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Maternal Biochemical Markers and Risk of Preeclampsia

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ABSTRACT

Preeclampsia is a pregnancy disorder associated with a numerous feto-maternal complication. This condition prevails in developing countries, where it is an important reason for feto-maternal morbidity and mortality. **Objective:** To assess the role of maternal biochemical markers in the development of preeclampsia during pregnancy. **Methods:** A comparative cross-sectional study was carried out after ethical approval from the Institutional Review Board. The study included 200 participants: 100 patients with preeclampsia and 100 normotensive pregnant women as controls. Preeclampsia was diagnosed based on blood pressure readings above 140/90 mmHg and proteinuria levels exceeding 300 mg/24h. Independentsample t-test was applied to see the differences in both groups in SPSS version 25. **Results:** Significantly higher mean levels of cholesterol, triglycerides, LDL and Sodium were observed in women with preeclampsia ($p < 0.0001$). Conversely, the mean levels of high-density lipoprotein cholesterol ($p = 0.0169$), magnesium, calcium and potassium were lower in women with preeclampsia ($p < 0.0001$). **Conclusions:** Total cholesterol, triglycerides lipid profile and levels of calcium and magnesium were significantly disrupted and showed strong correlations with the severity of the disease. In clinical practice, these biomarkers could facilitate the timely detection of at-risk cases, potentially reducing the rate of feto-maternal complications.

INTRODUCTION

Preeclampsia (PE) is a pregnancy disorder associatedwith high blood pressure, and proteinuria after the 5 months gestation in women who previously had normal blood pressure, posing a significant risk to both maternal and perinatal health [1]. It affects 2-8% of all pregnancies worldwide, while in Pakistan, it is accountable for 5-15% of pregnancies [2]. PE is prevalent in developing countries, where it is animportantreason for complications and mortality of mother and fetus [3]. The exact causes of preeclampsia remain unclear, but genetic factors are believed to play a significant role. PE results from interplay of multiple pathological conditions that cause disruption of regulatory systems of inflammation and endothelial function beyond the normal changes of pregnancy [4]. It is a serious health issue resulting in devastating consequences [5]. A research study on maternal serum triglyceride levels and preeclampsia indicates that elevated triglyceride levels may be a risk factor and/or predictor for preeclampsia [6]. The linkage between serum lipid profile abnormalities and PE is well-established. Abnormal lipid levels are strongly linked to atherosclerotic Cardiovascular Disease (CVD) and contribute directly to endothelial dysfunction [7]. In contrast to normal pregnancy, PE is characterized by elevated levels of triglycerides, total lipids, and LDL cholesterol [8]. The link between altered lipid profiles and endothelial dysfunction has emerged as a crucial area of research related to pregnancy complications, particularly PE [9].

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Hypertension, a key feature of PE, results from vasospasm affecting the kidneys, placenta, brain, and uterus. A decrease in the PGI2 ratio due to lipid profile changes may play a significant role in hypertension during pregnancy [10]. Electrolytes are essential for regulating blood pressure, and imbalances can make blood vessels overly responsive to vasoconstrictors like vasopressin and Antidiuretic Hormone (ADH), contributing to hypertension [11]. Disruptions in Sodium (Na) and Potassium (K) levels play a role in the development of PE. Moreover, magnesium is thought to influence angiogenic and inflammatory responses, which can lead to reduced vascular contraction and lower hypertension in preeclampsia [12]. Approximately 24% of all maternal deaths in Pakistan are attributed to hypertensive pregnancy disorders [13]. While various theories have been proposed regarding the cause of preeclampsia, no definitive cause has been identified. This uncertainty hampers efforts to prevent and treat the condition. Based on previous observations, we hypothesized that changes in lipid profile parameters and electrolyte imbalances in early pregnancy might be directly linked to the development of complications.

Purpose of the present study was to assess the role of maternal biochemical markers in the development of preeclampsia during pregnancy.

