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Review

Clinical and laboratory profile of HELLP Syndrome: Integrative Literature Review

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Abstract: The objective of this study is to gather information that corroborates the main clinical and laboratory findings involving Hellp Syndrome, its repercussions and consequences during pregnancy. An Integrative review was carried out in August 2024, using the digital library Scientific Electronic Library Online (SciELO), the Virtual Health Library (VHL) and PUBMED in the databases using the Boolean operators: AND and OR. The results were obtained through management with the Rayyan 16 QCRI application and were structured in PRISMA flowcharts. With the search in the databases, 219 articles were found, of which 122 were selected for reading and, according to the objective of the present work, 10 articles were included in the research. In the studies observed, it is concluded that among the main hypertensive syndromes in pregnancy, HELLP syndrome is a specific clinical and laboratory entity, requiring early diagnosis, precisely because of the repercussions at the maternal-fetal level, as it increases complications such as the syndrome from respiratory distress, infections and long-term developmental problems.

Keywords: Hypertensive syndromes of pregnancy; HELLP syndrome; Diagnosis and complications.

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1. Introduction

A significant number of women experience pregnancy-related health problems and conditions. Among these, the most prominent is pregnancy hypertension syndrome (PHS), characterized by clinical, biological, and laboratory manifestations of high blood pressure, which can appear as early as the 20th week of pregnancy and may progress to severe forms, such as HELLP syndrome. HELLP syndrome (Hemolysis, Elevated Liver Enzymes, and Low Platelets) is identified by the first letters of the English terms that refer to hemolysis (He), elevated liver enzymes (El), and thrombocytopenia (Lp). Several national and international studies suggest that this syndrome predominantly affects multiparous women who are older and in perimenopause, often presenting with gestational hypertension associated with preeclampsia and severe eclampsia. It is a rare but serious condition that leads to increased maternal and perinatal morbidity and mortality over a short period of time [1].

HELLP syndrome occurs in 5 to 9 out of every 1,000 pregnancies and in 10 to 20% of cases of severe preeclampsia. Some authors argue that this syndrome is unrelated to

preeclampsia, as it occurs without proteinuria or arterial hypertension in 15 to 20% of cases. In 70% of cases, HELLP syndrome manifests before childbirth; 80% of cases develop before the 37th week of pregnancy, and 10% before the 27th week. After delivery, most cases appear within the first 48 hours, although symptoms can manifest up to seven days postpartum [2].

The maternal mortality rate due to HELLP syndrome ranges from 24% in underdeveloped countries to 1.1% in developed countries. This deterioration typically occurs within 24 to 48 hours after delivery, with up to 31% of cases arising postpartum. It affects approximately 10 to 20% of patients with severe preeclampsia (0.5 to 0.9% of all pregnancies), leading to significant mortality and morbidity depending on the severity of the condition [1]. The most significant risk factor for developing HELLP syndrome is a history of hypertensive disorders in previous pregnancies, with the highest risk of recurrence occurring early in gestation. HELLP syndrome, considered an obstetric complication or a variant of severe preeclampsia, is marked by laboratory findings such as hemolysis (destruction of red blood cells), elevated liver enzymes (indicating liver damage), and thrombocytopenia (low platelet count).

Clinically, HELLP syndrome primarily involves arterial hypertension, with other symptoms such as epigastric pain and right upper quadrant pain, nausea and vomiting, blurred vision or temporary vision loss, excessive bleeding, and possible edema and weight gain due to hypertension and proteinuria. However, in most patients, clinical signs may vary or be non-specific, and diagnosis often relies on laboratory tests. Given the severity of this syndrome, the aim of this review is to inform healthcare professionals about its characteristic clinical and laboratory parameters and its complications during pregnancy, which require emergency management. Early diagnosis and prompt treatment are crucial to protect the health of both the mother and fetus.

2. Methods

This study is characterized as an integrative review, which allows the search, evaluation and synthesis of evidence on a given phenomenon [3]. To construct this study, the theme was first chosen, and the guiding question defined: "What is the clinical and laboratory profile of HELLP Syndrome?". The aim was to answer the main guiding question based on the PICO strategy (acronym for Patient, Intervention, Comparison and Outcome), that is, given this, PICO corresponds to, respectively, P = Patients with HELLP Syndrome; I = Clinical and laboratory profile; CO = Hypertensive syndromes in pregnancy. For selection, the Rayyan® platform (https://www.rayyan.ai/) was used.

