Available online at https://www.jhspract.com

Journalgurus© https://www.journalgurus.com

Original Article

Calcium Intake and the Risk of Developing Preeclampsia among Pregnant Women Receiving Antenatal Care at the Jos University Teaching Hospital

Chinedu G. Obikili[1], Amaka N. Ocheke[2], Patrick H. Daru[2].

[1] Department of Surgery, Zenith Medical and Kidney Center, Gudu, Abuja, FCT.
[2] Department of Obstetrics and Gynaecology, Jos University Teaching Hospital, Jos, Plateau State.

ABSTRACT

Background: Pre-eclampsia is a significant cause of maternal and fetal morbidity and mortality and steps have been made towards its prevention. In 2013 the WHO came up with a recommendation that calcium supplementation for prevention of pre-eclampsia be added as part of the antenatal care in populations with low calcium intake. However, calcium intake in our population is not known. **Method:** It was a hospital based cross sectional descriptive study. In this study, 206 women were recruited by convenience sampling technique, 24-hour dietary recall was taken from them after which dietary calcium was calculated using the West African food composition table. Their serum calcium levels were determined from samples taken in the antecubital vein without tourniquet. They were then followed up to determine the maternal and neonatal outcomes. Analysis was done using SPSS software version 20 and results calculated. **Results:** The mean calcium intake for the studied population was 529.6 +/- 312.08 mg/day, the mean serum calcium was 2.185 +/- 0.212 mmol/L. The incidence of pregnancy induced hypertension was 15.5% and the incidence of Pre-eclampsia was 2.8%. There was no statistically significant relationship between Calcium intake and Serum Calcium. Women who developed PIH and preeclampsia had an average lower calcium intake than those who had normotensive pregnancies, but this relationship was not statistically significant. There was no relationship between calcium intake, serum calcium and neonatal outcome. **Conclusion:** The oral calcium intake of women in our environment is lower than the recommended threshold of 900mg, thus, calcium supplementation should be given routinely as part of our ante-natal care in this environment. There appears to be a relationship between calcium intake and risk of pre-eclampsia in our environment, but no relationship between each of them and neonatal outcomes, though larger studies might be needed to confirm this assertion.

Key Words: Pre-eclampsia, Calcium intake, Calcium supplementation, Serum Calcium, Prevention.

INTRODUCTION

In 2013, the World Health Organization (WHO) came up with the recommendation that in populations where calcium intake is low, calcium supplementation as part of the antenatal care is recommended for prevention of pre-eclampsia among pregnant women, particularly among those at higher risk of hypertension (strong recommendation).[1]

This recommendation followed two Cochrane systematic reviews investigating whether calcium supplementation on a daily basis during pregnancy safely improves maternal and infant outcomes and found that this intervention significantly reduced the risk of pre-eclampsia and high blood pressure (with or without proteinuria).[2,3] Approximately 287,000 women died during pregnancy and childbirth in 2010, mostly due to maternal health complications, a significant amount of which is contributed by hypertensive disorders in

Corresponding Author:

Dr Chinedu George Obikili
Department of Clinical Services,
The Bridge Clinic, Port-Harcourt, Rivers State.
Phone: +2348036798227
obikilichinedu@gmail.com

pregnancy. These disorders complicate as high as 2-8% of pregnancies.[4]

The recommendation also states that the overall intake of calcium should not exceed locally established upper tolerable limits. In the absence of such standards an upper limit of calcium intake of 3g per day be used.[2, 5] Calcium intakes of 1200 mg per day is recommended by WHO and the Food and Agriculture Organization of the United Nations (FAO) [6]. The largest protective effects of calcium supplementation were found in populations with habitual calcium intake less than 900 mg per day[7].

From the logic behind these recommend-dations, it is evident that both extremes of low intake and excessive intake are harmful and can worsen maternal and perinatal outcomes thus it is paramount that calcium supplementation only be given in an evidence-based manner based on population studies. The study aimed to carry out the WHO recommendation of determining calcium intake at population level. It also used this calcium intake alongside serum calcium level to determine the effect calcium had on neonatal outcome in normotensive women and in those that developed hypertensive disorders of pregnancy.

