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PREVALENCE OF HYPOCALCAEMIA AND MATERNAL COMPLICATIONS AMONG ANTENATAL CLINIC ATTENDEES AT THE UNIVERSITY OF PORT HARCOURT TEACHING HOSPITAL.

[1]Eli S, [2]Enyindah CE, [2]Orluwene CG, [2]Ikimalo J, [2]Abam DS

Department of Obstetrics and Gynaecology, University of Port Harcourt Teaching Hospital, East-West Road, Choba, Port Harcourt.

ABSTRACT

BACKGROUND: Plasma Calcium level is not a routine laboratory test conducted during pregnancy.The role of calcium supplementation to prevent maternal complications of pregnancy such as pre-eclampsia and pregnancy induced leg cramps is conflicting.

OBJECTIVE: To determine the prevalence of hypocalcaemia and maternal complications among antenatal clinic attendees.

METHOD: Ten milliliters of blood sample were taken from each of the 90 pregnant women that met the inclusion criteria for the study.The plasma isolated from each woman was analyzed for calcium and albumin using calcium-albumin kit (lab 7225 spectrophotometer set Bran Scientific and Instrument Company, England). The data was analyzed using SPSS version 16.

RESULTS: The prevalence of hypocalcaemia was 25.6% at recruitment and 40% in the third trimester. Sixty-five percent of the subjects who had hypocalcaemia in third trimester developed pre-eclampsia. In the hypocalcaemic group, the frequency of leg cramps was 23.3% and 27.8% at recruitment and at the third trimester respectively. Eight out of the 23(34%) subjects had pre-eclampsia in the normotensive group.

CONCLUSION: The study revealed that high prevalence of hypocalcaemia was associated with advanced gestational age. In addition, there was a relationship between hypocalcemia, pre-eclampsia and pregnancy induced leg cramps.Thus calcium supplementation is recommended for those at risk of hypocalcaemia.

KEY WORDS; hypocalcaemia, maternal complications, pre – eclampsia, leg cramps.

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INTRODUCTION

Calcium (Ca^{2+}) which is mainly found in the bone, muscle and neuronal tissue is the fifth most prevalent element in the body[1, 2]. The recommended dietary allowance (RDA) for calcium is between 800mg to 1000mg per day for a male adult and 1000mg to 1200mg for female adult[3-7]. During pregnancy, dietary allowance of calcium increases by 300%[1, 8-13]. The Foetus retains 2530g of calcium mostly in the third trimester of pregnancy[1,2]. Calcium in ionic states are not routinely carried out and are expensive to run[4,5].

The estimated calcium intake during pregnancy from studies carried out in the United States of America is consistently low with a range of 43% to 49% of the recommended dietary allowance[12]. Low calcium intake was commoner among women of low income[14-17]. Prenatal supplements provided better calcium balance, which help to address the calcium nutritional status in pregnancy[10].

Hypocalcaemia when associated with maternal complications especially pre-eclampsia is one of the leading causes of maternal and perinatal morbidity and mortality, globally[18-22]. The estimated blood calcium level can therefore be estimated by the 50% ratio of the total calcium with fluctuations depending on the general blood acid—base balance. In acidosis (hence tourniquet should be avoided in taking blood samples), the ionized calcium will be higher than 50% of total blood calcium, while in alkalosis, it will be lower[23].

Ninety-eight to ninety-nine percent of body calcium is stored in the skeleton and teeth[1, 2]. The normal value for total calcium in the blood is 2.2-2.6mmol/L or ionized calcium level 1.11.4mmol/L. About 50% of the blood

Corresponding Author: Dr. Eli Sukarime
Department of Obstetrics and Gynaecology,
University of Port Harcourt Teaching Hospital,
East-West Road, Choba, Port Harcourt.
E-mail: elisukarime@gmail.com

(albumin)[24-27]. The ionized calcium which is difficult to measure independently of the total calcium is however the only component that can be used in the body in such vital processes as muscular contraction, cardiac function, transmission of nerve impulses and blood clotting[28].

