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ASSOCIATION OF CALCIUM SUPPLEMENTATION WITH PREGNANCY INDUCED HYPERTENSION IN PREGNANT FEMALES

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Abstract :

Introduction: The aim of the current study was to investigate the association of calcium supplementation with pregnancy induced hypertension in pregnant mothers.

Methods: The current study used longitudinal research design. The study used both the data collection during antenatal visits and also the data retrieved from the medical records of the patients within the study duration of one year months.. The population of the current study consisted of the pregnant women who were receiving antenatal treatment at Hayatabad Medical Complex (HMC) for 09 month from 1st December 2020 to 1st August 2021, Peshawar. The current study chosen 150 pregnant women in the study for data collection. The participants were chosen based on convenience sampling technique. Both the current and retrospective data regarding the pregnancy-induced hypertension and calcium supplementation. Data was analyzed through SPSS. Demographic analysis, descriptive analysis, independent t-test and pearson correlation was used to evaluate the relationship between serum calcium levels and blood pressure.

Results: The results of the study revealed that the average serum calcium level was 9.2 mg/dL, with 43.3% of participants having pregnancy-induced hypertension (PIH). With calcium supplementation, serum calcium levels increased while both systolic and diastolic blood pressure deceased across both trimesters. The independent t-test showed significantly lower serum calcium in hypertensive participants (8.7 mg/dL) compared to non-hypertensive ones (9.5 mg/dL, $t = -4.58$, $p < 0.001$). Pearson correlations revealed moderate to strong negative associations between serum calcium levels and both systolic ($r = -0.45$) and diastolic blood pressure ($r = -0.50$), indicating lower calcium is linked to higher blood pressure.

Conclusion: It was observed that there is significant level of the calcium between those having pregnancy-induced hypertension (PIH), with hypertensive women having lower serum calcium levels.The current study recommended that those women who are pregnant must ensure that they take adequate level of the calcium during the diet or through the supplements for managing blood pressure.

Keywords: calcium supplementation, pregnancy, pregnancy induced hypertension, PIH

Introduction

The human body relies on calcium for a wide variety of skeletal, cardiovascular, neurological, muscular, hormonal, and enzymatic processes, among many others. Calcium is needed for most metabolic processes, including muscle movement, nerve signaling, enzyme activity, and hormone function [1]. Skeletal system accounts for 99 percent of the body's calcium, which provides the structure and rigidity of bones. Intracellular and extracellular fluids account for the remaining 1%. Rickets in children, osteopenia and osteoporosis in adults, and an increased incidence of osteoporotic bone fractures (particularly in elderly people) are the main long-term effects of insufficient calcium consumption. The rate of increased intestinal calcium absorption by the mother more than doubles from the beginning to the end of pregnancy, which is necessary since a full-term infant's skeleton needs about 30 g of calcium, which is absorbed mostly by the mother. On the flip side, the main way that calcium is provided to the newborn via breast milk during breastfeeding is by the mother's skeletal calcium resorption [1].

Although dietary reference requirements for calcium differ by age group and life stage, the majority of recommendations suggest that adults (those 19 and above) consume 800–1300 mg of calcium per day. Some prenatal recommendations suggest increasing calcium consumption, while others claim that the metabolic changes that occur during pregnancy and breastfeeding more than make up for the fetus's calcium needs [2]. The European Union, the Food and Agriculture Organization of the World Health Organization, the American Heart Association, and Canada all agree that pregnant women should have between 1000 and 1300 milligrams of calcium per day, with a maximum of 2500 milligrams for women aged 19–50 and 3000 milligrams for those aged 14–18, respectively [3].

On the other hand, pregnancy-induced hypertension (PIH), which is described as systolic blood pressure (sBP) > 140 mmHg or diastolic blood pressure (dBP) > 90 mmHg, is a major cause of pre-eclampsia and eclampsia. Nearly 1.8% of the approximately four million instances of pre-eclampsia that occur annually result in maternal mortality [4]. The condition affects an estimated 3.2% of all live deliveries. It has long been known that taking calcium supplements while pregnant reduces the likelihood of developing pregnancy-induced hypertension (BP), with the first description of this correlation dating back to 1980. In light of the results of a meta-analysis of randomized controlled trials, the World Health Organization (WHO) has issued a recommendation

for all pregnant women, especially those from high-risk populations living in areas with low calcium intake, to take a daily supplement of 1500 to 2000 mg of calcium. This recommendation is effective from the 20th week of gestation onwards. The usual diet of the Bangladeshi populace does not include enough calcium, which contributes to their poor total calcium consumption. The government of Bangladesh has adopted the WHO calcium regimen, however there have been obstacles including poor compliance that have reduced the adoption rate [5].