METHODS

We selected lipid profile and electrolytes as biomarkers to evaluate causes of PE in pregnancy. Lipid profile was changed in PE, and has direct effects on the cardiovascular health. It results in endothelial damage and atherosclerotic changes that potentiate PE. Electrolytes imbalances affect PE by imparting their role in vascular tone and inflammatory responses. A comparative cross-sectional study was carried out at the Niazi Welfare Foundation Teaching Hospital in Sargodha, from 1st January, 2023 to 31st January 2024, following ethical approval from the Institutional Review Board (NM and DC-IRB-55). The sample size was determined based on a mean HDL level of 51.02 ± 16.01 in preeclampsia cases and 61.08 ± 25.03 in normotensive individuals, with a 90% confidence level and 80% power [14]. Using Open Epi, the calculated sample size was 98, rounded to 100. Therefore, the study included 200 participants: 100 patients with preeclampsia and 100 normotensive pregnant women as controls, all from the Obstetrics and Gynecology Department. Preeclampsia was diagnosed based on blood pressure readings above 140/90 mmHg and proteinuria levels exceeding 300 mg/24 hours or a + 1 on a dipstick test. Patients who were hospitalized were approached directly, and sociodemographic information was collected from both the patients and their attendants. Data collection was conducted using a consecutive sampling method, adhering to specific inclusion and exclusion criteria. Women aged 20 to 45 years with singleton pregnancies who developed hypertension with BP >140/90 mmHg on two separate occasions six hours apart and proteinuria >300 mg/24 hours or a +1 on a dipstick testduring pregnancy were included in the study. Exclusions were applied to women with chronic hypertension, gestational diabetes, cardiovascular disorders, renal disease, immunological disorders, PCOS, metabolic disorders, multiple pregnancies, or incomplete information. This study followed all ethical standardsto ensure safety and rights of participants. All the participants and their attendants were clearly explained regarding the purpose, procedure, potential risk and benefits related to this study. They were given free choice for participation and written informed consent was obtained from all participants and attendants. A 5 ml blood sample was drawn from the median cubital vein using aseptic techniques and placed into vacutainers without additives. The sample was then centrifuged at 3000 rpm for 10 minutes to separate the serum, which was stored in Eppendorf tubes at -20°C. The serum lipid profile and Ca++ and Mg++ levels were analyzed using a Beckman Coulter AU-680 chemistry analyzer via the spectrophotometric method. Serum electrolytes were assessed with an Easy Lyte analyzer using the ion-selective electrode (ISE) potentiometer method. All tests were conducted personally by the principal investigator in the Pathology/ Biochemistry Laboratory at NWFTH. The data were analyzed using SPSS version 25.0. For quantitative variables, Mean and Standard Deviation (SD) were computed. Qualitative variables were presented in frequencies and percentages, and presented in table. Independent t-test was used to see mean differences in two groups at 95% confidence interval, and p value <0.05. This methodology would help in finding and validating the biomarkersfor timely detection of PE, which could serve as a base for clinical practice in reducing feto-maternal consequences.

RESULTS

Demographics of control group showed man age of 30.0 ± 5.78 years, gestational age 30.21 ± .32 weeks, weight 74.04 ± 7.06 kg, BMI 26.83 ± 3.16, SPB 124.99 ± 3.12 mm/Hg while DBP 83.64 ± 1.80. Comparatively, study group presented with mean age 27.82 ± 6.36 years, gestational age 31.45 ± 2.81weeks, weight 81.63 ± 8.00 kg, BMI 29.51 ± 2.96, SPB 166.25 ± 11.21 mm/Hg while DBP 36.23 ± 20.85. p-values depicted significant differences in demographics of preeclampsia and normotensive group (Table 1).

Table 1: Demographic Variables of Cases and Control Groups (n=200)

Variables	Control (Mean ± SD)	Cases (Mean ± SD)	p-Value
Age (Years)	30.0 ± 5.78	27.82 ± 6.36	0.007
Gestational Age (Weeks)	30.21 ± .32	31.45 ± 2.81	0.003
Weight (Kg)	74.04 ± 7.06	81.63 ± 8.00	<0.001

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BMI	26.83 ± 3.16	29.51 ± 2.96	<0.001
SBP (mm/Hg)	124.99 ± 3.12	166.25 ± 11.21	<0.001
DBP (mm/Hg)	83.64 ± 1.80	36.23 ± 20.85	<0.001

In the normotensive pregnancy, TCwas found 174.88 ± 13.50 mg/dl, TGs184.65 ± 12.30 mg/dl, LDL 70.92 ± 2.62 mg/dl and HDL 40.08 ± 12.45 mg/dl. Whereas in preeclampsia group, TC were 210.14 ± 20.40 mg/dl, TGs 214.90 ± 15.59 mg/dl, LDL 101.78 ± 2.72mg/dl and HDL 34.23 ± 20.85 mg/dl. The mean levels of TC, TGs and LDL were significantly higher in women with preeclampsia compared to normal controls (p <0.0001), as shown in table 2. Conversely, the mean levels of HDL were significantly lower in women with preeclampsia than in normal controls (p = 0.0169). This study showed notable variations in lipid profileof cases and control group. The findings (mean ± SD) for these parameters are detailed in table 2.