Serum calcium levels are affected by parathyroid hormone and vitamins. Parathyroid hormone exerts direct effects on the bone to release calcium into the blood and on the kidneys to effect reabsorption by the proximal tubules while vitamin D increases serum calcium by stimulating absorption by intestines[1, 29]. The role of oestrogen in increasing bone calcium deposits and of androgens (like in hyper function of the adrenal cortex or thyroid) in causing hypocalcaemia and bone decalcifications are all regarded as permissive actions[30].

Hypocalcaemia has been shown to occur during pregnancy, reaching lowest level at the beginning of third trimester [2-6]. This reduction may be due to factors such as higher nutritional demands in pregnancy, inadequate intake in the diet and volume expansion and reduction in concentration of plasma proteins (especially albumin) in pregnancy. In addition, increase in maternal oestrogen production blocks bone re-absorption and increases calcium urinary excretion. As a compensatory mechanism, parathyroid hormone (PTH) tends to increase at term. However parathyroid hormone may indirectly increase intestinal absorption of calcium as the only compensatory process during pregnancy because of the action of oestrogen[1,2].

Calcium ions are released from bone into the blood stream or bound to proteins such as serum albumin. This means that in cases of hypoalbuminemia, there will be a corresponding hypocalcaemia [1,2].

Hypocalcaemia may also be due to hypomagnesaemia[1, 31]. This explanation is based on the fact that calcium is responsible for the transport of magnesium from the endoplasmic reticulum to the extracellular fluid. This invariably means that hypocalcaemia may result to low serum magnesium.

Hypocalcaemia in pregnancy is able to induce maternal and foetal consequences which may last throughout life [32-34]. Hypocalcaemia has been associated with disordered glucose metabolism, vascular disorders and electrolyte imbalance[1, 35]. It is important to note that studies have shown that hypocalcaemia has great effects on the process of parturition and on foetal growth and developme[1,2].

Hypocalcaemia causes uterine artery spasm and this has been linked to placental insufficiency which leads growth restriction[36-38]. In addition, hypocalcaemia has also been linked by some researchers to increased incidence of leg cramps; justifying the use of calcium supplements for many weeks until delivery in some centres[39].

The possible pathogenesis of hypocalcaemia in pre-eclampsia with associated morbidities has persistently been the subject of debate. Most of the available data on this insufficiently researched subject is outside our sub-region. The question to be answered is whether these data are a true reflection of what is obtainable in our environment[9, 10]. The prevalence of hypocalcaemia and maternal complications associated with hypocalcaemia among antenatal attendees will form the basis of this study.

It is important to note that often times due to practical ease of laboratory evaluations, it is total plasma calcium that is commonly measured in most laboratories. In view of the protein binding associated with calcium, principally by albumin, changes in plasma albumin levels thus affect total plasma level[1]. This warranted the concept of corrected plasma calcium to obviate any changes that low or high plasma albumin levels may have on the values gotten. Especially proteinuria being a feature of pre-eclampsia, the importance of corrected plasma calcium estimation becomes pertinent.

Heaney and Recker were among the early researchers to study calcium balance of pregnant women in the United States[40]. Towards the end of pregnancy, they noticed there was a tendency towards more and longer negative calcium balance, even when the women were on daily calcium intake. In addition, they concluded that intestinal calcium absorption is increased in late pregnancy[41].They studied 85 pregnant women residing in the United States of America and found that their daily calcium intake was less than the recommended daily allowance[40].

Most sea foods, cheese, yoghurt and milk are rich in calcium, as well as some shell fish, sardines, fortified foods and soya beans. In contrast, many refined foods, tubers, oils and fats contribute little to dietary calcium. Absorption of calcium can vary, especially depending on calcium intake[40, 41]. Calcium absorption appears to be greatest within the duodenum and ileum and occurs by both passive and active process[2, 42-44]. The kidney has a very significant role in calcium homeostasis. Active re-absorption of calcium takes place in the loop of Henle in the proximal tubules and this is influenced by urinary loss and probably the acid-base balance. Excess calcium is eliminated by the kidneys[2].

When dietary calcium intake is not sufficient to meet

mobilized and calcium deficiency in pregnancy can develop.

One of the first reports of serum calcium levels during pregnancy was in 1920 by Halluran and Spencer [45]. They found out that hypocalcaemia was associated with maternal complications such as pre-eclampsia and pregnancy-induced leg cramps.

