of pregnancy. *Am J Reprod Immunol* 1997;37:79.
 28. Flynn A. The role of dietary calcium in bone health. *Proc Nutr Soc* 2003;62(4):851-8.
 29. Harville EW, Schramm M, Watt-Morse M, Chantala K, Anderson JJ, Hertz-Picciotto I. Calcium intake during pregnancy among white and African-American pregnant women in the United States. *J Am Coll Nutr* 2004;23(1):43-50.
 30. Rasmussen S, Irgens LM. Fetal growth and body proportion in preeclampsia. *Obstet Gynecol* 2003;101(3):575-83.
 31. Maine D. Role of nutrition in the prevention of toxemia-. *Am J Clin Nutr* 2000;72(1):298S-300S.
 32. Lyell DJ. Hypertensive disorders of pregnancy: Relevance for the neonatologist. *NeoReviews* 2004;5(6):e240-e6.
 33. Ritchie LD, King JC. Dietary calcium and pregnancy-induced hypertension: is there a relation?-. *Am J Clin Nutr* 2000;71(5):1371S-4S.
 34. Seely EW, Wood RJ, Brown EM, Graves SW. Lower serum ionized calcium and abnormal calcitropic hormone levels in preeclampsia. *J Clin Endocrinol Metabol* 1992;74(6):1436-40.
 35. 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 Irial. *Aust N Z J ObstetGynaecol* 1999;39(1):12-8.