Table 2: Lipid Profiles of Preeclampsia and Normotensive Pregnant Women(n=200)

Variables	Control (Mean ± SD)	95% CI		Cases (Mean ± SD)	95% CI		p-Value
		Upper	Lower		Upper	Lower	
Total Cholesterol (mg/dL)	174.88 ± 13.50	177.419	172.363	210.14 ± 20.40	213.97	206.319	<0.001
Triglyceride (mg/dL)	184.65 ± 12.30	186.993	182.329	214.90 ± 15.59	218.804	210.996	<0.001
LDL (mg/dL)	70.92 ± 2.62	73.226	68.62	101.78 ± 2.72	104.701	98.87	<0.001
HDL (mg/dL)	40.08 ± 12.45	40.59	39.5	34.23 ± 20.85	36.76	35.72	0.017

Estimation of minerals and electrolyte values in table 3 revealed Mg levels of 2.40 ± 0.25 mg/dl, Ca 8.69 ± 0.54 mg/dl, Na 137.35 ± 3.04mEq/L and K 3.78 ± 0.26mEq/L in control group. In preeclampsiagroup, Mg levels were 1.37 ± 0.35mg/dl, Ca 7.55 ± 0.42mg/dl, Na 147.55 ± 4.26mEq/L and K .15 ± 0.37mEq/L. Statistically, magnesium, calcium and potassium levels were lower in cases presenting with preeclampsia compared to controls (p <0.0001). Comparatively, sodium levels were high in preeclampsia women(p<0.0001)as detailed in table 3.

Table 3: Electrolyte Parameters of Pre-eclampsia and Normotensive Pregnancy(n=200)

Variables	Control (Mean ± SD)	95% CI		Cases (Mean±SD)	95% CI		p-Value
		Upper	Lower		Upper	Lower	
Mg (mg/dL)	2.40 ± 0.25	2.45	2.358	1.37 ± 0.35	1.431	1.303	<0.001
Ca (mg/dL)	8.69 ± 0.54	8.795	8.594	7.55 ± 0.42	7.633	7.475	<0.001
Na (mEq/L)	137.35 ± 3.04	137.929	136.80	147.55 ± 4.26	148.35	146.80	<0.001
K (mEq/L)	3.78 ± 0.26	3.835	3.740	3.15 ± 0.37	3.195	3.055	<0.001

DISCUSSION

The thorough evaluation of the lipid profile, including TC, TGs, LDL-C, and HDL-C levels, along with key minerals such as sodium, potassium, magnesium, and calcium, highlights the multifaceted nature of preeclampsia. Notably, in this study, preeclamptic pregnant women exhibited significantly lower HDL-C levels. In this study, we observed significantly elevated TC, TGs, LDL in preeclampsia, indicating abnormal lipid metabolism. Preeclampsia is typically associated with hypertriglyceridemia. This study also found decreased HDL-cholesterol levels, which are consistent with findings from other research studies on preeclampsia women [6]. Similarly, Tesfa E *et al.*, established a connection between preeclampsia and elevated TG and LDL-C levels in the African population [14]. Yadav S *et al.*, found that preeclamptic patients had significantly higher levels of blood TGs and free fatty acids [15]. Li J *et al.*, observed similar results in the Chinese population [16]. Additionally, a study by Ebogo-Belobo JT *et al.*, in Africa and Sakarde A *et al.*, demonstrated that TC and LDL-C levels are linked to blood pressure, highlighting the complex interaction of lipid parameters in the endothelial damage associated with the pathogenesis of the disease [17, 18]. In the present study, preeclampsia patients exhibited decreased levels of magnesium, calcium, and potassium, while sodium levels were increased compared to the controls. Ahmed NA *et al.*, reported similar findings [19]. Additionally, Aslam F *et al.*, noted reduced calcium and magnesium levels in preeclamptic patients in the South-Punjab region of Pakistan [20]. This study provided valuable insights in identification of biomarkers that are potential basis for PE. In clinical practice, these biomarkers could facilitate the timely detection of at-risk cases, potentially reducing the rate of feto-maternal complications. Timely diagnosis allows for the implementation of targeted interventions, effectively managing the devastating effects of Preeclampsia (PE) in routine clinical practice. Despite identifying significant findings, the study has certain limitations, including being conducted in a single hospital; there is a risk of selection bias, which may hinder the generalization of the findings to other populations or healthcare setting. Measurement bias could also impact the generalizability. Despite using standard laboratory procedures to measure biochemical parameters, variations in manual techniques and equipment calibration could introduce inconsistencies that affect the accuracy and reliability of the results across different settings. In future, there is a need to conduct multi-centered studies to effectively evaluate the effect of biomarkers on preeclampsia.

CONCLUSIONS

The study reveals significant changes in the lipid profile and mineral levels in preeclampsia patients. Notably, TC and TGs within the lipid profile, as well as calcium (Ca) and magnesium (Mg) among minerals, all demonstrated a strong association with blood pressure. These findings suggest that these parameters could potentially serve as biomarkers for preeclampsia. Integrating these parameters in clinical approach provides effective perinatal outcomes.

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Authors Contribution

Conceptualization: MFJ
Methodology: MFJ, SS
Formal analysis: SR, JHQ
Writing, review and editing: SA[1], SA[2]

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

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