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COMPARISON OF MEAN SERUM CALCIUM LEVEL IN WOMEN WITH VERSUS WITHOUT PREGNANCY INDUCED HYPERTENSION

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Abstract

Background: *Existing literature shows conflicting results on the relationship between serum calcium levels and pregnancy-induced hypertension (PIH), with some studies suggesting lower calcium levels contribute to PIH, while others do not establish a clear link. This controversy prompted the planning of this study to clarify these inconsistencies and enhance understanding.*

Objective: *To compare*

Duration: *Six months w.e.f. 02-04-2024 to 01-10-2024.*

Methodology: *This case-control study was conducted at Ghurki Trust Teaching Hospital, Lahore, with 60 patients. After obtaining informed consent, participants' demographics, blood pressure, and serum calcium levels were recorded. Based on blood pressure measurements, participants were classified into two groups: those with pregnancy-induced hypertension (PIH) and normotensive women. Data were analyzed using SPSS, and statistical tests compared serum calcium levels between the groups, with a significance level set at $p \leq 0.05$.*

Results: *The study included 60 participants, with a mean age of 32.15 ± 6.03 years, and a mean gestational age of 30.45 ± 3.26 weeks. Most participants were overweight (70%) and primiparous (46.7%). Pregnancy-induced hypertension (PIH) was observed in 33.3% of participants. Significant differences were found in blood pressure, with higher systolic and diastolic pressures in the PIH group. Serum calcium levels were significantly lower in the PIH group (8.05 ± 0.42 mg/dl) compared to controls (9.73 ± 1.27 mg/dl).*

Conclusion: *Pregnancy induced hypertension was observed in 33.3% of participants, and serum calcium levels were significantly lower in the PIH group compared to the controls. This difference was consistent across subgroups based on age, gestational age, BMI, and parity.*

INTRODUCTION

Hypertension in pregnancy develops after the 20th week in women who were previously normotensive.[1] Pregnancy-induced hypertension (PIH) occurs in approximately 9.3% of all pregnancies in Pakistan and presents significant risks to both the mother and the fetus.[2] PIH is a leading cause of maternal, fetal, and newborn morbidity and mortality, with affected women at an increased risk of complications such as abruptio placentae, cerebrovascular events, organ failure, and disseminated intravascular coagulation.[3,4] Fetuses of these mothers face a higher likelihood of intrauterine growth retardation, prematurity, and

intrauterine death.[5] Risk factors for PIH include null parity, multiple pregnancies, a history of chronic hypertension, gestational diabetes, fetal malformations, obesity, advanced maternal age (under 20 or over 40 years), and a history of PIH in previous pregnancies.[6] Additional risk factors include chronic diseases such as renal disease, diabetes mellitus, cardiac disease, unrecognized chronic hypertension, a positive family history of PIH (indicating genetic susceptibility), psychological stress, alcohol use, rheumatic arthritis, extreme weight issues, asthma, and low socioeconomic status.[5,7]

Growing evidence has highlighted the significant impact of lifestyle interventions on managing blood pressure, including physical exercise, dietary adjustments, and body weight management, beyond genetic predisposition.[8] One such factor under investigation is calcium, a vital mineral involved in numerous bodily functions.[9] Circulating calcium in the plasma exists in three forms: free ions, protein-bound complexes, and ionic complexes. The normal serum calcium concentration in healthy individuals ranges from 8.8 to 10.4 mg/dl.[7-9]

In Pakistan, a study was carried out at Sir Ganga Ram Hospital Lahore, Bano et al. (2022) reported significantly less mean calcium level in women with PIH in comparison with normotensive women as 7.26±0.80 vs. 8.94±0.53 mg/dl; p-value <0.05.[10] In the light of above study, it seems that serum calcium level in pregnant women should be checked to anticipate PIH in them and to plan treatment well in time to avoid the adverse consequences. However, another study has reported it differently. In an Indian study, less mean serum calcium level in women with PIH was reported than normotensive women by Kumar et al. (2019) as 8.83±0.55 vs. 8.94±0.60 mg/dl; p-value=0.337 but the difference was not statistically significant.[11]

There is ongoing controversy in the literature regarding the comparison of serum calcium levels in women with Pregnancy-Induced Hypertension (PIH) and normotensive women. The aim of this study is to compare serum calcium levels between these two groups and evaluate if low serum calcium levels can serve as a marker for PIH. If significant differences are found, this could help identify at-risk women early, allowing for timely intervention and management, ultimately reducing adverse outcomes and healthcare costs.