Calcium intake is the most valid parameter used to assess the risk for pre-eclampsia as serum calcium concentrations are generally maintained within normal limits in the body and thus have limited use for assessment of calcium nutritional status at both individual and population levels[6]. On the other hand, varying studies exist, and a number of previous local studies have shown serum calcium levels to be lower than those in developed countries. However, works comparing Calcium intake with serum calcium levels are limited and it is important to ascertain the degree to which calcium homeostasis is maintained, this would also help explain the findings of low serum calcium in our environment and establish if it is related to calcium intake or if it is as a result something else which could be a subject for another follow up study[7,8].

Determination of the dietary calcium intake in an individual woman is a complex task. Calcium intake at population levels can be estimated through various means including dietary surveys using 24-hour recalls, food frequency questionnaires or food weighing, as well as through secondary data estimates derived from FAO food balance sheets or household consumption and expenditure surveys [9, 10]. The 24-hour dietary recall is the most practical here and was used for this study. Common West African foods have been assessed for contents of nutrients including calcium, one of such is the West African Food Composition Table[11].

METHODOLOGY

It was a hospital based cross-sectional study conducted at the Jos University Teaching Hospital (JUTH), a 600-bed tertiary health institution located in Jos, the capital of Plateau state in North Central Nigeria. The study comprised of 206 women in their early second trimester (from 13 weeks 0day till 20 weeks 0 days) presenting for booking at the Antenatal Clinic of the Jos University Teaching Hospital (JUTH)

In calculating the sample size, reference value from the study in Benin with similar characteristics and study design was used with a standard normal variant of 1.96 used, absolute error of 5% and a standard deviation based on the above study of 36.6.

Consenting eligible pregnant women who present to the antenatal clinic were recruited into the study by convenience sampling technique over a period of two months from July 2019 to August 2019. They were then followed up till delivery, over the course of 7 additional months till March 2020. The study was commenced in July 2019 and completed in March 2020.

A structured questionnaire was administered, and privacy was ensured while interviews were being conducted. Serial numbers were assigned to each patient to protect their identities and eliminate bias. The women were followed up till term and further data was inputted until delivery.

Nutrient intake, including total calorie and calcium intake was assessed using a 24-hour dietary recall questionnaire. The results were calculated using the West African food composition table.

A semi-quantitative comprehensive dietary history questionnaire was used to assess each woman's diet. Standardized food props[12] were used to more accurately estimate the quantity of every food the participant ingested. Daily intake of foods was calculated and selected nutrients (calcium) was estimated using an ad hoc algorithm for the questionnaire based on the standard West African food composition table. The calcium intake over the past 24 hours was calculated from this table and the sum of all the products was done. A standardized software was then used to convert their intake quantified in mls into grams based on the preparation pattern. The sum of intake cut off value of 900mg of calcium a day was considered to define adequate intake for pregnant women[2].

Venous blood (5ml) was taken from the antecubital vein without stasis (without the use of a tourniquet) and dispensed into a plain plastic bottle.

The serum calcium was analyzed and determined on the same day following separation after clotting. Calcium level in the serum was determined using Atomic Absorption Spectrophotometer.

The participants were followed up till the end of the puerperium. Their blood pressures and urinalysis for proteinuria was assessed at each visit and until 6 weeks postpartum. Upon delivery the gestational age at delivery, birth weight and APGAR scores were documented. Admissions to the neonatal unit were also noted alongside the indications for admission.

All statistical analysis was performed using SPSS software (version 20). Frequencies and percentages were computed for demographic and educational characteristics of the study population. Test for association for categorical and numerical data was done using Pearson's r test and student t test respectively. A P-value of <0.05 was taken as significant.

RESULTS

The socio-demographic characteristics of the women that participated in the study is shown in table 1. The overall mean age was 29.10 +/- 6.21 years with a median of 29 years and a range of 18 to 40 years. The largest number of women were in the age range of 20 – 29 as seen in table 1.

The average calcium intake was 529.6 +/- 312.08 mg per day with a range of 28 mg to 1616.7 mg per day. The mean serum calcium was 2.185 +/- 0.212 mmol/L with a range of 1.8 – 2.9 mmol/L

One hundred and forty-two women completed their follow up to the postnatal period whilst 64 women were lost to follow up at various points in their care. There was an incidence of 15.5% for PIH and 2.8% for pre-eclampsia. There was no case of eclampsia. There was no statistically significant relationship between Oral Calcium intake, Serum calcium and any of the Fetal outcomes.

