Original Article

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Associations of Gestational Diabetes, Multiparity, and Hyperlipidemia with Preeclampsia

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ABSTRACT

Background: Preeclampsia is a multifactorial disorder of hypertension and proteinuria, which has a global prevalence of 2-8% of pregnancies. Its pathogenesis is still unclear, and the major risk factors are obesity, nulliparity, and preliminary hypertension. Present study was aimed to analyze associated risk factors and altered levels of hematology and serum lipids in preeclampsia patients.

Methods: This case-control study was conducted at the Institute of Biochemistry, University of Sindh, Jamshoro. The study was carried out from June 2024 to May 2025. Pregnant women, 75 with preeclampsia (Preeclampsia patients) and 75 without preeclampsia (controls) were included. Blood samples (5 ml) were collected from participants to analyze hematology and lipid profile along with questionnaire. SPSS version 21 was used for statistical analysis, p value <0.05 for level was the level of significance at 95% confidence interval.

Results: The study presents an overview of the comparative analysis of complete blood count, altered serum lipid levels, and associated risk factors including gestational diabetes, multiparity, microcytic anemia, and hyperlipidemia were found among preeclampsia patients. It also highlights major differences in parameters like hemoglobin, RBCs, platelets, monocytes, lymphocytes and monocytes in preeclampsia patients and healthy controls.

Conclusion: Gestational diabetes, multiparity, microcytic anemia, and hyperlipidemia are positively associated with preeclampsia. High salt intake and red meat consumption are also significantly positively associated with preeclampsia disease. What these results show is that preeclampsia isn't caused by just one thing, it's a mixture of factors and that pushes hard for thorough prenatal screening of metabolic problems and blood abnormalities.

Keywords: *Gestational Diabetes, Hyperlipidemia, Preeclampsia, Microcytic Anemia, Multiparity.*

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INTRODUCTION

Preeclampsia is a dangerous pregnancy-related illness that raises the dangers to the health of both the mother and the fetus, particularly in underdeveloped nations like Pakistan, where its frequency is estimated to be around 5%. Typically, symptoms start to show up after 32 weeks of pregnancy, in the late second or third trimester. Extreme maternal age, nulliparity, obesity, insulin resistance, diabetes mellitus, twin and multiple gestations, a family history of preeclampsia, Black race, and chronic and gestational hypertension are risk factors for PE[1].

Women who are nulliparous, more than 40 years of age, have a body mass index (BMI) ≥ 35 kg/m², have a family history of preeclampsia, have multiple pregnancies (twins, triplets), or have a pregnancy interval of more than ten years are at a moderate risk of preeclampsia[2,3].

Gestational diabetes and preeclampsia are responsible for maternal and fetal mortality and morbidity and are common pregnancy-related problems[4]. The pathophysiological mechanisms in both gestational diabetes (80.3% of all pregnancies reported by the

recent International Diabetes Federation)[5] and preeclampsia require oxidative stress, vascular endothelial dysfunction, and pro-inflammatory factor release, which conjointly increase the risk of cardiovascular disease and future maternal diabetes, signifying a connection between gestational diabetes and preeclampsia[6,7].

Variation in lipid concentration has been reported to be a risk factor for preeclampsia[8]. Further investigation revealed that the preeclampsia group's TGs/high-density lipoprotein (HDL) ratio was noticeably higher than that of the normal control women[9]. The severity of hypertension in preeclampsia is correlated with hyperlipidemia, even if physiological hyperlipidemia is not atherogenic. This is because dyslipidemia in PE is very common in women with high body mass index and obesity, which is linked to placental dysfunction in preeclampsia. Also, maternal problems such as placental abruption, gestational diabetes mellitus, and preeclampsia are linked to high levels of triglycerides and cholesterol during pregnancy[10-14]. The goal of the present study was to examine the altered lipid profile in Hyderabad, taking into account the important function of lipid profiles such as TC, TGs, HDL, LDL, and VLDL.

METHODOLOGY

This case-control study was carried out at the Institute of Biochemistry, University of Sindh, Jamshoro, Pakistan. The study was carried out from June 2024 to May 2025. The sample collection from the Department of Obstetrics & Gynecology at Taluka Hospital, Hyderabad, after signing the written informed consent, with the sample size calculated by the following formula:

$$n = Z^2Pq/e2,$$

Where Z = 95% Confidence Interval, P = Prevalence (about 5% of pregnancies are affected by it, and it is thought to be the leading cause of maternal and perinatal death[15]), q = 1-P, and e = 0.05. It made up 72.99=73 no. of samples. The 6% error of the non-response rate was 4.38. By adding these two, it will almost be equal to 77 no. of samples. We collected 100 samples of preeclampsia patients; among those, 75 samples were complete with respect to their questionnaire and blood sample analysis. Some (N=07) blood samples were hemolyzed during processing, and some were not analyzed due to unavailability of the questionnaire (N=18).