The articles resulting from the search strategies were added, and two collaborators were invited to perform the blind selection based on the reading of the abstracts and titles. The inclusion criteria were relevance to the theme, adequate clinical intervention and results compatible with the objective of the study. The review of conflicts was released to all collaborators. After disagreements were resolved by consensus and following the inclusion criteria, the full texts of the included articles were read.

Then, the final inclusion of the articles was carried out. The inclusion criteria established: primary research article published in Portuguese, English or Spanish, with a time limit in the last 4 years (2020-2024). Letters to the editor, expert opinions, reviews, books, book chapters, experience reports, case studies, theoretical reflections, theses, dissertations, monographs and abstracts published in conference proceedings were excluded. The search was carried out in August 2024. At this stage, terms in Portuguese were chosen through the Health Sciences Descriptors (DeCs) and terms in English through the Medical Subject Heading (MeSH). The locations where the search would occur were established, as well as the inclusion and exclusion criteria for the studies.

The articles were selected via online access using the Scientific Electronic Library Online (SciELO), the Virtual Health Library (VHL) and the following health database: PUBMED, available on the Journals portal of the Coordination for the Improvement of Higher Education Personnel (CAPES) and obtained through the Federated Academic

Community (CAFe). The following Boolean operators were used to search the databases: AND and OR, to improve the search in the databases. For this purpose, we will use the following descriptors in Health Science (DeCS) and Medical Subject Headings (MESH): Hellp syndrome OR clinical and laboratory profile AND Hypertensive syndromes OR pregnancy AND diagnosis, which were performed in different combinations. For better understanding and transparency in the selection method, it was decided to present the flowchart of scientific articles through the Main Items for Reporting Systematic Reviews and Meta-Analyses (PRISMA) guide.

3. Results and Discussion

According to the results found in the study, for better understanding and transparency in the selection method, the flowchart of scientific articles was used through the Main Items for Reporting Systematic Reviews and Meta-Analyses (PRISMA) guide (Figure 1). The first phase consisted of searching the databases, totaling 219 articles. In the second phase, repeated articles were excluded, which were 97. In the third, titles and abstracts were read, 122 articles were selected. In the last phase of construction, an exploratory, selective and analytical reading of all studies and stratification of excerpts that answered the guiding question was carried out, totaling 10 articles that make up the sample. The data are presented in a descriptive way, aiming to gather and organize knowledge on the topic investigated. Table 1 presents an overview of the articles selected for the study and a summary of the main conclusions reached.

Figure 1. Schematic representation of synthesis and analysis of results (PRISMA).