Table 1. Relationship Between Socio-Demographic Data, Oral Calcium Intake and Serum Calcium

Characteristics	Frequency (Percentage)	Mean Calcium intake	Mean Serum Calcium
Age category			
< 20	10 (4.9)	672.318	2.210
20-29	98 (47.6)	539.440	2.214
30-39	88 (42.7)	518.719	2.158
40-49	10 (4.9)	386.208	2.120
Total	**206 (100.0)**	**529.600**	**2.185**
		Pearson's correlation: 0.123 p-value: 0.078	Pearson's correlation: 0.137 p-value: 0.049
Ethnicity			
Hausa-Fulani	91 (44.2)	574.849	2.208
Igbo			
Yoruba	6 (2.9)	547.067	2.067
Indigenous	9 (4.4)	472.789	2.144
Plateau tribe	74 (35.9)	496.650	2.170
Others			
Total	26 (12.6)	480.647	2.192
	206 (100.0)	**529.600;** p-value 0.600	**2.185;** p-value 0.846
Level of education			
None			
Primary	2 (1.0)	753.350	2.000
Secondary	11 (5.3)	686.018	2.073
Tertiary	105 (51.0)	535.725	2.200
Total	88 (42.7)	497.655	2.186
	206 (100.0)	**529.600**	**2.185**
		p-value 0.612	p-value 0.828
Occupation			
Housewife	63 (30.6)	560.859	2.213
Student	19 (9.2)	523.805	2.263
Trader	34 (16.5)	474.433	2.132
Self- employed			
Civil- Servant	34 (16.5)	528.594	2.150
Others			
	40 (19.4)	494.144	2.180
Total	16 (7.8)	621.413	2.188
	206 (100.0)	**529.600**	**2.185**
		p-value 0.349	p-value 0.645
Husband's level of education			
None	1 (0.5)	487.400	2.100
Primary	2 (1.0)	494.150	2.250
Secondary	94 (45.6)	538.861	2.194
Tertiary	109 (52.9)	522.651	2.178
Total	**206 (100.0)**	**529.600**	**2.185**
		p-value 0.333	p-value 0.746
Husband's occupation			
Unemployed	1 (0.5)	458.700	2.400
Student	2 (1.0)	535.600	2.050
Trader	50 (24.3)	554.116	2.206
Self- -employed			
Civil- Servant	56 (27.2)	511.084	2.161
Others			
Total	54 (26.2)	490.363	2.200
	43 (20.9)	575.853	2.177
	206 (100.0)	**529.600;** p-value 0.154	**2.185;** P-value 0.927

∗Correlation between age group and Serum Calcium is significant at 0.05 level (two tailed)

DISCUSSION

From the results above, the mean oral calcium intake was 529.6 +/- 312.08 mg/day with a range of 28 mg to 1616.7 mg/day. This is less than the WHO and FAO recommended daily calcium intake of at least 1200 mg per day[6] as well as being below the protective cut-off of 900 mg per day[7] below which calcium supplementation is recommended[2].

It correlates with previous findings which suggests that low calcium intakes at population levels occur frequently [13, 14], with critically low levels found in Asia and Africa.

It is similar to previous studies from Africa which had a Calcium intake range of 400-700 mg/day, while being higher than the average calcium intake in Asia which was 400mg/day, the lowest globally[15]. Though within the range for Africa, it was below the average calcium intake for low-income countries which is 647.6mg/day, and slightly below the second trimester levels for low-income countries of 565.5mg/day[16].

It is also slightly below the average calcium intake from Benin Republic which was 561 mg/day[17], and is in keeping with the study of

immigrant Nigerian women in Ireland which found inadequate dietary calcium intake[18].