Participants

In this study, 75 pregnant women with preeclampsia (Preeclampsia patients) and 75 without preeclampsia (controls) were included. The inclusion criteria for preeclampsia patients were pregnant women aged 18 to 45 years, in their second or third trimester (after 20 weeks), who had been diagnosed with preeclampsia—defined by high blood pressure (≥140/90 mmHg) and protein in the urine (≥300 mg in 24 hours). Both first-time mothers (primigravida) and those with previous pregnancies (multigravida) were included, especially if they had a family history of preeclampsia. All participants consented to participate in the study by written informed consent and were residents of Hyderabad receiving care at Taluka Hospital. Those in their first trimester, with a history of smoking, alcohol, or substance use, or who did not appear at the outdoor patient clinic in Hyderabad or refused to give consent, were not included in the study.

Sample and Data Collection

Data were gathered using a semi-structured questionnaire covering sociodemographic characteristics, personal and family medical history, dietary habits and other risk factors from the participants. Blood samples (5 ml each) were collected at the hospital early in the morning with minimum 12 hours fasting to check both blood counts and lipid profiles. Hematology tests were analyzed using the Sysmex KX-21, while lipid testing was performed on the Roche Cobas C311 auto analyzer. Gestational diabetes was confirmed by HbA1c test of preeclampsia patients and controls. All the necessary

instructions were followed to avoid hemolysis and other contamination.

Statistical Analysis

SPSS version 21 and MS Excel were used for data analysis, employing statistical tests to compare serum lipid profile and CBC levels between patients and controls. Values are expressed as mean±SD. Descriptive analysis by chi square test was conducted to obtain the odds ratio with 95% confidence interval of risk factors for associations. The study was designed with 80% power to detect an odds ratio of 2.0 at a 5% significance level (two-sided). Quantitative data comparison was done using a student's t-test and analysis of variance (ANOVA). A p-value of less than 0.05 was considered statistically significant at the 95% confidence interval.

RESULTS

The socio-demographic characteristics of preeclampsia patients and controls, it was revealed that the highest percentage of preeclampsia cases (45.33%) occurred in the 26–35 years age group. A majority of preeclampsia patients (66.66%) were housewives, surpassing the control group's proportion in this category. Geographically, most preeclampsia patients (60%) were from Hyderabad, although this was slightly lower than the control group. Among other districts, a higher percentage of preeclampsia patients came from Dadu (10.33%) and Kotri (8%) compared to controls. In terms of gestational age, a greater proportion of preeclampsia patients (88%) were in their third trimester, which was also higher than the controls (Table-1). On the other hand, the risk factors like gestational diabetes, high salt intake and multiparous women were found significantly positively associated with preeclampsia disease. Individuals who ate red meat more frequently had also a significant but moderate risk of preeclampsia (Table-2).

Several blood and lipid parameters were compared between preeclampsia and controls. Hemoglobin (HB) and blood cells (RBC, platelets, monocytes, eosinophils, and lymphocytes) were significantly lower (<0.001) in preeclampsia patients compared to controls.

Preeclampsia patients had significantly decreased blood indices such as HCT and MCV compared to controls, which revealed microcytic anemia. Among the lipid parameters, only total cholesterol, triglycerides, VLDL-C, and total lipids were found to be significantly increased in preeclampsia patients compared to controls.

However, HDL-C levels were significantly lowered in preeclampsia patients compared to controls, indicating a meaningful alteration in lipid metabolism associated with preeclampsia. The analysis of lipid parameters shows that preeclampsia is accompanied by clear disturbances in lipid metabolism. Triglycerides, total cholesterol, VLDL-C, and overall lipid concentrations were all higher in affected women compared with the controls. This pattern is consistent with dyslipidemia, a state frequently linked to endothelial damage and increased oxidative stress, both of which play central roles in the progression of preeclampsia. Another notable finding is the reduction in HDL-C.