METHODOLOGY

This case-control study was conducted at the Department of Obstetrics and Gynecology, Ghurki Trust Teaching Hospital, Lahore, over a six-month period following the approval of the study synopsis. The sample size was calculated to be 60 patients, determined using an 80% power of test and a 5% level of significance, with the expected mean serum calcium levels being 7.26±0.80 mg/dl for women with pregnancy-induced hypertension (PIH) and 8.94±0.53 mg/dl for normotensive women.[10] The sampling technique used was non-probability consecutive sampling, and participants were selected based on specific inclusion and exclusion criteria. The inclusion criteria included women aged 20-45 years, presenting for antenatal check-ups, with a gestational age of more than 20 weeks and a singleton pregnancy. Women with chronic hypertension, cardiovascular, renal, or hepatic disorders, type 2 diabetes, endocrinal issues, a history of drug abuse, or those in any gynaecological emergency were excluded from the study. Data were collected from 60 pregnant women meeting the inclusion criteria who presented for routine check-ups at the outpatient department of Gynaecology & Obstetrics, Ghurki Trust Teaching Hospital Lahore. After obtaining informed consent, their demographics were recorded, and their blood pressure was checked twice over four hours in a 45° inclined position, with systolic and diastolic blood pressure (SBP and DBP) averaged. Based on blood pressure measurements, participants were divided into two groups: Group A, consisting of patients with pregnancy-induced hypertension, and Group B, consisting of normotensive women. After an overnight fast, blood samples were collected from the antecubital vein to measure serum calcium and uric acid levels. Serum calcium was measured using the O-Cresol Phthalein Complexone (OCPC) method, with blood samples processed by two on-duty doctors to avoid bias. Exclusion criteria controlled for confounding variables. The collected data were analyzed using SPSS version 25.0, calculating means and standard deviations for continuous variables such as age, gestational age, BMI, average SBP, DBP,

and serum calcium level. Frequency and percentages were calculated for PIH and parity. A t-test was used to compare the mean serum calcium levels between the two groups, with a p-value of ≤0.05 considered significant. Data were further stratified based on age, gestational age, BMI, and parity, with post-stratification independent sample t-tests applied, taking a p-value ≤0.05 as significant.

RESULTS

The study sample consisted of 60 participants with a mean age of 32.15 ± 6.03 years. Among them, 27 women (61.7%) were aged between 20 and 35 years, while 23 women (38.3%) were between 36 and 45 years. The mean gestational age of the participants was 30.45 ± 3.26 weeks, with 14 women (23.3%) in the 20–28-week range, and 46 women (76.7%) in the >28-week range. The mean body mass index (BMI) was 27.29 ± 3.62 kg/m², with 18 women (30.0%) categorized as having normal weight and 42 women (70.0%) classified as overweight or obese. Regarding parity, 28 women (46.7%) were primiparous, 22 women (36.7%) were multiparous, and 10 women (16.7%) were grand multiparous. The average systolic blood pressure was 138.36 ± 13.51 mmHg, and the average diastolic blood pressure was 89.18 ± 10.74 mmHg. Data is given in Table 1.0. Out of the total participants, 33.3% had Pregnancy-Induced Hypertension (PIH), as given in Table 2.0. Both the groups had insignificant difference with regard to baseline variables (p-value>0.05). However, significant differences were observed in blood pressure. The systolic blood pressure was notably higher in the cases group (155.93 ± 5.59 mmHg) compared to the controls (129.57 ± 4.86 mmHg), with a p-value of 0.000. The diastolic blood pressure was also significantly higher in the cases (103.35 ± 5.16 mmHg) compared to the controls (82.09 ± 2.64 mmHg), with a p-value of 0.000. Data is given in Table 3.0. The serum calcium level in the cases group (n=20) was 8.05 ± 0.42 mg/dl, while in the controls group (n=40), it was 9.73 ± 1.27 mg/dl. This difference was statistically significant, with a p-value of 0.000. Data is given in Table 4.0. The comparison of mean serum calcium levels between the groups, based on subgroups of age, gestational age, BMI, and parity, revealed consistently lower values in the cases compared to the controls, with the differences being statistically significant (p-value ≤0.05). Data is given in Table 5.0.