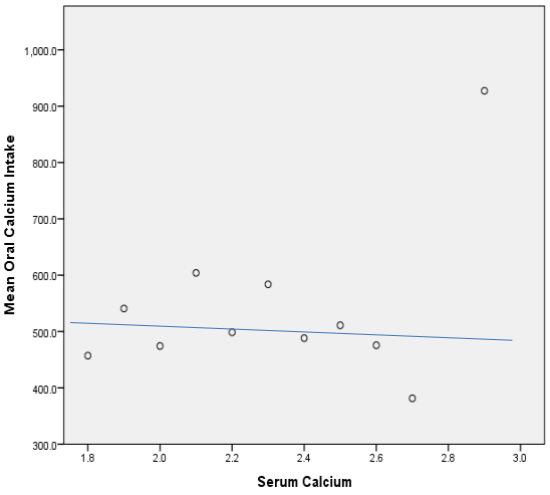

Figure 2. Scatter graph showing relationship between calcium intake and serum calcium level with Correlation coefficient (Pearson's r) = 0.008

Table 2. Showing Relationship Between Maternal Outcome, Oral Calcium Intake and Serum Calcium

Maternal Outcome	Frequency (%)	Mean Calcium intake (std)	Mean Serum Calcium (std)
Normotensive	116(81.7)	561.614(325.6)	2.187 (0.2037)
Pregnancy Induced Hypertension	22(15.5)	476.181(285.7)	2.218 (0.2363)
Pre-eclampsia	4(2.8)	447.575(455.0)	2.225 (0.3500)
Total	**142(100.0)**	**545.165(322.9)**	**2.193 (0.2119)**

Table 3. Bivariant Analysis Using Pearson's R Correlation Showing No Statistically Significant Relationship Between Oral Calcium Intake, Serum Calcium and Maternal Outcome.

		Oral Calcium Intake	Serum Calcium	Maternal Outcome
Oral Calcium Intake	Pearson Correlation	1	0.008	-0.107
	P-value. (2-tailed)		0.904	0.207
	N	206	206	142
Serum Calcium	Pearson Correlation	008	1	0.057
	P-value. (2-tailed)	0.904		0.498
	N	206	206	142
Maternal Outcome	Pearson Correlation	-.0107	0.057	1
	P-value. (2-tailed)	0.207	0.498	
	N	142	142	142

This result, however, is significantly lower than the calcium intake among White American women which was as high as 1671mg/day[19]. This disparity is unsurprising as most developing countries have been found to have low calcium intake, due to the limited access to calcium rich foods in many low income settings[20]. Though, the study from Immigrant Nigerian women in Ireland would suggest that, besides availability, cultural dietary habits would play a role in Calcium intake.

In this study, the mean serum calcium was 2.185 +/- 0.212 mmol/L with a range of 1.8 – 2.9 mmol/L. This is within the normal range of serum calcium of 2.12 – 2.62mmol/L[21] in previous studies as well as within the normal recommended range for normal physiological processes which is 2.18 – 2.55 mmol/L[22]. This also closely resembles Serum calcium levels in previous works done in Nigeria with a mean value of 2.28 for normal pregnant women[23].

There was no direct association between dietary calcium intake and serum calcium. All these are not different from what is expected as despite lower dietary calcium intakes, calcium metabolism maintains Serum Calcium at a fairly constant level with increased absorption, reduced excretion and resorption where necessary [6]. This homeostasis is maintained with the actions Vitamin D, Parathyroid hormone (PTH) and calcitonin (CT).

This however does not affect its causative effect in the pathophysiology of preeclampsia, as the mechanism is believed to be by the presence of circulating serum factors with calcium which increases the vascular smooth muscle tone[24]. Though, it must be stated that the exact mechanism remains unclear[2].

The results showed wide ranges of variations in the sociodemographic factors which affect dietary calcium intake. Factors analyzed for possible correlation included age, ethnicity, educational level, occupation, husband's level of education and husband's occupation. There was no statistically significant relationship between any of these variables and the level of calcium intake. This means that the characteristics of this population did not significantly affect the quantity of calcium they consumed and thus, there can be some validity to assume that this center-based study can be used to deduce the average calcium intake in the overall population in this environment.

There was a statistically significant relationship between age groups of the women and their serum calcium levels, with older women having slightly lower levels of serum calcium despite still being within the range for normal as seen in Table 1. This correlates with previous studies which show that serum calcium progressively decreases with age[25]. This would also, partly explain why and how age is a risk factor for preeclampsia. Serum levels of calcium have been associated with preeclampsia from previous works [23,26]. The other demographic factors were not

statistically associated with the serum calcium levels.