But many researches proved that taking a 500 mg calcium tablet daily may help with PIH. Notable findings were found in a systematic review that examined the effects of low-dose calcium consumption on pre-eclampsia. A higher impact was seen among high-risk people, according to the evaluation, which included research from both low-risk and high-risk populations. The authors urged for more large-scale trials to validate the finding [6,7] as the data used to compile this study mostly came from smaller research. Prior studies have also shown that better adherence to a lower dosage regimen can lead to a larger cumulative dose of calcium intake. Practical obstacles, such as the size and quantity of traditional calcium tablets needed to achieve the necessary daily amount (3 to 4 tablets), possibly explain why high dose supplementation has not been widely embraced, as advised by the WHO. Also, since calcium inhibits iron absorption, you can't take iron and calcium pills at the same time[8].

Given the high prevalence of PIH in Pakistan and the potential role of calcium supplementation in reducing its incidence, it is essential to explore the association between calcium intake and hypertensive outcomes in pregnant women. Furthermore, while there is international evidence supporting the role of calcium in reducing hypertensive complications, there is limited research conducted in the local context of Pakistan, particularly in the Peshawar region. This study provide region-specific data, contributing to the growing body of evidence on the importance of calcium supplementation during pregnancy.

Study Objective

- To investigate the association of calcium supplementation with pregnancy induced hypertension in pregnant mothers.

Materials and Methods

The current study used longitudinal research design for investigating the association of calcium supplementation with pregnancy-induced hypertension (PIH) in pregnant women. The study used both the data collection during antenatal visits and data retrieved from the medical records of the patients for accessing the relation of calcium intake and PIH within the study duration of 1ST December 2020 to 1st August 2021 .

The population of the current study consisted of the pregnant women who were receiving antenatal treatment at Hayatabad Medical Complex (HMC), Peshawar. The inclusion criteria consisted that any pregnant women who was at any age of gestational, having low calcium serum level and was given calcium tablets during antenatal care were included in the current study. While women taking already antihypertensive medications, diagnosed with kidney diseases, or such medical condition that could cause increased blood pressure.

The current study chosen 150 pregnant women in the study for data collection. The participants were chosen based on convenience sampling technique that is non-probability sampling technique, which ensured that the participants were present during their antenatal visits. Below formula was used to estimate the sample size.

$$\mathbf{n = Z^2 \times p \times (1-p)/d^2}$$

Z = Z-value for 95% confidence (1.96)

p = estimated prevalence of PIH (assumed to be 10%, or 0.10)

d = margin of error (5%, or 0.05)

$$\mathbf{n = (1.96)^2 \times 0.10 \times (1-0.10)/(0.05)^2}$$

$$n = 138$$

While considering the non-responses possibility, the sample size was set to be 150 participants.

The data for the current study was collected through both structured questionnaire and medical records of the patients. Both the current and documented data regarding the pregnancy-induced hypertension and calcium supplementation was used, as shown in the below table.

Table1: Data Collection Tools

Data Collection Tool	Category	Variables/Information Collected	Source
Structured Questionnaire	Demographics	Age, Gestational Age, Parity, Socioeconomic Status	Participant's Self-Report
	Calcium Supplementation	Current and past use of calcium supplements (dosage and duration).	Participant's Self-Report
	Medical History	Prior pregnancy-induced hypertension, family history of hypertension, use of antihypertensive medication	Participant's Self-Report
Medical Records	Blood Pressure History	Retrospective data on systolic and diastolic blood pressure from prior antenatal visits	Medical Records
	Serum Calcium Levels	Historical serum calcium levels, if available from previous tests	Medical Records
	Pregnancy-Related Conditions	Records of preeclampsia and eclampsia, based on clinical diagnoses during pregnancy	Medical Records

Data Analysis

Data was analyzed through SPSS. Demographic analysis was conducted to examine the demographic characteristic of the study participants. Descriptiveanalysis was conducted for variablesi.e., as calcium supplementation, PIH diagnosis, and preeclampsia/eclampsia status, independent t-test was used to compare serum calcium levels between hypertensive and non-hypertensive groups. Lastly, Pearson correlation was used to evaluate the relationship between serum calcium levels and blood pressure.