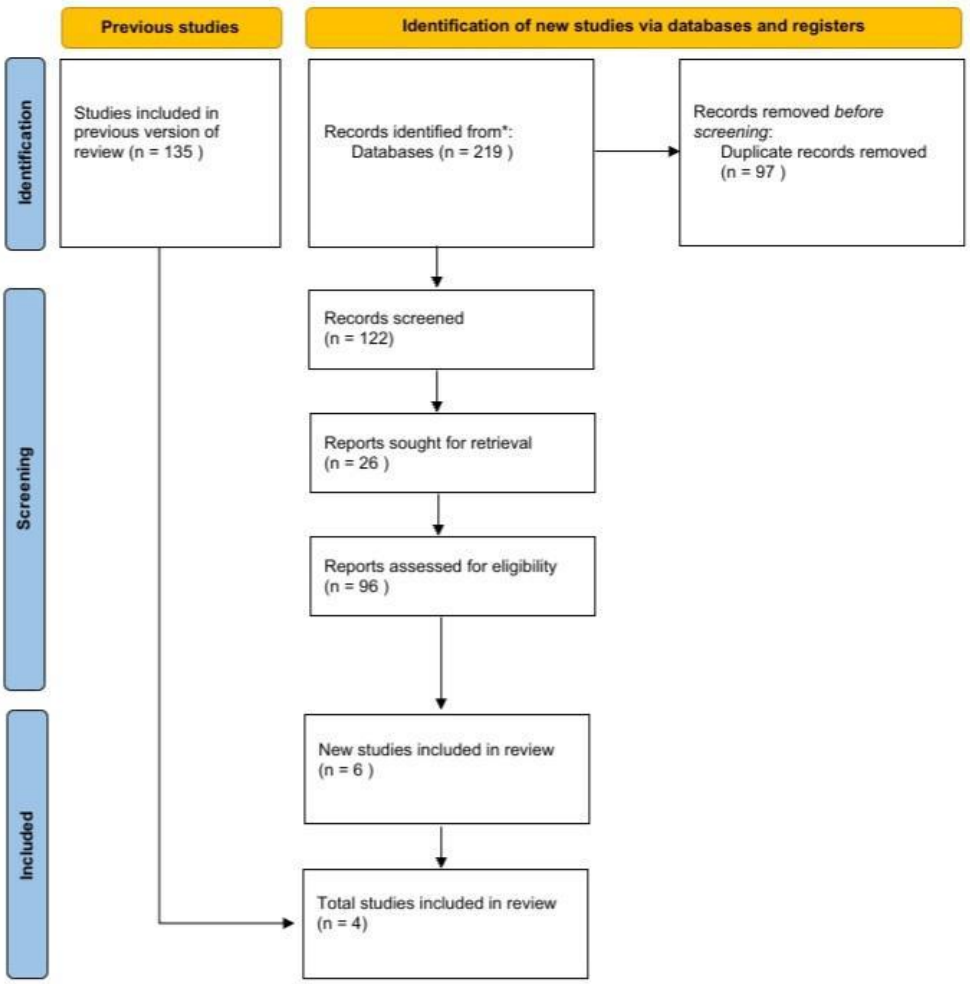

Table 1. Studies selected for sample, according to Rayyan identification, title, authors, objectives and main results.

References	Objectives	Main Results
[5]	From January 1 to December 31, 2020, the medical records of 130 pregnant and post-partum patients admitted with Hypertensive disorders in pregnancy (HDP) in a census method of sampling were retrieved, while 83.1% (108) were suitable for analysis in an institutional cross-sectional retrospective study in the department of obstetrics and gynecology at the John F. Kennedy Maternity Center, Liberia.	There was an institutional prevalence of 3.0% of HDP. The maternal fatality rate was 12.3%, while the perinatal mortality rate was 14.3%. There was a significant association between HELLP syndrome and Severe pre-eclampsia with maternal death, P< 0.001. Prematurity, first minutes Apgar score <5, NICU admission, and low birth weight were associated with perinatal deaths (P <0.001).
[6]	The aim of the study is to analyze the care of patients with gestational hypertensive disorders, essential conclusions.	Hypertensive disorders in pregnancy (HDP) are a group of conditions—including chronic hypertension, gestational hypertension, preeclampsia with and without end-organ damage, and acute complications, which include HELLP (hemolysis, elevated liver enzymes, and low platelets) syndrome and eclampsia—that could lead to severely adverse outcomes for both mother and fetus. The incidence of HDP has increased, affecting one out of seven delivery hospitalizations. Physicians should be aware of HDP for early identification and proper treatment to improve patient outcome
[7]	To review literature and estimate the occurrence of preeclampsia and its complications in Brazil.	We retrieved 304 studies after the initial search; of those, 10 were included in the final analysis, with a total of 52,986 women considered. The pooled prevalence of preeclampsia was 6.7%, with a total of 2,988 cases reported. The frequency of eclampsia ranged from 1.7% to 6.2%, while the occurrence of HELLP syndrome was underreported. Prematurity associated to hypertensive disorders ranged from 0.5% to 1.72%.
[8]	The objective of index study is to review the available literature on hepatic rupture or hematoma in hypertensive disorders of pregnancy to find the incidence, associated risk factors, clinical presentation, mode of management and feto-maternal outcome	Unawareness of the hepatic rupture in pregnancy by an obstetrician demands high index of suspicion for diagnosis and requires specialized, focused and exhaustive management for optimal feto-maternal outcome. Laparotomy and perihepatic packing is a viable option in patients with unstable vitals and is feasible even in lim-