Carmina et al studied 9 healthy Brazilian women who habitually consumed 500mg calcium per day and concluded that calcium homeostasis appears to be attained by a more efficient intestinal calcium absorption during pregnancy and by renal calcium conservation during both pregnancy and lactation[46-50].

Several cardiovascular changes occur during pregnancy among which is 40% of blood volume expansion[1, 2]. There is the possibility that alteration in calcium metabolism may be responsible for some of the physiological changes during pregnancy and many other diseases linked to cardiovascular abnormalities. Evidence has shown that a compromised calcium status may be involved in some disorders during pregnancy such as pre-eclampsia/pregnancy induced hypertension and muscle cramps.

Studies done in western Nigeria established a link between hypocalcaemia and pr-eeclampsia[32]. Physiological effects of calcium in hypertension/pre-eclampsia have been established by some biological mechanisms[2]. A relatively low calcium level creates an intracellular imbalance between calcium and magnesium, which results in increased vascular tone in the smooth muscle of the artery and therefore increased blood pressure[16,17].

The relationship between pre-eclampsia and hypocalcaemia has long been recognised[51-53]. Researchers have shown that there is undisputable link between pregnancy induced hypertension and calcium deficiency[1,2].

Heaney studied the plasma and intracellular calcium concentrations in pre-eclamptic and normal pregnant women[2,5]. They found plasma calcium levels were not so different but that in preeclamptic women, calcium deficiency was a common finding. These two groups showed lower plasma level of calcium concentrations than non-pregnant values and the pre-eclamptic group had a significantly lower calcium concentration when compared to the normal pregnant women. Thus they suggested that hypocalcaemia might contribute to the vascular lesions of pre-eclampsia[1,54]. In addition, Bezerra in another study demonstrated that subjects who developed pre-eclampsia showed decrease in gestational age[55].Worthy of note however is that this has not been consistent with some researchers who concluded that hypocalcaemia had no role to play in the pathogenesis of pre-eclampsia[13].

In a study done at North East Nigeria, there was 10% to 15% decline in the serum level of total calcium among 30 pregnant women[56]. The reduced calcium level may be due to haemodilution of pregnancy, poor absorption or excessive urinary loss from increased glomerular filtration rate[1,2].

In spite of this conflicting data, many authorities have suggested the supplementation of calcium to pregnant women who become hypocalcaemic[4,47].

In a meta-analysis conducted by Patrelli, which was a randomised controlled trial conducted to demonstrate calcium supplementation and prevention of pre-eclampsia, he concluded in the study that pre-eclampsia is likely to be a multi-factorial disease[57,58]. However, inadequate calcium intake represents a factor associated with an increased incidence of hypertensive disease. The results further demonstrated that additional calcium during pregnancy is an effective measure to reduce the incidence of pre-eclampsia, especially in populations at high risk of pre-eclampsia due to ethnicity, gender, age, high body mass index and in those with low baseline calcium intake[40].

However, more studies are needed to confirm the relationship between calcium supplementation and reduction in incidence of pre-eclampsia.

In another study conducted by Berasis in Nigeria, it was noted that pre-eclampsia is a pregnancy specific syndrome and is one of the most common causes of electrolyte imbalance vis-a-vis hypocalcaemia, hypomagnesaemia, hypokalaemia and hyponatraemia[40].

Calcium supplementation has been advocated by some authorities to be beneficial in the treatment of pregnancy induced leg cramps[12, 17]. In addition it has been shown by some authorities that in cases of maternal hypocalcaemia administration of oral calcium has been associated with reduction in incidence of pregnancy-induced leg cramps[39].Young and Jewell in a Cochrane review later concluded that if a woman found cramps troublesome in pregnancy, the best evidence was for calcium supplement to be given[6,9].

It is appropriate to prevent hypocalcaemia in pregnancy because of the presumed association of

pre-eclampsia and pregnancy-induced leg cramps. In addition, these maternal complications increase maternal and perinatal mortality. However, preventive measures of hypocalcaemia have been disappointing. Many strategies used to prevent hypocalcaemia have been evaluated. In general, none of these have been found to be clinically efficacious.

