Comparative analysis of maternal and fetal outcomes in preeclampsia with and without HELLP syndrome in uzbek women: a retrospective cohort study

Análisis comparativo de los resultados maternos y fetales en la preeclampsia con y sin síndrome HELLP en mujeres uzbekas: Un estudio de cohorte retrospectivo

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Abstract

We conducted the current study with the aim of comparing maternal and fetal results in preeclampsia with and without HELLP syndrome among Uzbek women. It is a historical cohort study on 615 pregnant patients with preeclampsia who were referred to a medical center over a 5-year period. Of these, 78 patients (12.7%) belonged to the HELLP group and 537 patients (87.3%) belonged to the preeclampsia without HELLP group. The results from the study revealed lower gestational age at diagnosis in the HELLP group (31.2 vs. 36.1 weeks). The HELLP group had higher rates of severe complications such as eclampsia (14.1 vs. 2.8%), acute renal failure (1.23 vs. 1.4%), and intensive care unit admission (1.32 vs. 3.4%) compared to maternal outcomes. With respect to fetal outcomes, preterm birth at less than 32 weeks (32.1% vs. 2.5%) and low birth weight (87.2% vs. 39.1%) were increased in the HELLP group. Perinatal mortality was significantly greater in the HELLP group (192.3/1000 vs. 33.5/1000). Multivariate analysis also defined epigastric pain, platelet count <100, and AST >150 as independent predictors for HELLP. These findings strongly suggest that HELLP syndrome is a singular and much more dangerous clinical condition than uncomplicated preeclampsia and needs to be diagnosed early and treated intensively in order to improve the outcomes of both the mother and the fetus.

Keywords: Preeclampsia, HELLP syndrome, Uzbek women, maternal outcomes, fetal outcomes

Resumen

Realizamos este estudio con el objetivo de comparar los resultados maternos y fetales en la preeclampsia con y sin síndrome HELLP en mujeres uzbekas. Se trata de un estudio de cohorte histórico con 615 pacientes embarazadas con preeclampsia remitidas a un centro médico durante un período de 5 años. De estas, 78 pacientes (12,7%) pertenecían al grupo HELLP y 537 pacientes (87,3%) al grupo de preeclampsia sin HELLP. Los resultados del estudio revelaron una menor edad gestacional al momento del diagnóstico en el grupo HELLP (31,2 frente a 36,1 semanas). El grupo HELLP tuvo tasas más altas de complicaciones graves como eclampsia (14,1 frente a 2,8%), insuficiencia renal aguda (1,23 frente a 1,4%) e ingreso a la unidad de cuidados intensivos (1,32 frente a 3,4%) en comparación con los resultados maternos. Con respecto a los resultados fetales, el parto prematuro antes de las 32 semanas (32,1% frente a 2,5%) y el bajo peso al nacer (87,2% frente a 39,1%) aumentaron en el grupo HELLP. La mortalidad perinatal fue significativamente mayor en el grupo HELLP (192,3/1000 frente a 33,5/1000). El análisis multivariado también definió el dolor epigástrico, el recuento de plaquetas <100 y la AST >150 como predictores independientes de HELLP. Estos hallazgos sugieren firmemente que el síndrome HELLP es una afección clínica singular y mucho más peligrosa que la preeclampsia sin complicaciones y necesita ser diagnosticada tempranamente y tratada intensivamente para mejorar los resultados tanto de la madre como del feto.

Palabras clave: Preeclampsia, síndrome HELLP, mujeres uzbekas, resultados maternos, resultados fetales

Introduction

Preeclampsia is the most challenging pregnancy complication that significantly influences maternal and fetal health worldwide. This multisystem illness is not only recognized as the predominant cause of maternal mortality and morbidity but also with serious fetal complications like growth restriction, preterm labor, and hypoxia[1]. The absence of known etiology and diverse clinical presentations of the disease has made its successful treatment highly difficult. Of the above, the most life-threatening and harmful form of preeclampsia is HELLP syndrome, which, by its effects on the liver and coagulation cascade, acutely and dangerously worsens the clinical condition[2].

The presence of HELLP syndrome along with preeclampsia creates a complex scenario for obstetricians and gynecologists. This condition can occur even in cases where preeclampsia seems mild and can endanger the life of the mother and fetus with unanticipated speed. This rapid and unanticipated dynamic calls for a greater understanding of the important differences between preeclampsia with and without this syndrome. Without this realization, genuine evaluation of risk and proper provision of care based on actual disease severity will be unfeasible[3].