		ited resource settings.Short interval between diagnosis and management may enhance the feto-maternal survival rate and prevent further morbidity or mortality.
[9]	To map evidence on nursing care for women with HELLP syndrome.	Of the 129 studies, ten were selected, which made up the final sample. The studies date from 2004 to 2022, with a predominance of English language and clinical case studies. A greater occurrence of the syndrome was observed in second-time pregnant women in the second decade of life, with a gestational age from 32 weeks, which resulted in an emergency cesarean section, and all newborns were discharged accompanied by their mothers. Studies that described nursing diagnoses and focused on nursing care were retrieved. From the review, 39 nursing care were identified.
[8]	The main objective of this study is to evaluate the agreement of obstetricians regarding the management of pre-eclampsia/eclampsia and HELLP syndrome, as recommended by some Portuguese institutions and international organizations.	In most categories, the disagreement between guidelines was partial (medians of "0.50"). The least concordant categories were "criteria for admission in pre-eclampsia", "criteria for severity of pre-eclampsia" and "guidance in HELLP syndrome" between protocols and guidelines (medians of "0.00"). The lack of agreement among obstetricians regarding clinical guidelines is reported in other studies.
[9]	To analyze the correlation between the profile, clinical and gynecological conditions of the pregnant woman and maternal mortality caused by HELLP (Haemolysis, Elevated Liver Enzymes and Low Platelets) syndrome.	The clinical conditions of the current pregnancy that showed significant correlations with maternal mortality resulting from the syndrome were: modes of delivery (p= 0.023), eclampsia (p= 0.000), at least two symptoms of severity and complication (p= 0.005), as well as the time between diagnosis of the syndrome and delivery (p= 0.015).
[10]	The aim of the present study was to determine the risk factors for patients with pre-eclampsia (PE) with severe features to develop hemolysis, elevated liver enzymes and low platelets (HELLP) syndrome and to design a prediction score model that incorporates these risk factors.	Overall, 445 patients were included, of whom 69 patients were in the study group and 376 in the control group. A multivariate logistic analysis regression showed that maternal age <40 (OR = 2.28, 95% CI: 1.13-5.33, P = 0.045), nulliparity (OR = 2.22, 95% CI: 1.14-4.88, P = 0.042), mild hypertension (OR = 2.31, 95% CI: 1.54-4.82, P = 0.019), epigastric pain (OR = 3.41, 95% CI:

		1.92-7.23, P < 0.001) and placental abruption (OR = 6.38, 95% CI: 1.29-35.61, P < 0.001) were independent risk factors for HELLP syndrome. A prediction score model reached a predictive performance with an area under the curve of 0.765 (95% CI: 0.709-0.821).
[11]	The goal of this updated evaluation is to provide the most up-to-date molecular advances in the pathophysiology of PE/HELLP syndromes. Recent medical data on vWF:Ag levels in patients with PE, ADAMTS-13, and dysregulation of the complement system, are highlighted and evaluated.	Recent medical data on vWF:Ag levels in patients with PE, ADAMTS-13, and dysregulation of the complement system, are highlighted and evaluated. Furthermore, we discuss the relationship between those entities and the progression of the disease, as well as their significance in the diagnostic process. Finally, considering the difficulties in analyzing and controlling those symptoms in pregnant women, we can provide a current diagnostic and therapeutic algorithm.
[12]	The objective of this study is to evaluate the agreement between obstetricians regarding guidelines on pre-eclampsia/eclampsia and HELLP syndrome, published by national clinical centers and international organizations.	The results suggest the need to develop national guidelines for clinical conduct in hypertensive diseases typical of pregnancy, including screening and prevention, obtained through the consensus of a group of obstetricians from various maternity hospitals in the country.
[13]	To analyze the correlation established between the profile, clinical and gynecological conditions of the pregnant woman and maternal mortality caused by HELLP syndrome (Haemolysis, Elevated Liver enzymes and Low Platelets).	Only four variables regarding the clinical conditions of the current pregnancy interfered with maternal mortality due to HELLP syndrome, such as the correlation with the time between diagnosis and delivery, which is unprecedented in the scientific literature.

