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Factors that Lead to HELLP Syndrome in Preeclampsia

Author: Carla Andrea Vargas Vargas

Affiliation/Institution: Universidad Nacional del Oriente
Orcid ID: https://orcid.org/0009-0003-1131-8057

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Abstract: This study reveals the most detailed information about the pathology of preeclampsia and HELLP syndrome. The possibility of generating more information and gathering everything related to the pathology lays the groundwork and theoretical foundations to later contribute a practical model to the scientific community.

This literature review focuses on the most prominent aspects of preeclampsia and the factors that contribute to the development of HELLP syndrome in pregnant women. The inclusion criteria considered for this study were that the bibliographic documents examined in databases such as Google Scholar, Scielo, PubMed, and Redalyc were no more than 10 years old from their publication date, written in either English or Spanish, and contained keywords and abstracts with relevant and topic-appropriate information.

The theoretical method used was the analysis-synthesis method, which emphasizes its application as a deconstructive approach to the object of study and a reorganizer of the same phenomenon.

The inductive-deductive method was employed for the collection of both abstract and concrete information.

The results obtained in this study are purely descriptive and reveal extensive information validated by significant bibliographic sources. Preeclampsia and HELLP syndrome represent significant clinical challenges in obstetric care due to their high maternal and perinatal morbidity and mortality. These conditions highlight the need for thorough monitoring during pregnancy, especially in women with identifiable risk factors.

Both entities share a pathophysiology centered on placental dysfunction and systemic endothelial damage. These mechanisms trigger a spectrum of clinical manifestations ranging from hypertension and proteinuria to severe complications such as hemolysis.

Keywords: *HELLP, Preeclampsia, Pregnant Woman, Pregnancy.*

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I. INTRODUCTION

Preeclampsia is a pregnancy-specific hypertensive disorder that represents one of the leading causes of maternal and perinatal morbidity and mortality worldwide. This multisystemic syndrome, which partially manifests after 20 weeks of gestation, is characterized by arterial hypertension and organ dysfunction, affecting organs such as the liver, kidneys, and the hematological system.

Its pathophysiology is closely related to abnormal placentation, endothelial dysfunction, and an exacerbated inflammatory response, highlighting its systemic and complex impact. Among the most severe complications of preeclampsia is HELLP syndrome (Hemolysis, Elevated Liver Enzymes, and Low Platelet Count), a condition that occurs in approximately 10-20% of severe preeclampsia cases.

HELLP syndrome, considered a severe variant of preeclampsia, is associated with a significantly increased risk of liver failure, disseminated intravascular coagulation, placental abruption, and other maternal and fetal complications. The relationship between both conditions lies in their common pathophysiological origin, characterized by placental dysfunction and oxidative stress, with HELLP syndrome representing a more advanced spectrum of systemic damage. Given its impact on maternal and fetal health and the need for rapid and effective interventions, it is crucial to understand the underlying mechanisms, diagnostic

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strategies, and available therapeutic options to reduce its incidence and severity.

This article explores the clinical and pathophysiological characteristics of preeclampsia and its relationship with HELLP syndrome, highlighting the importance of early diagnosis and timely management.

The formulation of a problem, such as understanding *What is the relationship between preeclampsia and HELLP syndrome?* leads us to conduct a descriptive and observational literature review.

II. METHODOLOGY

This literature review focuses on the most prominent aspects of preeclampsia and the factors that lead to the development of HELLP syndrome in pregnant women. The inclusion criteria considered for this study were that the bibliographic documents examined in databases such as Google Scholar, Scielo, PubMed, and Redalyc were no more than 10 years old from their publication date, written in either English or Spanish, and contained keywords and abstracts with relevant information aligned with the proposed topic.

The theoretical method used was the analysis-synthesis method, which emphasizes its application as a deconstructive approach to the object of study and a reorganizer of the same phenomenon.

The inductive-deductive method was employed for the collection of both abstract and concrete information.

III. RESULTS AND DISCUSSION

Preeclampsia is a relatively common hypertensive disorder during pregnancy, with a progressive presentation, an unknown cause, and frequently associated with severe maternal and perinatal complications. It is characterized by vasospasm and endothelial activation and is defined by the presence of hypertension and proteinuria after the 20th week of gestation. (1)

It is a hypertensive disorder of pregnancy that occurs after 20 weeks of gestation and is characterized by arterial hypertension (≥140/90 mmHg) and proteinuria (≥300 mg in 24-hour urine). It can occur in the absence of proteinuria if accompanied by organ dysfunction (elevated transaminases, thrombocytopenia, renal insufficiency, etc.).