Results

Table2: Demographic Analysis of the socio-demographic information of the study participants.

Demographic Characteristic	Category	Frequency (n)	Percentage (%)
Age (years)	18-25	40	26.7%
	26-30	50	33.3%
	31-35	35	23.3%
	36-40	20	13.3%
	Above 40	5	3.3%
Gestational Age (weeks)	< 20 weeks	30	20.0%
	20-28 weeks	50	33.3%
	29-36 weeks	45	30.0%
	> 36 weeks	25	16.7%
Parity	0 (Primigravida)	55	36.7%
	1	40	26.7%
	2-3	35	23.3%
	More than 3	20	13.3%
Socioeconomic Status	Low-income	45	30.0%
	Middle-income	75	50.0%
	High-income	30	20.0%

Demographic Characteristic	Category	Frequency (n)	Percentage (%)
Educational Level	No formal education	20	13.3%
	Primary	40	26.7%
	Secondary	60	40.0%
	Higher education	30	20.0%

Table 2 showed that;

- The majority of the participants 33.3% were in the age group of 26-30 years, followed by 23.3% in the 31-35 years range. Only 3.3% were above 40 years of age.
- Most participants were in the second trimester (20-28 weeks), representing 33.3% of the sample, followed by 30% in the 29-36 week range.
- A significant portion of participants (36.7%) were primigravida, while only 13.3% had more than three pregnancies.
- Half of the participants (50.0%) belonged to the middle-income group, while 30.0% were from low-income families.
- 40.0% of the participants had a secondary level education, while 26.7% had primary education, and 13.3% had no formal education. 20.0% had higher education.

Table 3 of the study showed that the results of the descriptive analysis of the current study.

Variable	Mean (M)	Standard Deviation (SD)	Minimum	Maximum
Calcium Supplementation (mg/day)	800 mg	300	500 mg	1500 mg

Variable	Mean (M)	Standard Deviation (SD)	Minimum	Maximum
Serum Calcium Level (mg/dL)	9.2 mg/dL	1.2	7.0 mg/dL	11.5 mg/dL
Systolic Blood Pressure (mmHg)	125 mmHg	15.5	100 mmHg	160 mmHg
Diastolic Blood Pressure (mmHg)	85 mmHg	10.3	70 mmHg	110 mmHg
Pregnancy Induced Hypertension (PIH)	Yes = 65, No = 85	N/A	N/A	N/A
Preeclampsia/Eclampsia Diagnosis	Yes = 30, No = 120	N/A	N/A	N/A

Table 3 showed the results for the below variables

1. Calcium Supplementation:

The average daily calcium intake was 800 mg/day, with a standard deviation of 300 mg, indicating moderate variability in supplement intake.

2. Serum Calcium Levels:

The mean serum calcium level of the participants was 9.2 mg/dL, which is within the normal range (8.5-10.5 mg/dL). The standard deviation of 1.2 mg/dL showed some variation in calcium levels.

3. Blood Pressure:

The mean systolic blood pressure was 125 mmHg with a standard deviation of 15.5 mmHg, while the mean diastolic blood pressure was 85 mmHg with a standard deviation of 10.3 mmHg.

4. Pregnancy-Induced Hypertension (PIH):

Out of 150 participants, 65 (43.3%) were diagnosed with pregnancy-induced hypertension (PIH), while the remaining 85 (56.7%) did not have PIH.

5. Preeclampsia/Eclampsia Diagnosis:

A total of 30 participants (20%) were diagnosed with preeclampsia or eclampsia, while 120 (80%) were not diagnosed with these conditions.

Thus, the data showed a significant percentage of women experiencing pregnancy-induced hypertension (43.3%) and a smaller portion with preeclampsia/eclampsia (20%).Similarly, average calcium supplementation intake was fairly high, and the mean serum calcium levels suggest that most participants maintained a normal calcium status.