Primary prevention of hypocalcaemia involves avoiding the occurrence of derangement of calcium prior to pregnancy. This entails carrying out full evaluation of the patient.

Secondary prevention of hypocalcaemia is the breaking off of the disease process before the emergence of associated maternal complications. Since the aetio-pathogenesis of hypocalcaemia have been explained earlier; secondary prevention entails correction of the pathophysiology.

These measures may be nutritional or pharmacological.

A study conducted by Heany had suggested that diet rich in calcium taken early in pregnancy may reduce the risk of hypocalcaemia[13]. A more recent study has shown that diet rich in calcium such as most seafood, cheese, yoghurt and milk given within the third trimester of pregnancy may lead to reduction of the incidence of hypocalcaemia[43,44].

Calcium supplementation appears to be beneficial to women at high risk of hypocalcaemia and in communities with low dietary calcium intake[9,10]. These benefits are conformed by several small trials. One of the largest trials on calcium supplementation as it concerns one of the maternal complications associated with hypocalcaemia was the calcium for pre-eclampsiaprevention (CPEC) trial[10].CPEC trial suggested that calcium supplementation during pregnancy did not prevent pre-eclampsia or reduce perinatal outcomes in healthy nulliparous women[10].

The advantage of the study above was its large sample size and also the highest dose of calcium (2 gram) was used compared to previous studies. However, the drawback of this study was that it was conducted in a low-risk population with adequate intake of calcium. This means that most probably hypocalcaemia was ruled out.

The CPEC study with respect to hypocalcaemia and maternal complication of pre-eclampsia still leaves open the possibility that calcium supplement may be useful as the women included in the trial were already taking higher than average levels of calcium than is

was a need for a confirmatory trial to be conducted in a high-risk population especially those at risk of hypocalcaemia. Such a trial, the World Health Organization randomized trial of calciu supplementation among low calcium intake pregnant women, was done involving 8325 women. It tends to support the motion that 1.5g calcium/day supplement did not prevent one of such maternal complication associated with hypocalcaemia but did reduce its severity, maternal morbidity and neonatal mortality.

The results of the WHO trial are related to many West African women with inadequate dietary calcium intake in relationship to hypocalcaemia with associated maternal complications.

AIM AND OBJECTIVE OF THE STUDY

To determine the prevalence of hypocalcaemia and maternal complications among antenatal clinic attendees at the University of Port Harcourt Teaching Hospital.

METHODOLOGY

This study was conducted in the University of Port Harcourt Teaching Hospital. It is a800 bed hospital located at Alakahia in Obio-Akpor Local Government Area of Rivers State, South-South Nigeria, about 15 kilometres from Port Harcourt city along the Port Harcourt axis of the East-West Road. It is a tertiary health institution that provides all levels of health care services to Rivers, Bayelsa, Delta, Imo, Abia and Akwa-Ibom States. The Obstetrics and Gynaecology department is one of the major clinical departments of the hospital with twenty-two (22) Consultant Staff.

On the average between 400 and 450 patients are booked for antenatal care every week in the hospital, while follow-up attendance rate is between 250 and 300 patients per week. The delivery rate in the hospital in the last few years has been about 3600 yearly, which gives an average monthly rate of 300.

The hospital has a chemical pathology department staffed by consultants, resident doctors, laboratory scientists and interns. Over thirty various tests are conducted in the chemistry laboratory including serum calcium and albumin estimations. The present cost of doing single serum calcium estimation is about three US dollars. Serum total calcium is usually requested together with albumin for the purpose of estimating the corrected calcium level. Ionized calcium (the active component) is also measured.

STUDY DESIGN

This is a case control cross sectional study of patients attending antenatal care at the University of Port

be healthy pregnant women with uncomplicated pregnancies at the time of enrolment. These patients had 10 mls of venous blood specimen drawn into a Lithium Heparin specimen bottle and centrifuged at 3000 rpm. Plasma will be collected for estimation of total calcium, albumin and ionized calcium fraction. These samples were centrifuged within one hour of collection and batch analysed. This was done at enrolment and thereafter at the third trimester. It is important to note that tourniquet was not be applied when collecting blood samples to ascertain the level of Plasma calcium because this may contribute to error in the analysis of the result due to the role of Calcium in the pathogenesis of muscle contractility. They were subsequently followed up till third trimester.