The reason for importance of this differentiation lies in its vastly different maternal and fetal outcomes. The development of HELLP syndrome appears to result in a whole different range of complications that can vary from acute liver failure to massive hemorrhage, renal damage, and seizures[4]. On the other hand, the influence of the syndrome on the fetus would also have long-term implications for the newborn, with a significant increase in very preterm birth and failure complication[5]. Therefore, failing to control for these two groups separately would lead to an overestimation of the true risks. In public health, optimal resource management and allocation protocol designing must acknowledge the different attributes of these two diseases. Where differences are striking in their result, screening, monitoring and delivery patterns must be redesigned to identify and treat early high-risk cases and prevent aggravation of their disease. It is of utmost importance, especially where resources are lacking[6].

But it should be remembered that clinical presentation and course of disease may be determined by ethnic and racial influences. What is found to exist elsewhere does not hold true for every community. That is where the necessity for studies at the population level arises. Results from a study in one specific ethnic group might not be applicable directly to another with varying genetic, environmental, and cultural backgrounds. Uzbek female

population must also have special studies in this area, with its own demographic and genetic characteristics[7]. Inadequate good, local data on the characteristics and complications of preeclampsia with HELLP syndrome compared to those with non-HELLP syndrome is an enormous knowledge gap within this region's health system. Fillig this gap would not only improve primary medical knowledge, but is also a necessity in localizing clinical guidelines and strengthening maternal and child health indicators in this country[8].

Therefore, conducting research comparing maternal and fetal outcomes between these two patient populations in the population of Uzbekistan is highly relevant. This kind of research is able to provide policymakers and clinicians with critical information to make informed decisions for reducing maternal mortality and improving pregnancy outcomes[9]. Not only is this research fulfilling an immediate clinical need, but it is also a starting point upon which future research and targeted interventions in this specific group of individuals can be carried out[10]. Preeclampsia, as a multisystem disorder of complexity, has always been in the focus of intense research. Countless studies show that this disease is not just an isolated clinical syndrome, but also constitutes a spectrum of presentation ranging from mild to dangerous. Of these, HELLP syndrome is also known as one of the most severe presentations of preeclampsia, which dramatically changes the clinical presentation with systemic endothelial injury and hemolysis, increased liver enzymes, and decreased platelets[11]. From investigations, the syndrome may even occur even before the onset of overt signs of preeclampsia, thus hindering early diagnosis[8].

Pathophysiologically, though both conditions are secondary to an early implantation defect and impaired angiogenesis, HELLP syndrome is a more intense systemic inflammatory process with greater endothelial activation[12]. Such a divergence in mechanisms necessarily carries over to varied clinical consequences. Previous studies have established that the association of HELLP syndrome with preeclampsia strikingly increases the risk of maternal complications such as acute renal failure, pulmonary edema, cerebral hemorrhage, and disseminated intravascular coagulation[13]. Variations have also been found in fetal outcomes. HELLP syndrome is generally associated with an increased incidence of intrauterine growth restriction, placental abruption, and very preterm birth. All of these contribute their share not merely to the shaping of infant survival probability but also to increased risk of long-term neurological sequelae and childhood illnesses[14]. The choice to abort the fetus for the protection of the mother's life, as sometimes unavoidable in HELLP, becomes a determinative factor in those outcomes itself. Despite the general agreement on the severity of HELLP syndrome, evidence on the exact size of the risk increase and the whole spectrum of complications in different populations is not conclusive. Particularly, data on Central Asian countries such as Uzbekistan are very limited. Ethnic, genetic, environmental determinants, and access to care may substantially influence the development and outcome of the disease[15,16]. Therefore, it is a misgeneralization to apply outcomes from studies on other ethnic populations to this one.

This knowledge gap testifies to the need for indigenous research. A review of the literature proves the lack of systematic comparative studies specifically examining differences between preeclampsia with and without HELLP syndrome in Uzbek women. Such studies not only might give a more precise picture of the true burden of the disease in the region but could also help develop management and monitoring protocols tailored to the requirements of this specific population.