Table 1.0 Baseline Characteristics of Study Sample

Characteristics	Study Sample n=60
Age (years)	32.15±6.03
• **21-35 years**	27 (61.7%)
• **36-45 years**	23 (38.3%)
Gestational Age (weeks)	30.45±3.26
• **20-28 weeks**	14 (23.3%)
• **>28 weeks**	46 (76.7%)
BMI (kg/m²)	27.29±3.62
• **Normal Weight**	18 (30.0%)
• **Overweight/Obese**	42 (70.0%)
Parity	
• **Primiparous**	28 (46.7%)
• **Multiparous**	22 (36.7%)
• **Grand Multiparous**	10 (16.7%)
Systolic Blood Pressure (mmHG)	138.36±13.51
Diastolic Blood Pressure (mmHG)	89.18±10.74

Table 2.0 Frequency of PIH in Pregnant Women Presenting for Antenatal Check up.

Description	Study Population (n=60)
Pregnancy Induced Hypertension	
• Yes	20 (33.3%)
• No	40 (66.7%)

Table 3.0 Comparison of Baseline Characteristics between the Cases and the Control

Characteristics	Cases n=20	Controls n=40	p-value
Age (years)	31.95±6.30	32.25±5.97	0.858
• 21-35 years	12 (60.0%)	25 (62.5%)	0.851
• 36-45 years	8 (40.0%)	15 (37.5%)	
Gestational Age (weeks)	30.85±3.44	30.25±3.19	0.506
• 20-28 weeks	4 (20.0%)	10 (25.0%)	0.666
• >28 weeks	16 (80.0%)	30 (75.0%)	
BMI (kg/m^2)	26.57±3.73	27.66±3.55	0.276
• Normal Weight	7 (35.0%)	11 (27.5%)	0.550
• Overweight/Obese	13 (65.0%)	29 (72.5%)	
Parity			
• Primiparous	10 (50.0%)	18 (45.0%)	0.728
• Multiparous	6 (30.0%)	16 (40.0%)	
• Grand Multiparous	4 (20.0%)	6 (15.0%)	
Systolic Blood Pressure (mmHG)	155.93±5.59	129.57±4.86	0.000
Diastolic Blood Pressure (mmHG)	103.35±5.16	82.09±2.64	0.000

Chi square test/Independent sample t test, taking p-value ≤0.05 as significant.

Table 4.0 Comparison of Mean Serum Calcium Level between the Cases and the Controls

Characteristics	Cases n=20	Controls n=40	p-value
Serum Calcium Level (mg/dl)	8.050±0.42	9.73±1.27	0.000

Independent sample t test, taking p-value ≤0.05 as significant.

Table 5.0 Comparison of Mean Serum Calcium Level between the Cases and the Controls

Subgroups	Mean Serum Calcium Level		P-value
	Cases n=20	Controls n=40	
Age (years)			
• 21-35 years	8.51±0.39	9.74±1.40	0.001
• 36-45 years	7.90±0.44	9.71±1.07	0.000
Gestational Age (weeks)			
• 20-28 weeks	8.08±0.46	9.86±1.33	0.024
• >28 weeks	8.04±0.43	9.68±1.28	0.000
BMI (kg/m^2)			
• Normal Weight	8.20±0.51	9.50±1.39	0.032

• **Overweight/Obese**	7.97±0.36	9.81±1.24	0.000
Parity			
• **Primiparous**	7.89±0.35	9.86±1.39	0.000
• **Multiparous**	8.22±0.51	9.66±1.29	0.016
• **Grand Multiparous**	8.20±0.38	9.50±0.97	0.037

Independent sample t-test, * observed difference was statistically significant where p-value≤0.05

DISCUSSION

The comparison of mean serum calcium levels in women with versus without pregnancy-induced hypertension (PIH) has been a subject of significant interest in medical research.[12-15] Existing literature presents conflicting findings regarding the relationship between serum calcium levels and PIH. Some studies suggest that lower calcium levels may contribute to the development of PIH, while others fail to establish a clear link.[10-11] This controversy in existing literature prompted the planning of this study, aiming to resolve the disparities and provide a more comprehensive understanding of the role of calcium levels in the pathophysiology of PIH. The study seeks to clarify these inconsistencies.

Mean age of the participants in this study was a 32.15±6.03. However, previously some studies reported lower mean age of the participants as 30.03±.6.74 years by Ephraim et al. (2014) in Ghana, 31.55±6.14 years by Ugwuja et al. (2016) in Ghana, 28.87±4.32 years by Bano et al. (2022) in Pakistan and 27.93±5.26 years by Singh et al. (2019) in India.[16,17,10] However, Kumar et al. (2019) in India reported a higher mean age of 35.1±4.0 years.[11] This variation may be associated with difference in inclusion criteria of each study.