For the benefit of the mother, expedited delivery is currently the only therapy for pregnancies with severe preeclampsia and HELLP syndrome. (2)

HELLP syndrome is a severe complication of preeclampsia that includes hemolysis (H), elevated liver enzymes (EL), and thrombocytopenia (LP).

Diagnostic Criteria: Hemolysis: Presence of schistocytes in the blood smear, increased indirect bilirubin, and decreased haptoglobin, **e**levated liver enzymes: Elevated transaminases (AST and ALT >70 U/L), **t**hrombocytopenia: Platelets <100,000/mm³.

Preeclampsia is secondary hypertension specific to pregnancy and is characterized by proteinuria, with or without associated edema. In its severe form, it includes oliguria, pulmonary edema, liver dysfunction, coagulation disorders, elevated serum creatinine, visual disturbances, and epigastric pain.

Patients with preeclampsia may progress to eclampsia, which is characterized by convulsive episodes without prior neurological disease and occurs in 0.3% of deliveries. Some pregnant women also develop HELLP syndrome, which is characterized by biochemical alterations indicating hemolysis, elevated liver enzymes, and thrombocytopenia. (3)

- *Risk Factors:*

Primigravidity, history of preeclampsia, multiple pregnancies, obesity, a dvanced maternal age, pre-existing conditions (chronic hypertension, diabetes, autoimmune diseases).

The syndrome of preeclampsia and eclampsia has been known for over 2,000 years, as it was identified in antiquity by the Egyptians and the Chinese. The clinical presentation was graphically described by Hippocrates during the second half of the 19th century. Until the first two or three decades of the 20th century, toxemia, as it was also called, was often mistaken for glomerulonephritis. During this same period, various surveillance studies were conducted, and most authors reported chronic nephritis as a sequela of the disease. However, in 1927, Corwin and Erick ruled out glomerulonephritis as a common condition during pregnancy, concluding that the lesion associated with eclampsia was primarily vascular and not renal. This finding was later highlighted by Rate and Tell, as well as by Eric and Tylman in 1939 and 1935, respectively. (4)

It is worth noting that preeclampsia is a gestational syndrome that causes many deaths worldwide. For a long time, it was poorly understood, and its causes were unknown. However, numerous studies have described preeclampsia in a more pathophysiological manner, identifying it as an endothelial dysfunction. This understanding has significantly benefited the processes of diagnosis, management, and monitoring.

For several years, the etiology of preeclampsia was unknown. However, it is now understood that the issue originates during placental development. In the first stage, placental trophoblastic cells fail to adequately invade the decidua and spiral arteries, preventing the necessary transformation to increase fetoplacental blood flow. During the second stage, poor placental perfusion occurs due to inadequately transformed arteries. (5)

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In a study conducted in February 2009, which aimed to compile maternal deaths caused by eclampsia and HELLP syndrome, a total of 304 deaths were identified: 100 due to eclampsia, 117 due to eclampsia/HELLP, and 87 associated with HELLP syndrome. Among the total deaths, 71.3% of the women experienced seizures, and 67.1% developed HELLP syndrome. In high-income countries, 3.9% of deaths were attributed to eclampsia without HELLP syndrome, while in low-income countries, this figure was 42.5% ($P < 0.0001$). The presence of HELLP syndrome in women who died from eclampsia was 90.6% (29/32) in high-income countries compared to 47.6% (88/185) in low-income countries ($P < 0.001$). (6)

Indicating that HELLP syndrome poses a significant risk to the pregnant mother.

The typical clinical symptoms of HELLP syndrome are pain in the upper right quadrant of the abdomen or epigastric region, nausea, and vomiting. The upper abdominal pain may be intermittent, resembling colic. Up to 30-60% of patients experience headaches, and around 20% have visual symptoms. In the postpartum period, HELLP syndrome generally develops within the first 48 hours in women who have had proteinuria and hypertension prior to delivery. (7)

Gestational Hypertension the onset of hypertension after 20 weeks of gestation without any of the characteristics of preeclampsia, or within the first 24 hours postpartum. It typically normalizes within 10 days after delivery, although, by definition, blood pressure should return to normal within 12 weeks after the end of pregnancy.

Chronic Hypertension pre-existing hypertension identified before pregnancy or before 20 weeks of gestation, with blood pressure readings of systolic ≥140 mmHg or diastolic ≥90 mmHg, or both. It persists for more than 12 weeks postpartum and may involve the use of antihypertensive medication before pregnancy.