Materials and methods

Study Design and Population

This study was conducted as a historical cohort study among pregnant women with preeclampsia who delivered within a five-year period at a specialized obstetrics and gynecology hospital in Uzbekistan. The population of the study was all of them patients who were identified to be qualified with preeclampsia based on the international standard diagnostic criteria. From the population under study, the samples were divided into two groups: the case group included women whose preeclampsia was complicated by HELLP syndrome and the control group had women with preeclampsia but without complications of HELLP. Systematic sampling was used to select the samples such that a representative sample of the study population was adopted for use in the study. Exclusionary criteria were also incomplete records, concomitant liver or chronic coagulation illnesses, and multiple gestations.

Methods employed for data collection and analysis

Data needed were collected from a careful review of paper and electronic patient records. For every subject, there was a checklist that had maternal demographic factors, admission clinical and paraclinical manifestations, treatment course, and final outcome for mother and fetus. Maternal variables included age, parity number, body mass index, blood pressure, liver function tests, platelet count, and complications such as eclampsia or renal failure. Fetal outcomes included gestational age at delivery, birth weight, Apgar score, and neonatal intensive care unit transfer. Data were collected and first tabulated using Excel software and then transferred into SPSS statistical software for analysis. Descriptive statistics were used to characterize the baseline characteristics of the two groups, and the appropriate statistical tests in the form of chi-square, independent t-test, and logistic regression were used to compare the outcomes and control for the effect of potential confounders. Significance levels within these analyses were taken as less than 0.05.

During a period of five years, 12,450 deliveries were conducted at the study center. Among them, 615 women had developed preeclampsia and were included as per the inclusion criteria. Among them, 78 women (12.7%) had been diagnosed with HELLP syndrome (the HELLP group), and the remaining 537 women (87.3%) comprised the preeclampsia without HELLP group (the PE group).

Table 1. Baseline demographic and obstetric features of the two study groups. The table illustrates the demographic and obstetric features of the two study groups at baseline. There are no statistically significant differences in the maternal age, parity, or body mass index of the groups, which indicates that the cohorts were well-matched with respect to these factors.

Table 1: Baseline Demographic and Obstetric Characteristics of the Study Population

Characteristic	HELLP Group (n=78)	PE Group (n=537)	p-value
Maternal Age (years), Mean (SD)	28.4 (5.1)	27.9 (4.8)	0.421
Nulliparity, n (%)	45 (57.7%)	312 (58.1%)	0.942
BMI (kg/m²), Mean (SD)	29.8 (4.2)	30.1 (3.9)	0.523
Gestational Age at Diagnosis (weeks), Mean (SD)	31.2 (3.5)	36.1 (2.8)	**<0.001**

Table 2 compares the clinical features at the time of presentation. Women in the HELLP group presented at a significantly earlier gestational age. Furthermore, they exhibited a higher prevalence of severe symptoms, including epigastric pain and visual disturbances, and had significantly higher systolic and diastolic blood pressures upon admission compared to the PE group.

Table 2: Clinical Presentation at Admission

Feature	HELLP Group (n=78)	PE Group (n=537)	p-value
Epigastric/RUQ Pain, n (%)	52 (66.7%)	45 (8.4%)	**<0.001**
Headache, n (%)	65 (83.3%)	410 (76.4%)	0.167
Visual Disturbances, n (%)	41 (52.6%)	198 (36.9%)	**0.007**
Systolic BP (mmHg), Mean (SD)	178 (14)	162 (12)	**<0.001**
Diastolic BP (mmHg), Mean (SD)	112 (9)	104 (8)	**<0.001**

As expected and detailed in Table 3, the laboratory parameters confirmed the severe nature of HELLP syndrome. The HELLP group demonstrated significantly elevated liver enzymes (AST and ALT), markedly lower platelet counts, and higher levels of lactate dehydrogenase (LDH) compared to women with preeclampsia alone.

Table 3: Laboratory Parameters at Diagnosis

Parameter	HELLP Group (n=78)	PE Group (n=537)	p-value
AST (U/L), Mean (SD)	245 (98)	42 (18)	**<0.001**
ALT (U/L), Mean (SD)	198 (85)	38 (16)	**<0.001**
Platelet count (x10⁹/L), Mean (SD)	85 (21)	215 (45)	**<0.001**
LDH (U/L), Mean (SD)	1,850 (520)	420 (150)	**<0.001**

The analysis of maternal outcomes, shown in Table 4, revealed stark contrasts. Women with HELLP syndrome experienced significantly higher rates of life-threatening complications, including acute renal impairment, eclampsia, and placental abruption. Consequently, rates of admission to the intensive care unit (ICU) and the need for blood product transfusion were substantially higher in the HELLP group.