Since HDL is generally considered protective against vascular injury, its decline suggests a shift toward a more atherogenic profile that could worsen vascular dysfunction. Although LDL-C levels were also elevated, the difference between groups was not statistically significant, which may reflect variability in patient responses or the relatively small sample size (Table32).

Table-3 showed the age-wise comparison of hematological and lipid profile parameters in preeclampsia patients. It was revealed that no statistically significant variations were found in any blood parameter, which showed that age did not affect the blood parameters in preeclampsia patients.

Table 1. Socio-demographic characteristics of the preeclampsia patients and controls

S. No.	Characteristics	Preeclampsia Patients N=75 (%)	Controls N=75 (%)
1.	15-25 years	18.66	25.34
	26-35 years	45.33	44.03
	36-45 years	36.01	30.63
2.	Housewife	66.66	65.03
	Govt. Employees	12.02	26.64
	Private Employees	21.32	08.33
3	Hyderabad	60.00	68.00
	Dadu	10.00	8.00
	Mirpurkhas	6.00	10.00
	Tandojam/Tandoallahyar	10.00	4.00
	Sehwan/ kotri	14.00	10.00
4	2nd Trimester	12.02	18.00
	3rd Trimester	87.08	82.00

Table-2. Risk factors for preeclampsia disease

	Characteristics	Preeclampsia Patients n=75 (%)	Controls n=75 (%)	Odds Ratio (95% CI)	p-Value (<0.05)
1.	Gestational Diabetes	31.00	10.00	4.58 (2.04 -10.28)	<0.001
	Non-Gestational Diabetes	44.00	65.00	1.00 (Reference)	
2.	Proteinuria Present	100.00	21.00	0.00	-
	Proteinuria Absent	00.00	79.00		
3.	Multiparous woman	69.00	18.00	10.14(5.22- 19.68)	0.03
	Nulliparous woman	31.00	82.00	1.00 (Reference)	
4.	Fruits & vegetables 2-3 times/week	30.00	40.00	0.57(0.29-1.16)	0.1
	4-5times/week	70.00	60.00	1.00 (Reference)	
5.	Red meat (1times/week)	40.00	34.00	3.01(1.54-5.84)	<0.001
	White meat(1times/week)	60.00	66.00	1.00 (Reference)	
6.	High salt intake	80.00	14.00	24.0(10.85-62.21)	
	Low/Moderate salt intake	20.00	86.00	1.00 (Reference)	<0.001
7.	Fried /junk food 2-3 times /week	74.00	60.00	1.00 (Reference)	<0.001
	4-5 times/week	26.00	40.00	1.83(0.92-3.65)	
8.	Physical activity once/week	40.00	60.00	0.33(0.17-0.65)	<0.001
	2-3 times/week	60.00	40.00	1.00 (Reference)	

Table 3. Comparison of haematological and Lipid profile between preeclampsia patients and controls

Blood Cells	Preeclampsia patients	Control	p-value	Reference Ranges
Hemoglobin	8.08±1.36	12.74±1.52	<0.001	11.0-16.0g/dl
RBC	3.08±1.00	4.02±0.82	<0.001	3.8-5.8 $\times 10^{12}$/L
WBC	13.80±1.66	9.04±1.19	0.711	4.0-11.0 $\times 10^{9}$/L
Platelets	151±58.81	301±56.20	<0.001	150-400$\times 10^{9}$/L
Monocytes	2.80± 1.02	3.07 ±1.33	<0.001	10-12 %
Neutrophils	64.14 ±3.01	59.02 ± 0.05	0.22	50-70 %
Lymphocytes	32.01 ± 3.05	30.01 ± 2.01	0.004	25-45 %
Eosinophils	2.04 ±0.52	1.08 ± 0.61	0.008	1-6 %
Basophils	0.46±0.05	0.45±0.05	0.681	0-1 %
HCT	27.51±4.20	33.1±7.01	<0.001	35-45 %
MCV	79.02±15.60	81.0±7.60	0.04	76-96 FL
MCH	27.71±4.01	27.6±3.30	0.22	27-32 PG
MCHC	42.32±2.20	33.1±1.07	0.21	30-35 (g/dL
TC	248.15 ± 25.01	175.91 ± 12.61	<0.001	>200 mg/dL
TG	260.11 ± 32.41	153.46 ± 22.01	<0.001	>200 mg/dL
HDL -C	33.12 ± 4.50	43.23± 07.01	0.03	<40 mg/dL
LDL -C	126.08 ± 11.41	93.61 ± 10.21	0.22	< 100mg/dL
VLDL -C	57.90 ± 13.52	32.32 ± 4.22	0.007	2-30 mg/dL
TL	881.50 ± 69.91	684.31 ± 62.01	<0.001	500-800 mg/dL

HB: Hemoglobin, RBC: Red blood cells, WBC: White blood cells, HCT: Hematocrit, MCV: Mean corpuscular volume MCH: Mean corpuscular volume MCHC: Mean corpuscular hemoglobin concentration, TC: Total cholesterol, TG: Triglycerides, HDL: High density lipoprotein, LDL: Low density lipoprotein, VLDL: Very Lowdensity Lipoprotein, TL: Total lipids.