The results from this study, as seen in Table 2, showed that lower calcium intake levels were associated with worse maternal pregnancy outcomes, with normotensive pregnancy outcomes having the highest average calcium intake and pre-eclamptic pregnancy outcomes having the lowest average calcium intake. This would suggest a relationship between calcium intake and development of hypertensive disorders of pregnancy. Though the association in this study was not statistically significant, it is similar to previous studies which have shown that populations with low calcium intake are more likely to develop pre-eclampsia [27]. A larger sample size might be needed to ascertain if a statistically significant relationship exists between oral calcium intake and pre-eclampsia, as the studies that these conclusions on causality were drawn from, were of larger sample sizes [2, 24, 28].

Paradoxically, the mean serum calcium levels slightly progressively increased from the women who went on to have normotensive pregnancies to those that had pregnancy induced hypertension and highest in the group that developed pre-eclampsia. This might seem contrary to the previous studies that have shown lower serum calcium levels in women with pre-eclampsia [26,29,30], however, of note is that these studies all assessed calcium levels of women who had already developed pre-eclampsia. This study assessed serum calcium intake in the second trimester prior to development of pre-eclampsia. These findings suggest that prior to onset of PIH and preeclampsia, the serum calcium levels remain normal or might even be slightly higher in women who eventually develop these hypertensive disorders in pregnancy. Larger sized studies might be needed to ascertain if this paradoxical link indeed exists.

Previous prospective studies comparing calcium levels and neonatal outcomes in normotensive women and women with hypertensive disorders in pregnancy showed that maternal hypocalcemia was associated with adverse perinatal outcomes in women that developed hypertensive disorders of pregnancy. However, other works showed that the evidence for improved outcome with supplementation was limited [30,31]. Findings from this study however, showed no statistically significant relationship between calcium intake and neonatal outcomes such as gestational age at delivery, birth weight, APGAR scores and admission into the NICU. There was also no statistically significant relationship between serum calcium levels and these neonatal outcomes.

Thus, though the development of pregnancy induced hypertension and pre-eclampsia have been associated with poorer neonatal outcomes[32], a direct relationship between calcium intake, serum calcium and neonatal outcome could not be drawn from this study. However, a follow up study to test the neonatal benefits of calcium supplementation might be necessary to demonstrate the link between calcium and neonatal outcome, this benefit has been demonstrated by meta-analysis of previous works[33].

The incidence of pre-eclampsia in this study was 2.8%, this correlates with the global average of 2-8%[4]. However, it is lower than the incidence in a study from the same center which was 8.8%[34]. Though the average calcium intake of the studied population was low, it did not translate to an increased incidence of pre-eclampsia as compared to the global average or in places with adequate calcium intake [35]. Previous studies however, have shown an increased incidence of pre-eclampsia in developing countries and in Nigeria in particular[34]. A possible explanation for this finding is that this sample size may not be appropriate for an incidence study for a condition as common as pre-eclampsia, and as much as 31.6% of women were lost to follow up before the end of the puerperium thus these findings may not reflect the true incidence of pre-eclampsia.

Though the incidence of hypertensive disorders of pregnancy from this study is 18.3%, which is in keeping with previous studies in our environment, with an incidence of 17% reported in a Nigerian study. It is also within the global average range of 1 – 35%.

The limitations of the study were that it was hospital based and its findings might not be generalizable to the overall population and women with medical conditions that affect calcium metabolism could not be excluded, also calciuria could have been a better reflection to compare oral calcium intake with but would require 24 hour urinary sample which would be cumbersome and impractical for an out-patient sample collection. The major strength were the significant findings which could help standardize practice regarding calcium supplementation, the use of a local food composition table was also a strength as well as the laboratory analysis which was carried out in an ISO certified laboratory.

Recommendations

1. Calcium supplementation should be considered as routine practice as part of the antenatal care for pregnant women in our environment.

2. More work needs to be done to ascertain the pattern of serum calcium in the first and second trimesters of pregnancy, to determine if early changes in pregnancy can be used as a predictor for occurrence of pre-eclampsia.
3. Larger scale studies need to be done in our environment to clearly show the relationship between calcium intake and serum calcium with maternal and neonatal outcomes.
4. A follow up study needs to be done in a similar environment to assess the beneficial effects calcium supplementation will have in pregnancy outcomes.