STUDY LOCATION

The subjects in the study were patients attending antenatal care in the University of Port Harcourt Teaching Hospital and delivery will be during the course of the study period. All patients who meet the criteria for inclusion were counselled and given a consent form, and those who elected to participate in the study will be enrolled until the sample size is achieved. Counselling on the nature of the study was done, the amount of blood to be drawn, the details of the subsequent follow up, and the time of termination for each patient will be given. The women were told that participation was voluntary and that they were free to withdraw at any time. They were also told that their decision to participate or not participate in the study will not affect their care. Their written consent was obtained if they decide to join the study.

STUDY GROUP

Patients evaluated were between gestational ages 8 to 20 and 26 to 36 weeks. The reason was that these periods was in agreement with most existing data, indicating that hypocalcaemia occurred in early pregnancy[1,2]. However, others revealed a fall in serum calcium level in the third trimester.

This suggests that the effects due to changes in serum calcium levels in pregnancy may be marked in the latter half of pregnancy.

The participants were recruited over two (2) weeks, and were followed up till the third trimester. Routine antenatal care was given unless complications arise. Routine antenatal investigations and drugs were prescribed. All complications in pregnancy and outcome of delivery was noted. The participants were advised to avoid taking calcium supplements.

All patients were assessed for occurrence of features of pre-eclampsia and leg cramps in pregnancy and need

At the end of the study the prevalence of hypocalcaemia among antenatal clinic attendees was ascertained. In addition, maternal complications link with patients presenting with hypocalcaemia was also ascertained. It is important to note that treatment was offered to patients with hypocalcaemia. This was necessary to avoid the ethical issues concerning withholding treatment should any of the patients have a laboratory report of hypocalcaemia as determined by the standards of the study.

INCLUSION CRITERIA

All healthy patients of gestational age between 8 to 20 weeks and between 26 weeks to 36 weeks attending antenatal care in the UPTH during the study period were eligible. For all subjects, sociodemographic data including age, parity, occupation and level of education of the patient and her spouse, estimated gestational age, as well as relevant clinical parameters were entered into a data extraction sheet and used to generate a data base. The social classes of the women were determined from Olusanya et al classification, making use of educational status of the woman and her husband's occupation[59]

EXCLUSION CRITERIA

The patients with the following conditions were excluded from the study: those with chronic hypertension, chronic renal disease/renal osteodystrophy, intrauterine growth restriction, multiple pregnancy, retroviral infection/acquired immunodeficiency syndrome, sickle cell anaemia, diabetes mellitus, gestational diabetes mellitus, metabolic syndrome and thyroid disease.

SAMPLE SIZE DETERMINATION

In a similar study conducted by Aruna Patel et al at G.M Hospital, Rewa, the prevalence of Hypocalcaemia with maternal complication vis-a-vis pre-eclampsia was 94%[61]. Therefore, the minimum sample size for simple proportion with 5% accuracy and 95% level of confidence will be calculated below as[62]:

$$n = \frac{Z^2 \times P(1-P)}{d^2}$$

Where:

n = the desired sample size,

z = the standard normal deviate, usually set at 1.96, which corresponds to 95% confidence level, p = the proportion (prevalence) in the target population estimated to have a particular characteristic, d = is the tolerance i.e. how close the proportion of interest is to the desired estimate e.g. within 0.05.

$$n = \frac{(1.96)^2 \times 0.94(0.6)}{(0.05)^2} = 88$$

The calculated sample size will be 88 which will be rounded up to 90.

STATISTICAL ANALYSIS

All results were entered into a questionnaire and analysis was done with a personal computer using the SPSS for windows version 16. Categorical variables were expressed as absolute numbers and percentages and significant difference was determined using the Chi square test or Fisher exact test where appropriate, while continuous variables were presented as means with standard deviations and significant differences were determined with the student "t" test. The level of significant difference was set as $p < 0.05$.