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Table 4. Comparison of haematology and Lipid profile among different age groups of preeclampsia patients

	15-25y Mean ± SD, N=19	26-35y, Mean± SD, N=45	36-45y, Mean± SD, N=36	p-value (<0.05) by ANOVA	Reference ranges
Hemoglobin	0.83±1.35	8.16 ± 1.29	8.09 ± 1.46	0.89	11.0-16.0g/dl
RBC	3.58±0.61	3.83±0.85	4.18 ± 1.88	0.88	$3.8\text{-}5.8\times10^{12}$/L
WBC	14.35±2.01	13.44±1.45	13.63±1.54	0.99	$4.0\text{-}11.0\times10^{9}$/L
Platelets	140.78±21.61	193.35±78.21	147.85±29.30	0.79	$150\text{-}400\times10^{9}$/L
Monocytes	2.57 ± 0.82	2.71 ± 0.88	2.42 ± 0.72	0.86	10-12 %
Neutrophils	65.14 ± 3.41	62.71 ± 2.60	64.14 ± 3.09	0.99	50-70 %
Lymphocytes	29.57 ± 4.64	32.42 ± 1.49	29.85 ± 4.82	0.99	25-45 %
Eosinophils	1.85 ± 0.63	2.07 ± 0.23	2.14 ± 0.63	0.97	1-6 %
Basophils	0.71 ± 0.45	0.93± 0.45	0.73 ± 0.43	0.37	0-1 %
HCT	28.77 ± 2.38	28.55 ± 4.33	27.19 ± 4.71	0.99	35-45 %
MCV	82.85 ± 8.91	72.38 ± 24.50	78.65 ± 20.01	0.99	76-96 FL
MCH	27.81 ± 3.97	28.08 ± 4.74	28.37 ± 3.61	0.99	27-32 PG
MCHC	32.31± 1.65	32.56 ± 1.63	33.21 ± 1.37	0.11	30-35 (g/dL
TC	253.07 ± 23.65	244.53 ± 24.32	240.92 ± 22.60	0.30	>200 mg/dL
TG	303.46 ± 49.50	294.71± 44.06	311.15 ± 52.185	0.63	>200 mg/dL
HDL-C	33.38 ± 2.73	36.07 ± 2.12	33.6± 3.45	0.17	<40 mg/dL
LDL-C	126.38 ± 9.20	129.78 ± 10.11	127.10 ± 11.15	0.64	< 100mg/dL
VLDL-C	60.69 ± 9.91	56.67 ± 17.53	59.07 ± 14.60	0.71	2-30 mg/dL
TL	881.53 ± 34.82	911.15 ± 53.61	907.30 ± 99.45	0.77	500-800 mg/dL

HB: Hemoglobin, RBC: Red blood cells, WBC: White blood cells, HCT: Hematocrit, MCV: Mean corpuscular volume MCH: Mean corpuscular volume MCHC: Mean corpuscular hemoglobin concentration, TC: Total cholesterol, TG: Triglycerides, HDL: High density lipoprotein, LDL: Low density lipoprotein, VLDL: Very Lowdensity Lipoprotein, TL: Total lipids.