Table4 showed the calcium levels and blood pressure before and after supplementation

Trimester	Measurement	Before Supplementation	After Supplementation	Mean Difference	p-value
First Trimester	Serum Calcium Level (mg/dL)	8.5	9.5	1.0	0.002
	Systolic Blood Pressure (mmHg)	130	120	-10	0.001
	Diastolic Blood Pressure (mmHg)	85	80	-5	0.05
Second Trimester	Serum Calcium Level (mg/dL)	9.0	10.0	1.0	0.001
	Systolic Blood Pressure (mmHg)	125	115	-10	0.003
	Diastolic Blood Pressure (mmHg)	82	78	-4	0.08

- In 1st trimester, serum calcium levels increased significantly from 8.5 mg/dL to 9.5 mg/dL ($p = 0.002$), indicating effective supplementation.
- Systolic blood pressure showed a significant decrease from 130 mmHg to 120 mmHg ($p = 0.001$). Diastolic blood pressure also decreased from 85 mmHg to 80 mmHg ($p = 0.05$).
- In 2nd trimester, serum calcium levels rose significantly from 9.0 mg/dL to 10.0 mg/dL ($p = 0.001$). Systolic blood pressure dropped from 125 mmHg to 115 mmHg ($p = 0.003$).

- Diastolic blood pressure decreased from 82 mmHg to 78 mmHg (p = 0.08), indicating a trend toward improvement, although not statistically significant.

Table 5 showed the results of the independent sample t-test

Group	n	Mean Serum Calcium Level (mg/dL)	Standard Deviation (SD)	t-value	p-value
Hypertensive (PIH)	65	8.7 mg/dL	1.1	-4.58	< 0.001**
Non-Hypertensive (No PIH)	85	9.5 mg/dL	1.0		

Note: $p < 0.05$ indicates statistical significance.

- Table 5 showed that the mean serum calcium level for the hypertensive group (those diagnosed with pregnancy-induced hypertension) was 8.7 mg/dL with a standard deviation of 1.1 mg/dL.
- The non-hypertensive group (those without pregnancy-induced hypertension) had a higher mean serum calcium level of 9.5 mg/dL, with a standard deviation of 1.0 mg/dL.
- The independent t-test resulted in a t-value of -4.58, with a p-value < 0.001, indicating that the difference in mean serum calcium levels between the hypertensive and non-hypertensive groups is statistically significant

Table 6 showed the results of the Pearson correlation.

Variable	Serum Calcium Levels	Systolic Blood Pressure	Diastolic Blood Pressure	Blood
Serum Calcium Levels	1.00			
Systolic Blood Pressure	-0.45**	1.00		

Variable	Serum Calcium Levels	Systolic Blood Pressure	Diastolic Blood Pressure
Diastolic Blood Pressure	-0.50**	0.62**	1.00

Note: Correlation coefficients are significant at $p < 0.01$

The Pearson correlation coefficient between serum calcium levels and systolic blood pressure is -0.45, which indicates a moderate negative correlation. The correlation between serum calcium levels and diastolic blood pressure is -0.50, showing a moderate to strong negative correlation. While, the Pearson correlation coefficient between systolic and diastolic blood pressure is 0.62, indicating a strong positive correlation.

The significant negative correlations between serum calcium levels and both systolic and diastolic blood pressure suggest that lower serum calcium levels may be related to higher blood pressure. This supports the notion that calcium may play a role in blood pressure regulation.

Discussion

The results of the study revealed that the average serum calcium level was 9.2 mg/dL, with 43.3% of participants having pregnancy-induced hypertension (PIH). With calcium supplementation, serum calcium levels increased while both systolic and diastolic blood pressure deceased across both trimesters. The independent t-test showed significantly lower serum calcium in hypertensive participants (8.7 mg/dL) compared to non-hypertensive ones (9.5 mg/dL, $t = -4.58$, $p < 0.001$). Pearson correlations revealed moderate to strong negative associations between serum calcium levels and both systolic ($r = -0.45$) and diastolic blood pressure ($r = -0.50$), indicating lower calcium is linked to higher blood pressure. The results are consistent with the result of the previous studies. Free calcium supplements were distributed to pregnant women in Dailekh, Nepal, via prenatal care services and counselling by community health volunteers. The pilot research found that this approach was both practicable and successful, with a high coverage rate of 94.6% in the district [9]. Of the women who received calcium, 67.3% took the complete course, which consists of two 500 mg pills daily beginning at 4 months of gestation and continuing for 5 months or until birth. In all, 82.3% of the women who received calcium took it. Just 10% of pregnant women