CONCLUSION

The mean calcium intake in this study was 529.6mg/day, which is less than the WHO threshold of 900mg below which calcium supplementation is recommended. The average serum calcium level was 2.185mmol/L which was normal, and no relationship was found between calcium intake and serum calcium.

The only significant determinant of serum calcium was maternal age, while there was no socio demographic determinant of calcium intake. Lower dietary calcium intake was found to be associated with development of pregnancy induced hypertension and pre-eclampsia, with women developing pre-eclampsia having the lowest average calcium intakes.

No relationship was found between calcium intake, serum calcium and neonatal outcomes.

Acknowledgements

The authors acknowledge the contributions of Dr Nnorom Onome Chidinma who assisted in proofreading the manuscript, Dr Benjamin Ebi who helped with data collation and some stages of analysis, Christiana who worked as research assistant and helped with Data Collection

Disclosures

There are no conflicts of interests and there was no sponsorship for this work.

REFERENCES

1. Resolution WHA65.11. Nutrition. Maternal, infant and young child nutrition: draft comprehensive implementation plan In: sixth-fifth World Health Assembly, Geneva, 21-26 May, 2012. Resolutions, decisions and list of participants. Geneva. World Health Organization. 2012
2. WHO Guideline: Calcium supplementation in pregnant women. Geneva, World Health Organization. 2013.
3. Imdad A, Jabeen A, Bhutta ZA. Role of Calcium Supplementation during Pregnancy in reducing risk of developing gestational hypertensive disorders: a meta-analysis of studies from developing countries. BMC Public Health. 2011; 11(3):513
4. Duley L. The Global impact of pre-eclampsia and eclapmsia. Seminars in perinatology. 2009; 33(3):130-137.
5. World Health Organization, food and agricultural organization of the United Nations. Vitamins and mineral requirements in human nutrition, 2nd Ed. Geneva. World Health Organization. 2004.
6. National institute of medicine. Dietary reference intakes for calcium and vitamin D. New York. National Academics Press. 2011.
7. Calcium Supplementation in pregnancy for prevention of pre-eclampsia. Nutritional International. 2017
8. Ingec M, Nazik H, Kadanali S. Urinary Calcium excretion in severe pre-eclampsia and eclampsia. Clin Chem Lab Med. 2006; 44:51-56
9. Dary O, Imhoff-Kunsch B. Measurement of food consumption to inform food fortification and other nutrition programs; an introduction to methods and their application. Food and Nutrition Bulletin. 2012; 33(3):141-145
10. Fiedler JL. Household Consumption and Expenditures Surveys (HCES): a primer for food and nutrition analyst in low- and middle-income countries. Food and Nutrition Bulletin. 2012; 33 (3):170-184
11. Stadlmayer B, Charrondiere UR, Victor N, Enujivgha RG, Fagborun EG, et al. West African Food Composition Table. 2012; 1-148
12. Slimani N, Ferrari P, Ocke M, et al. Standardization of the 24-hour diet recall calibration method used in the European prospective investigation into cancer and nutrition (EPIC): General concepts and preliminary results. European Journal of Clinical Nutrition. 2000; 54(12):900-917.
13. Gibson RS, Cavalli-Sforza T. Using reference nutrient density goals with food balance sheet data to identify likely micronutrient deficits for fortification planning in countries in the western pacific region. Food and Nutrition Bulletin. 2012; 33(3): 214-220
14. Broadly MR. Dietary requirements for magnesium but not calcium are likely to be met in Malawi based on National food supply data. International Journal of Vitamin and Nutrition Research. 2012; 82(3):192-199.
15. Balk EM, Adam GP, Langberg VN, Early A, Clark P. for the IOF Calcium steering committee. Global dietary calcium intake among adults: a systematic review. Osteoporosis Int. 2017; 28(12):3315-3324.
16. Cormick G, Betran AP, Romero IB, Lombardo CF, Gulmezog UA. Global inequities in dietary calcium intake during pregnancy: a systematic review and meta-analysis. BJOG: An international Journal of obstetrics and gynaecology. 2019; 126(4)
17. Victoria DA, Madeleine FT, Charles S, Clemene M, Colette M, Colette A. Dietary calcium intake and associated factors among pregnant women in southern Benin in 2014. Food and Nutrition Sciences. 2015; 6:945-954