RESULTS

In the study 90 participants were recruited. All 90 participants remained in the study till the third trimester.

Table 1 shows the level of hypocalcaemia in the study population. The mean plasma calcium level at recruitment was 2.22 mmol/L while at the third trimester was 2.13mmol/L.

The prevalence of hypocalcaemia at recruitment was 25.6% with 23 out of the 90 subjects having serum calcium levels less than 2.2mmol/L at recruitment. The frequency however increased to 36 out of the 90 subjects (40%) in the third trimester, though this difference in proportion was not significant (P=0.07). Fifteen out of the 28 subjects who subsequently had hypocalcaemia at the third trimester developed preeclampsia in the course of the pregnancy. There were 9 other patients with preeclampsia whose serum calcium levels remained normal. Eight patients were taking selfprescribed multivitamin among the subjects in spite of this 4 of them had hypocalcaemia. Table 2 depicts the frequency of hypocalcaemia with maternal socio-demographic characteristics. The age of the subject ranged from 19years to 36 years with a mean age of 29.78. There were 2 subjects under the age of 20years and all of them had hypocalcaemia (P=0.00).

The other age group with significant level of hypocalcaemia was 30-39 years with a frequency of 63.3% (P=0.216). Most of the patients were para 1-4 and contributed 66.7% of those who had hypocalcaemia, while nulliparas contributed to 33%. There were more cases of hypocalcaemia among Para 1 to 4 but this observation was not statistically significant (P= 0.648).

social class 1. They also made the highest number of patients with hypocalcaemia (P=0.00).

There were 15 patients in the social class 4 and all 15 them had hypocalcaemia (P=0.00). The prevalence of obesity at recruitment was 33 out of a total of 90 subjects (35.6%); of which 8 of these mothers had hypocalcaemia (P=0.126).

Table 3 shows the maternal adverse outcome related to hypocalcaemia. The development of preeclampsia was significantly higher in the hypocalcaemia group where 15 out of the 23 (62.2%) patients had preeclampsia compared with 8 out of 23 patients in the normocalcaemic group (P= 0.01)

There were no patients in which symphysio-fundal height was smaller than date at the third trimester in both the normocalcaemia and/hypocalcaemic groups. The level of preterm birth was low in this study, 2out of 90 (0.2%). All the subjects in this study delivered after 34 weeks gestation. There were 3 out of a total of 23 in the hypocalcaemia group in the third trimester that delivered before 37 weeks while one patient in the normocalcaemic group delivered preterm. This was not statistically significant (P= 0.03).

The occurrence of leg cramp was significant more in the hypocalcaemia group compared with patients who had normocalcaemia (P= 0.01).

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TABLE 1 Frequency Table

Statistics							
	AGE	parity	ht	wt	BMI	CALCIUM AT RECRUITMENT	CALCIUM AT TERM
Mean	29.78	1.69	1.6113	75.6022	29.0867	2.2278	2.1300
Std. Error of Mean	.427	.161	.00551	1.45120	.52243	.01850	.01791
Median	30.00	2.00	1.6000	73.2500	28.1000	2.3000	2.2000
Mode	32	0	1.60	70.00	27.30	2.30	2.20
Std. Deviation	4.047	1.526	.05224	13.7672 5	4.95622	.17548	.16990
Variance	16.377	2.329	.003	189.537	24.564	.031	.029

	Frequency	Percent (%)	P VALUE
Calcium level at recruitme nt			
Hypocalcemia	23	25.6	
Normal	67	74.4	
Calcium level at 3RD TRIMESTER			
hypocalcaemia	36	40.0	0.07
Normal	54	60.0	
Total	**90**	**100.0**	
	3rd trimester pre eclamptic subject		
Hypocalcaemia	**15**		
Normal	**8**		

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	AGE	parity	ht	wt	BMI	CALCIUM AT RECRUITMENT	CALCIUM AT 3RD TRIMESTER
Mean	29.78	1.69	1.6113	75.6022	29.0867	2.2278	2.1300
Range	17	5	.23	75.00	25.10	.90	.70
Minimum	19	0	1.50	53.00	21.00	1.80	1.70
Maximum	36	5	1.73	128.00	46.10	2.70	2.40