Chronic Hypertension with Superimposed Preeclampsia a patient with chronic hypertension who develops preeclampsia at some point during pregnancy.

Chronic Hypertension with Proteinuria During Pregnancy a chronically hypertensive patient who develops proteinuria during pregnancy.

Chronic Hypertension with Chronic Proteinuria a chronically hypertensive patient with chronic proteinuria who experiences an increase of more than 30 mmHg in systolic blood pressure and more than 15 mmHg in diastolic blood pressure during pregnancy, or an increase in proteinuria above 300 mg. Preeclampsia occurs after 20 weeks of gestation, during labor, or within the first 2 weeks postpartum, with blood pressure above 140/90 mmHg associated with proteinuria (more than 30 mg in a single sample or more than 300 mg in a 24-hour sample). (8)

The pathophysiology of preeclampsia is complex and not fully understood, but it includes the following main mechanisms:

- *Defect in Placentation:*
  Abnormal trophoblast invasion of the uterine endometrium results in poor placental perfusion. This leads to placental hypoxia, which triggers the release of anti-angiogenic factors.

- *Endothelial Dysfunction:*
  Anti-angiogenic factors, such as soluble fms-like tyrosine kinase-1 (sFlt-1) and soluble endoglin, disrupt the angiogenic balance, affecting the integrity of blood vessels.

- *Oxidative Stress:*
  Placental hypoxia generates free radicals that exacerbate cellular damage and promote systemic inflammation.

- *Systemic Inflammatory Response:*
  An increase in pro-inflammatory cytokines and activation of the maternal immune system causes multi-organ dysfunction.

- *Regarding a Clinical Case, the Following Describes the Case of a 39-Year-Old Woman:*
  A 39-year-old woman with three previous uncomplicated pregnancies presented at 33 weeks of gestation with acute cortical blindness. Based on clinical and laboratory evaluation, a diagnosis of preeclampsia with HELLP syndrome was made. A computed tomography (CT) scan of her head revealed ischemic lesions in her basal ganglia, extending superiorly to involve the posterior parietal and occipital regions.

Magnesium sulfate and hydralazine infusions were initiated, and an urgent cesarean section was performed under spinal anesthesia after the placement of an arterial line and intravenous hydration. The anesthesia and surgical course were uneventful, and she delivered a live baby girl weighing 1540 g.

By the next morning, she had regained some vision, and her visual recovery was complete 72 hours after delivery. A magnetic resonance imaging (MRI) scan with angiography was performed on the first postpartum day. Ischemic lesions were confirmed in the same locations identified on the CT scan, but all major cerebral vessels were patent, and no significant vascular abnormalities were observed.

Her postoperative course was uneventful, and she was discharged home seven days after delivery with a prescription for labetalol for persistent hypertension. (9)

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The complications that may arise are the following:

➢ *For the Mother:*

Eclampsia (seizures). Premature placental abruption. Liver or kidney failure. HELLP syndrome.

➢ *For the Fetus:*

Intrauterine growth restriction'. Preterm birth. Fetal death.

This variant of hypertensive disease is considered high risk for target organ damage, especially the liver, and represents a significant cause of maternal-fetal mortality. It is estimated that HELLP syndrome occurs in 10% to 20% of women with severe preeclampsia and is associated with widespread and significant endothelial damage. Additionally, eclampsia and HELLP syndrome are important predictors of other organ dysfunctions and mortality. (10)

The treatment that could be promoted among mothers at risk of developing these pathologies might include:

- Blood Pressure Control:
- First-line drugs: Labetalol, nifedipine, or hydralazine. Seizure prevention:
- Magnesium sulfate as an anticonvulsant agent.

Delivery management: Termination of pregnancy is the only definitive treatment. In cases of mild preeclampsia and preterm pregnancy, expectant management with monitoring.

➢ *Monitoring:*

Continuous maternal-fetal monitoring, including assessment of severity signs and fetal well-being.

IV. CONCLUSIONS

Preeclampsia and HELLP syndrome represent significant clinical challenges in obstetric care due to their high maternal and perinatal morbidity and mortality. These conditions highlight the need for thorough monitoring during pregnancy, especially in women with identifiable risk factors.

Both entities share a pathophysiology centered on placental dysfunction and systemic endothelial damage. These mechanisms trigger a spectrum of clinical manifestations ranging from hypertension and proteinuria to severe complications such as hemolysis.

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