continued taking their calcium supplements up until they gave birth. This was due to various reasons such as feeling ill, experiencing adverse effects, forgetting to take the supplement, finding it inconvenient to take the supplements daily, or struggling with the large-sized pills. Pregnant women in two rural regions of Ethiopia participated in a small-scale calcium supplementation acceptance experiment. They were randomly allocated to one of three regimens, with dosage and timing variations, and then given the option to choose their regimen [10]. The purpose of this study was to identify factors that help or hurt adherence and to find out whether pregnant women would take more calcium if their supplement regimens were easier to follow. There was no significant difference in adherence between regimens with 2 (81.1% of women), 3 (83.4%), or 4 (77.1%) pill-taking events, but women favoured 2 event regimens over 3 or 4 event regimens. The variables that affect the delivery and absorption of calcium supplements were investigated in another research involving 32 pregnant women in Kenya. The results were similar when looking at the effects of reminder items and adherence partners, who both helped patients remember to take their medication [11]. In order to successfully include calcium supplementation into prenatal care, this research also suggested a steady supply of supplements, high-quality counselling from healthcare practitioners, materials for women to keep at home as reminders, and support from family members [12, 13]. In a cluster-randomized experiment conducted in Bangladesh, an intervention focussing on nutrition known as "Maternal, Neonatal, and Child Health" was contrasted with a routine program. The intervention included interpersonal counselling during home visits and one-on-one prenatal care sessions. Women included in the more rigorous program took more calcium and IFA pills, and more of them went to their early prenatal appointments. In the nutrition-focused intervention arm, participants' husbands' knowledge, attitudes, norms, self-efficacy, and support for their wives were enhanced when men were included in the interventions via counselling, husbands' forums, and films [14]. The World Health Organisation now recommends taking calcium supplements in large dosages (1.5-2 g), which often means taking 500 mg three to four times a day [15, 16]. Doses shown to be effective in clinical studies formed the basis for this advice. But there hasn't been any study to determine the lowest effective dosage [17, 18]. Implementing calcium supplementation in contexts where it is considered too expensive and demanding can be hindered by this large dosage and its three-times-daily dosing regimen[19].

Conclusion

The current study shown that the lower levels of the serum calcium have association with higher level of the systolic and diastolic blood pressure in pregnant women. It was observed that there is significant level of the calcium between those having pregnancy-induced hypertension (PIH), with hypertensive women having lower serum calcium levels. With calcium supplementation, serum calcium levels increased while both systolic and diastolic blood pressure deceased across both trimesters. It is supported by the findings that role of calcium in blood pressure regulation during pregnancy. Also, adequate calcium intake may help manage blood pressure and reduce the risk of PIH and related conditions.

Recommendations

The current study recommends that those women who are pregnant must ensure that they take adequate level of the calcium during the diet or through the supplements for managing blood pressure. Similarly, the healthcare providers should also monitor their serum calcium levels as the part of their routine antenatal care, especially in the women who are at the risk of the PIH. Lastly. The future studies should investigate the optimal calcium dosage and its impact on blood pressure and pregnancy outcomes.

Limitations

The current study has several limitation including that the study was relied on the self-reported data for the calcium supplementation and also the dietary intake, and this can introduce the bias in the reporting. Similarly, the cross-sectional design limited the causal inference between the hypertension and the calcium levels. Lastly, the sample size was limited the single medical facility, thus affecting generalizability.

Significance

The results underscore the importance of adequate calcium intake for managing blood pressure and improving maternal and fetal health. By integrating calcium monitoring into prenatal care, healthcare providers can enhance pregnancy outcomes and reduce complications associated with

hypertension.This study highlights the potential link between serum calcium levels and blood pressure regulation during pregnancy. Identifying low calcium levels as a risk factor for pregnancy-induced hypertension could lead to better preventive strategies.

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