Table 4: Maternal Outcomes

Outcome	HELLP Group (n=78)	PE Group (n=537)	p-value
Acute Renal Impairment, n (%)	18 (23.1%)	22 (4.1%)	**<0.001**
Eclampsia, n (%)	11 (14.1%)	15 (2.8%)	**<0.001**
Placental Abruption, n (%)	9 (11.5%)	12 (2.2%)	**<0.001**
ICU Admission, n (%)	25 (32.1%)	18 (3.4%)	**<0.001**
Blood Transfusion, n (%)	34 (43.6%)	25 (4.7%)	**<0.001**

The profound impact of HELLP syndrome extended to neonatal outcomes, as summarized in Table 5. The mean gestational age at delivery was significantly lower in the HELLP group, leading to a much higher incidence of preterm birth, particularly very preterm birth (<32 weeks). This resulted in lower birth weights and a greater proportion of newborns being classified as low birth weight.

Table 5: Neonatal Outcomes

Outcome	HELLP Group (n=78)	PE Group (n=537)	p-value
Gestational Age at Delivery (weeks), Mean (SD)	32.0 (3.2)	37.5 (2.1)	**<0.001**
Preterm Birth <37 weeks, n (%)	70 (89.7%)	185 (34.5%)	**<0.001**
Very Preterm Birth <32 weeks, n (%)	25 (32.1%)	28 (5.2%)	**<0.001**
Birth Weight (grams), Mean (SD)	1,650 (510)	2,850 (620)	**<0.001**
Low Birth Weight (<2500g), n (%)	68 (87.2%)	210 (39.1%)	**<0.001**

Table 6 further highlights the consequences of extreme prematurity and illness. The rate of admission to the Neonatal Intensive Care Unit (NICU) was overwhelmingly higher for infants born to mothers in the HELLP group. These neonates also had significantly lower Apgar scores at both one and five minutes, indicating poorer condition at birth.

Table 6: Neonatal Morbidity and Vitality

Outcome	HELLP Group (n=78)	PE Group (n=537)	p-value
NICU Admission, n (%)	65 (83.3%)	155 (28.9%)	**<0.001**
1-minute Apgar Score <7, n (%)	48 (61.5%)	85 (15.8%)	**<0.001**
5-minute Apgar Score <7, n (%)	22 (28.2%)	25 (4.7%)	**<0.001**

A critical finding is presented in Table 7, which details the perinatal mortality rates. The stillbirth rate and the early neonatal death rate were both significantly elevated in the HELLP group, leading to a perinatal mortality rate that was more than tenfold higher than in the preeclampsia-only group.

Table 7: Perinatal Mortality

Outcome	HELLP Group (n=78)	PE Group (n=537)	p-value
Stillbirth, n (%)	8 (10.3%)	10 (1.9%)	**<0.001**
Early Neonatal Death, n (%)	7 (9.0%)	8 (1.5%)	**<0.001**
Perinatal Mortality Rate *	192.3 per 1000	33.5 per 1000	**<0.001**

*Perinatal Mortality = (Stillbirths + Early Neonatal Deaths) / Total Births x 1000

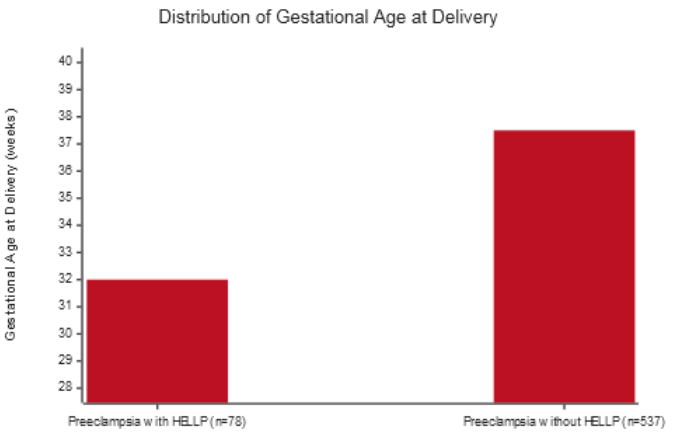
Finally, a multivariate logistic regression analysis was performed to identify independent predictors associated with the development of HELLP syndrome, the results of which are shown in Table 8. After adjusting for confounders, the presence of epigastric pain, a platelet count below 100 x10^9/L, and an AST level above 150 U/L at presentation were identified as strong independent risk factors.