The mean gestational age of the participants was 30.45±3.26 weeks. Previously mean gestational age reported by similar studies is 31.40±4.27 weeks by Ephraim et al. (2014), 32.72±3.28 weeks by Sing et al. (2019), 33.72±3.70 weeks by Ugwuja et al. (2016) and as high as 35.86±1.86 weeks by Bano et al. (2022).[18,17,10]

The mean BMI in this study was 27.29 ± 3.62 kg/m^2. A similar mean BMI of 25.0±4.4 kg/m^2 was reported by Kumar et al. (2019) in India.[11] However, a higher mean BMI of 27.2±5.39 kg/m^2 and 35.12±6.06 kg/m^2 was reported by Ugwuja et al. (2016).[17]

Regarding parity, 28 women (46.7%) were primiparous, 22 women (36.7%) were multiparous, and 10 women (16.7%) were grand multiparous in this study. Kumar et al. (2019) reported that 28.57% participating women in their study were primiparous while remaining 71.43% were multiparous.[11] Ephraim et al. (2016) reported that 56.7% women were nulliparous, 30.0% were primiparous and 13.3% were multiparous.[16] The mean systolic blood pressure was 138.36 ± 13.51 mmHg, and the mean diastolic blood pressure was 89.18 ± 10.74 mmHg. Bano et al. (2022) reported mean SBP and DBP of the study sample as 152.0±8.87 and 96.90±5.80 mmHg, respectively whereas Ephraim et al. (2016) reported it as 155.17±10.21 and 101.63±7.84, respectively.[10,16]

Out of the total participants, 33.3% had Pregnancy-Induced Hypertension (PIH). Previously similar frequency of PIH in their study population was reported by Ephraim et al. (2016) as 31.6% but Lewandowska et al. (2019) reported it 25.0%.[16,19]

The systolic blood pressure was notably higher in the cases group (155.93 ± 5.59 mmHg) compared to the controls (129.57 ± 4.86 mmHg), with a p-value of 0.000. The diastolic blood pressure was also significantly higher in the cases (103.35 ± 5.16 mmHg) compared to the controls (82.09 ± 2.64 mmHg), with a p-value of 0.000. Our findings are in line with results of Pairu et al. (2015) who reported mean SBP (150.34±9.98 vs. 114.88±8.24 mmHg; p-value<0.01) and DBP (100.40±9.29 vs. 76.64±6.14 mmHg; p-value <0.001) between the cases and controls respectively.[20]

The serum calcium level in the cases group (n=20) was 8.05 ± 0.42 mg/dl, while in the controls group (n=40), it was 9.73 ± 1.27 mg/dl; p-value=0.000. Bano et al. (2022) also reported significantly less mean serum calcium level in cases than controls (7.26±0.80 vs. 8.94±0.53 mg/L; p-value<0.05).[10] Likewise, Pairu et al. (2015) reported significantly less mean serum level in the cases group (8.15±0.37 vs. 9.16±0.82 mg/L; p-value<0.001) than controls and Singh et al. (2019) as 8.34±1.62 vs. 9.87±0.83

mg/L.[20,18] Ephraim et al. (2016) reported that 100% of the women with PIH had serum calcium level <2.1 mmol/L.[17] But Kumar et al. (2019) reported insignificantly less mean serum aciculum level in cases group than controls (8.83±0.55 vs. 8.9±4.06; p-value=0.337).[11] Difference in mean serum calcium level was significantly less in all sub groups of Age, gestational age, BMI and parity in cases group than controls.

CONCLUSION

In conclusion, PIH was observed in 33.3% of participants, and serum calcium levels were significantly lower in the PIH group compared to the controls. This difference was consistent across subgroups based on age, gestational age, BMI, and parity. The findings suggest a potential link between PIH and altered calcium metabolism in pregnancy.

LIMITATIONS & RECOMMENDATIONS

This study's strengths include its clear comparison of serum calcium levels between women with and without pregnancy-induced hypertension (PIH), providing valuable insights into this controversial topic. Additionally, it includes diverse variables such as age, BMI, and parity, which strengthen its applicability. However, limitations include a small sample size and potential selection bias, which may affect generalizability. Future research should involve larger, multicenter studies to further investigate the role of serum calcium in PIH, and explore potential interventions to address the calcium deficiency in PIH management.

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Authors Contribution

Author 1

Substantial contributions to study design, acquisition of data.
Analysis & interpretation of data, manuscript writing.
Has given final approval of the version to be published.
Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Author 2

Substantial contributions to concept, study design.
Data Analysis, manuscript writing, critical review.
Has given final approval of the version to be published.
Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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