	Calcium level at recruitment			**Calcium level at 3RD TRIMESTER**			**Frequency**	**Percent (%)**
	Hypocalcemia	Normocalcaemia	**P-Value**	Hypocalcemia	Normocalcaemia	**P-Value**		
Age Group								
<20	2	0	**0.024**	2	0	**0.216**	2	2.2
20-29	5	26		12	19		31	34.4
30-39	16	41		22	35		57	63.3
Parity								
0	6	24	**0.393**	13	17	**0.648**	30	33.3
1-4	17	43		23	37		60	66.7
Social class								
1	4	40	**0.000**	12	32	**0.000**	44	48.9
2	1	24		5	20		25	27.8
3	4	2		4	2		6	6.7
4	14	1		15	0		15	16.7

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	8 -20 wks (n=90)	26 – 36 wks (n=90)	P-value
Hypertension/preeclampsia	6(6.67%)	30(33.3%)	0.01
Leg cramps	21(23.3%)	25(27.8%)	0.01
Preterm labour	--	2(2.2%)	0.03

DISCUSSION

The main study revealed that 25.6% of the pregnant women had hypocalcaemia as revealed by the plasma level at recruitment (8-20 weeks). The definition of normal plasma calcium level for the population was 2.2 to 2.6 mmol/L[24-27]. Hence this prevalence may be different from figures reported by other investigators working in different populations. Sanchez PA reported 10 to 15 % decline in the plasma level of calcium amongst 30 pregnant women in a community based cross sectional study in north eastern Nigeria,[56] while a previous study conducted in the United States of America, involving 85 pregnant women revealed that their daily calcium intake was less than the recommended daily allowance.[40] This study evaluated second trimester, which is not in keeping with the work by Aruna Patel et al who recruited women from first trimester of pregnancy and this can explain the high levels of hypocalcaemia reported in the study[61]: the prevalence of hypocalcaemia in the present study was lower probably due to the involvement of mainly urban dwellers in a teaching hospital setting.

In this study being a teenager was significantly associated with hypocalcaemia and to a lesser degree the age group 30-39 years as also correlated with hypocalcaemia. This may explain the similarity with findings of Aruna Patel et al who had majority of their study subjects in the age group (18-24 years) [61]. This study has also explained the higher frequency of hypocalcaemia in the para1-4 but this association not statistically significant. This is closely related to the findings of Carmina et al that there was a decrease in serum calcium with increase in parity[46]. In their study, pregnant women with parity 2 or more had significantly lower serum calcium level compared to nullipara. To explain this relationship some investigations have proposed that frequent cycle of reproduction exert a significant stress that leads to a greater risk of malnutrition[47-50].

Social class 4 was significantly correlated with occurrence of hypocalcaemia in the study. This is similar to previous reports that lower income women had lower calcium intake, which results in a higher negative calcium balance hence the association of low socioeconomic status has also been associated with preterm labour/delivery which have been linked to hypocalcaemia[13]. It is most likely that low social class imposes a status of inadequate calcium consumption in the diet because low consumption of diets rich in calcium such as soya bean, legumes and vegetables[13, 30]. The intake of multivitamin supplement by a small group of the subjects in this study was not associated with a better plasma calcium status. This is in agreement with previous studies which have shown no improvement in plasma calcium level by intake of multivitamin during pregnancy[8, 9]. It is important to note that subjects who took additional multivitamin drugs did not aim to take calcium supplements and should calcium be present in these multivitamins the content is likely not to be significant and this may explain the lack of association observed in this study as the use of additional multivitamin did not appear to improve calcium balance in these subjects.

The occurrence of pre-eclampsia was significantly associated with hypocalcaemia in the study. Several researchers in the past have also reported a link between calcium depletion and hypertension in pregnancy in both animals and human studiesr[20, 21, 31, 48]. This link is attributed to vascular muscle spasm in the uterus which is thought to be due to calcium deficiency. Golmohammad et al in their study demonstrated that all subjects who eventually developed preeclampsia showed decrease in serum calcium concentrations with increasing gestational age[36]. In the present study 15 patients with hypocalcaemia at recruitment developed pre-eclampsia another 9 patients who had normocalcaemia at enrolment eventually developed pre-eclampsia, and this in agreement with the study of Sukonpan K[51].