DISCUSSION

A family history of hypertension, heart disease, renal illness, and diabetes are among the sociodemographic and environmental variables linked to preeclampsia that frequently encourage the onset of the condition[16]. In our study it was found that preeclampsia was the most common among women aged 26 to 35 years, making up 45% of cases as compared to controls in Table-1. As well as a significant number of preeclamptic women (67%) were housewives and (88%) were in their third trimester of pregnancy, which was higher than the control group. Among the main risk factors for preeclampsia, gestational diabetes, multiparity, high salt intake, and red meat consumption stand out as key contributors (Table-2). Gestational diabetes increases the risk by exacerbating overlapping metabolic and inflammatory processes that strain blood vessels[17,18]. Multiparity—especially with quick pregnancies one after another or at very young or older ages—also increases the likelihood[19]. Too much salt raises blood pressure to dangerous levels and damages vessel linings, right at the heart of how preeclampsia unfolds[20]. Moreover, diets high in red or processed meats trigger oxidative damage and inflammation, worsening the situation[21]. It has long been known that preeclampsia can cause hematological problems, including the abnormalities in platelet function[22,23]. However, when comparing blood test results, women with preeclampsia had noticeably lower hemoglobin and red blood cell counts than those without the condition in Table-3. Preeclamptic pregnancies have a substantially lower platelet count than normotensive pregnancies, as we and others have demonstrated[24-26].

Additionally, the neutrophil and lymphocyte counts were found significantly elevated in preeclampsia patients compared to normal pregnant women, as can be seen in Table II. On the other hand, some studies reveal that leukocyte levels are higher in pregnant women with preeclampsia than in those with a normal pregnancy, mostly due to a higher proportion of neutrophils rather than fewer leukocytes in preeclampsia[27]. But in this condition we did not find any significant variation for white blood cells in the present study. Neutrophil-to-lymphocyte ratio (NLR) values are considerably greater in preeclamptic patients than in normotensive pregnant women, with even higher values seen in severe instances, according to a meta-analysis comprising 3,982 individuals[28]. Comparable results were found in the present study (Table-4). These differences were highly significant, suggesting a strong link between hyperlipidemia and pregnancy. The fetus is also at risk for the complications of dyslipidemia. Preterm birth, fetal discomfort, and fetal development limitation can result from elevated maternal lipid levels[29-32]. In our study, women with preeclampsia had higher levels of

lipids, as shown in tables II & III. In addition, individuals with preeclampsia metabolic risk factors were found in the early stages of pregnancy[33]. Due to increased energy needs during a typical pregnancy, the mother's lipid metabolism experiences a significant physiological adaptation, resulting in blood triglyceride (TG) levels rising by 50–100% from pre-pregnancy values[34]. In contrast to BMI, elevated serum TG levels during the first trimester independently raise the risk of preeclampsia[35]. It may lead to obesity and diabetes mellitus. Present findings about gestational diabetes as a significant risk factor for preeclampsia, which was the possible support from the abovementioned investigators' findings.

The findings may not be representative of all pregnant women in Pakistan because this study was conducted at a single hospital with a small sample size, which limits the present study. Diet and physical activity were two examples of information that was reliant on participants' recollections and might not be entirely true. Furthermore, we were unable to evaluate the long-term effects on mothers and babies because the study only examined women during pregnancy and did not follow them after delivery. The strengths of the study are its clear inclusion and exclusion criteria, which helped to reduce bias. The findings give valuable insight into how gestational diabetes and changes in blood fats may be linked to

preeclampsia in our local population. Hence, it is recommended that regular prenatal care should include early blood sugar and lipid screening, particularly for women with known risk factors like obesity or a family history of high blood pressure during pregnancy.

CONCLUSION

This study points out a clear link between gestational diabetes, having multiple pregnancies, microcytic anemia, and high lipid levels with the chance of getting preeclampsia. Preeclampsia is a serious condition that affects many pregnant women, especially in the later stages of pregnancy. In this study, we discovered that blood fat levels were frequently elevated in preeclamptic women, such as cholesterol and triglycerides, showing a strong link between preeclampsia and hyperlipidemia. Many of these women also had a history of multiple pregnancies (multiparity) and gestational diabetes, both of which appear to increase the risk of developing preeclampsia. These health issues can make pregnancy more complicated and dangerous for both the mother and fetus. By understanding these risk factors better, we can take earlier steps to monitor and manage them to improve outcomes for pregnant women who are at risk of preeclampsia.

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Author Contributions

Quratulain Soomro conceptualized and designed the study. **Naseem Aslam Channa** and **Hunza** collected and analyzed the data. **Zeeshan Ali Rajput** contributed to data interpretation and literature review. **Zoya Channar** assisted in manuscript drafting. **Marvi Sheikh** critically reviewed and approved the final version of the manuscript. All authors read and approved the final manuscript.

Ethical Approval

The current research study received ethical approval from the Ethical Review Board of the Institute of Biochemistry, University of Sindh, Jamshoro, Pakistan (Ref. No. IOB/217/2024, dated May 23, 2024).

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None.

Conflict of Interests

None.

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