18. Lindsay KL, Gibney ER, McNutty BA, McAuliffe FM. Pregnant immigrant Nigerian women; an exploration of dietary intakes. Public Health. 2014; 128(7):647-653
19. Emily WH, Margaret S, Margaret W, Kim Chantal, et al. Calcium intake during pregnancy among white and African American pregnant women in the United States. Journal of the American College of Nutrition. 2004; 23(1): 43-50.
20. Moshood OO, Katherine LD, Kimberly OO. Calcium supplementation to prevent pre-eclampsia: Translating Guidelines into practice in low-income countries. Adv Nutr. 2016; 7(2):275-278
21. Almaghams A, Almalki MH, Buhary BM. Hypocalcemia in pregnancy: A clinical Review Update. Oman Med J. 2018; 33(6):453-462
22. Abbassi-Ghanavati M, Greer LG, Cunningham FG. Pregnancy and laboratory studies: a reference table for clinicians. Obstet Gynecol. 2009; 114(6):1326-31
23. Omotayo OL, Nura A, Waheed-Olajide OA, Funsho AI, Adekunle DK, Abayomi BS. Study on comparison of serum levels of calcium, magnesium and uric acid in mild pre-eclamptics, severe pre-eclamptics and normal pregnant women in Illorin, Nigeria. Niger J Exp Clin Biosci. 2015; 3:71-77
24. Green J, Assady S, Nakhoul F, Bick T. Differential effects of sera from normotensive and hypertensive pregnant women on Ca (2+) metabolism in normal vascular smooth muscle cells. J Am Soc Nephrol. 2000; 11:1188-1198.
25. Pagana KD, Pagana TJ, Pagana TN. Mosby's Diagnostic and Laboratory Test Reference. 14th Ed. St Louis MO: Elsevier. 2019
26. Udenze IC, Arikawe AP, Azinge EC, Okusanya BO, Ebueh OA. Calcium and Magnesium metabolism in pre-eclampsia. West Afr J Med. 2014; 33(3):178-182.
27. Attallah AN, Hofmeyr GJ, Duley L. Calcium supplementation during pregnancy for preventing hypertensive disorders and related problems. Cochrane Database System Review. 2000
28. Vanwijka M. Vascular function in pre-eclampsia. Cardiovascular Research. 2000; 47:38-48.
29. Ikechukwu IC, Ojareve OI, Ibhagbemion AJ, Okhoare OF, Oluwatomi OB, Akhalufo OS, Oluwagbenga AT, Chigaekwu MN. Blood lead, calcium and phosphorus in women with preeclampsia in Edo state, Nigeria. Arch Environ Occup Health. 2012; 67(3):163-169.
30. Hofmey GL, Lawrie TA, Atollah AN, Torlon MR. Calcium supplementation during pregnancy for preventing hypertensive disorders and related problem. Cochrane Database of Systematic Reviews. 2018. Issue 10. ANN:CD001059.
31. Kumar N, Singh AK. Maternal serum uric acid and calcium as predictors of hypertensive disorders of pregnancy: A case control study. Taiwan J Obstet Gynecol. 2019; 58(2):244-250.
32. Adinma J, Umeononihu OS, Umeh MN. Maternal nutrition in Nigeria. Trop J Obstet Gynaecol. 2017; 34:79-84.
33. Anmerlmdad AJ, Zulfigar AB. Role of calcium supplementation during pregnancy in reducing risk of developing gestational hypertensive disorders: a meta-analysis of studies from developing countries. BMC Public Health. 2011;11(3): 18.
34. Musa J, Mohammed C, Ocheke A, Kahansim M, Pam V, Daru P. Incidence and risk factors for pre-eclampsia in Jos, Nigeria. Afr Health Sci. 2018; 18(3):584-595
35. Anath CV, Keyes KM, Wapner RJ. Pre-eclampsia rates in the United States. 1980-2010: age-period-cohort analysis. BMJ. 2013; 347:64-65