The relationship between hypertension and hypocalcaemia has led to some researchers to advocate for the use of calcium supplement to reduce the risk of developing hypertension and hypocalcaemia[42, 49].

Patients who had hypocalcaemia in this study were more likely to report leg cramps. This finding is in agreement with reports of several other studies.[41]In a prospective group of women before and after

showed that oral calcium supplement was associated with a significant decrease in the leg cramps. Similarly, a Cochrane review by Young and Jewell also supported evidence for calcium lactate in the treatment of muscle cramps in pregnancy[41].

The risk of having preterm birth did not have any correlations with hypocalcaemia, although some other studies showed calcium deficiency with preterm delivery, hence application of calcium in the treatment of preterm labor[34]. Symphysiofundal height discrepancy during pregnancy did not predict hypocalcaemia in this study.

CONCLUSION AND RECOMMENDATIONS

This study found the prevalence of hypocalcaemia to be 26.67% and revealed that pregnancy is associated with reduced serum calcium level as gestation advanced.

The factors in these women which contribute to the degree of hypocalcaemia were shown in this study to include young age, high parity and low socio-economic status. The relationship of a negative calcium balance to pre-eclampsia and muscle cramps in pregnancy was significant in this study. It is important to note that maternal health from stand point of preeclampsia and leg cramps remains significant in our locality.

The findings from this study suggest calcium balance needs to be improved in our pregnant women. An important way to reduce the prevalence of hypocalcaemia will be the achievement of normal calcium balance in pregnancy.

I recommend that the average diet in this environment be evaluated in a nutritional study to determine the content of calcium. The diet with the highest amount of calcium can be advised for pregnant women who are at risk of calcium deficiency, in addition calcium supplements may be prescribed to pregnant women at risk of hypocalcaemia.

The assay of calcium ion is not routinely done and is expensive but plasma calcium which was assayed in this study is a reliable indicator of active calcium. However, it is also likely that many women who are hypocalcaemic may not show it early because less than 1% of the body calcium found in the blood; so that doing a blood test may not necessarily identify a deficiency state. It is quite possible to completely miss a hypocalcaemic patient as shown in this study. At risk patients who are so identified will thus benefit from either dietary advice or calcium supplementation. Evidence supports the use of calcium supplementation in women who have hypocalcaemia hence some units throughout pregnancy. To ascertain the calcium content of our local diet may be difficult because of the diversity of our diets which is influenced by our socio-cultural backgrounds. A possible way to overcome t is the supplementation of the diet with oral calcium. The findings from this study revealed that calcium lack is likely pronounced in the third trimester.

All patients should be given oral calcium supplements from the second trimester pregnancy or calcium rich diet especially consisting of leaves, nuts, peas or shellfish is advised from this stage of pregnancy.

I recommend that this policy of routine supplementation of calcium in pregnancy be directed at younger lower income women or those with high parities commenced in the second trimester of pregnancy as these are women who have been shown to be at higher risk of negative calcium balance in this study. It is perceived that prescribing drugs or diet to enhance calcium status at a particular time in pregnancy is most likely to be accepted as a useful intervention after proper counselling of these women as prophylaxis against hypocalcaemia similar to giving haematinics or antimalarial in pregnancy. It is important to emphasize the need for a balanced diet during pregnancy as other micronutrients remain vital to the metabolic needs of the woman and her baby.

It is important to stress that discouragement of teenage pregnancy will help reduce the risk of hypocalcaemia in young mothers further, observing a standard period of birth spacing to allow the body to replenish its stores of essential nutrients including calcium will help to reduce the prevalence of hypocalcaemia in pregnancy. In addition, improving the socio-economic status of every woman through education and economic empowerment will help improve the calcium status of pregnant women in our environment.

I recommend that a population based cross sectional study be conducted to strengthen the findings of this study. This is important because the sample size will be larger and likely to be more representatives so that the drawbacks from a hospital based study will be reduced to the barest minimum. In addition, nutritional survey studies can be carried out to prove the efficacy of dietary counselling in pregnancy.

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