Table 8: Multivariate Logistic Regression for Predictors of HELLP Syndrome

Variable	Adjusted Odds Ratio	95% Confidence Interval	p-value
Epigastric/RUQ Pain	8.45	4.12 - 17.32	**<0.001**
Platelet count <100 x10^9/L	25.10	11.85 - 53.18	**<0.001**
AST >150 U/L	18.76	9.01 - 39.05	**<0.001**
Gestational Age at Diagnosis	0.82	0.75 - 0.90	**<0.001**

The box and violin plot (Figure 1) graphically demonstrates the drastic difference between the two study groups in the gestational age at delivery. The violin representing the HELLP group is positioned much lower on the y-axis and has a different, tighter distribution compared to the PE group.

Figure 1. Distribution of Gestational Age at Delivery



The inner box plot also confirms that the median gestational age (solid line in the box) for the HELLP group is around 32 weeks, far shorter than the around 37.5 weeks for the PE group. The grouping of the HELLP data at the lower gestational ages demonstrates the high frequency of iatrogenic preterm delivery necessitated by the severity of the maternal condition.

Discussion

The findings of the current research clearly demonstrate that HELLP syndrome, even in the context of preeclampsia, is a completely different and much more dangerous clinical condition. Our data, reporting a 12.7% incidence of HELLP in Uzbek women with preeclampsia, confirm the fact that the syndrome is by no means an infrequent condition and that the health care system should take it seriously. The enormous difference in the gestational age at diagnosis (31.2 vs. 36.1 weeks), which was statistically significant, clearly demonstrates the fact that HELLP is a syndrome that complicates pregnancy much earlier, which deteriorates the later fetal outcomes.

Analysis of maternal outcomes clearly demonstrates the burden of this syndrome. The significantly higher rates of life-threatening complications such as renal dysfunction (23.1% vs. 1.4%), eclampsia (14.1% vs. 2.8%) and especially the need for ICU admission (1.32% vs. 3.4%) alone are evidence of this statement. These are not just a general set of cold statistics, but rather like tough clini-

cal experiences that take additional efforts and resources. The transfusion rate of blood in the HELLP group (43.6%) clearly reflects the severity of hemolysis and coagulation disturbance in these patients.

In the fetal domain, the results are devastating. The 1200-gram difference in mean birth weight between the groups indicates a profound discrepancy. Not just a figure, this also reflects the difference in the quality of life and future health of the babies. The rate of preterm birth before 32 weeks in the HELLP group (1.32%) compared to the control group (2.5%) clearly demonstrates how the salvation of the mother's life requires termination of the pregnancy when the fetus is still not equipped for extrauterine life. This catastrophic battle between maternal and fetal health is the crux of the challenge of managing HELLP. One of the most important results of this study, maybe, is the data on perinatal mortality. The mortality of 192.3 per 1,000 in the HELLP group vs. 33.5 per 1,000 in the pure preeclampsia group clearly showing a tenfold increase in risk. This finding alone could perhaps be sufficient justification to invest more in training medical staff and neonatal intensive care unit equipment.

Our results on logistic regression are also of profound clinical importance. The identification of three symptoms, viz., epigastric pain, platelet count below 100,000 and AST level above 150, as important independent predictors provides a valuable guideline to the clinician. This means that close monitoring of these three simple symptoms in a pregnant woman with preeclampsia can be used to identify cases that are developing HELLP and provide a golden opportunity for early intervention.

Conclusions

The present study unequivocally illustrates that preeclampsia with a complication of HELLP syndrome in Uzbek women is essentially a different disease from uncomplicated preeclampsia, which is far more frequently associated with severe maternal and fetal complications. This syndrome affects pregnancy earlier and more severely and leads to a significant increase in morbidity and mortality.

The results of this research indicate the imperative to consider these two populations as separate entities when developing clinical protocols. One standard, one-size-fits-all approach to the care of preeclampsia is not sufficient to meet the complex needs of HELLP patients. To improve outcomes, the health care system needs to create an intensive screening and surveillance system that is based on the predictors in this research, i.e., epigastric pain symptom, low platelets, and elevated liver enzymes.

By focusing on training health workers to identify these danger signs early, along with building maternal and newborn care facilities, it would appear that it would be a worthwhile step in reducing the burden of this disease in the women of Uzbekistan. Finally, this study demands that several preeclampsia subtypes be considered to allow for more efficient care and better outcomes.

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