Hypertensive disorders of pregnancy (HDP) are major obstetric complications associated with high rates of maternal and fetal mortality and morbidity, especially in resource-limited settings. These disorders include gestational hypertension, pre-eclampsia, eclampsia, and chronic hypertension. Their incidence has increased due to the rising prevalence of related risk factors such as obesity, gestational diabetes, and advanced maternal age. HDP affects one in seven hospitalizations for childbirth and is currently the leading cause of pregnancy-related death in developed countries. Among the major complications of preeclampsia, HELLP syndrome is the leading cause of death in parturients, characterized clinically and by laboratory findings, including three main manifestations: hemolysis (destruction of red blood cells), elevated liver enzymes (indicating liver damage), and low platelet count (affecting blood clotting).

In a study conducted by Odunvbun WO et al. at the John F. Kennedy Maternity Center (JFKMC) Hospital in Liberia, the institutional prevalence of HDP was 3.0%. The maternal fatality rate was 12.3%, while the perinatal mortality rate was 14.3%. There was a significant association between HELLP syndrome and severe preeclampsia with ma-

ternal death (p<0.001). Prematurity, a 1-minute Apgar score <5, NICU admission, and low birth weight were associated with perinatal deaths (P < 0.001) [5, 6].

In other words, in the obstetric clinical context, HELLP syndrome stands out for its high mortality and morbidity. Timely diagnosis is crucial to mitigate the risk of potentially fatal events. In Latin America, preeclampsia affects 2% to 8% of all pregnancies and accounts for a quarter of all maternal deaths in the region. Preeclampsia and other hypertensive syndromes also contribute to the majority of medically indicated preterm births, and complications related to prematurity are the leading cause of death up to the fifth year of life in Brazil. The pathophysiology of preeclampsia (PE) is complex, with the precise underlying cause not fully elucidated, though it is likely heterogeneous.

Gardikioti A et al. state that PE can be further complicated by hemolysis and thrombocytopenia, leading to the emergence of HELLP syndrome, and its pathogenesis is associated with an excessive maternal inflammatory response and increased endothelial activation [7, 8]. Arduini PS et al., in agreement with this study, note that in most cases, the etiopathogenesis is unknown. However, factors such as nulliparity or multiparity, age over 30 years, a history of HELLP syndrome in a previous pregnancy, chronic hypertension, pre-gestational diabetes, heart disease, obesity, chronic liver disease, placental alterations, and congenital anomalies are identified as risk factors for the emergence of HELLP syndrome.

Gilboa I et al. identified distinct risk factors associated with the development of HELLP syndrome in patients with severe features of PE, including maternal age under 40 years, nulliparity, mild hypertension, epigastric pain, and premature placental abruption, which were established as independent risk factors for HELLP syndrome [9, 10]. A detailed medical history plays a crucial role in differentiating between various clinical entities. It is believed that a personal history of preeclampsia, thrombophilia, or chronic hypertension, along with primiparity, very young age or age over 35 years, obesity, and multiple pregnancies, predisposes individuals to the development of preeclampsia. In fact, preeclampsia occurs not only in previously healthy pregnant women but also in those with underlying pathological conditions.

Delivery is the treatment of choice for patients with HELLP syndrome or preeclampsia, with improvement expected 1–2 days postpartum. However, if there is no resolution, or if there is a worsening of clinical manifestations or laboratory parameters (persistent anemia, neurological symptoms, additional thrombocytopenia) within the first days after delivery, intervention is necessary [11]. Therefore, screening and prevention of pre-eclampsia are essential areas of study given the high morbidity and mortality associated with these conditions and the limited effectiveness of therapeutic options. The absence of preeclampsia-specific protocols underscores the need to review and update them, though prudence is needed in adopting recommendations with robust scientific backing. Patient care records, including sociodemographic data, health characteristics, prenatal monitoring, and obstetric history, play a vital role in protecting the rights of patients and healthcare professionals in legal or administrative situations, but most importantly, they contribute to providing quality care that meets the needs of this population [12, 13].

In seeking to gather as much pertinent information as possible to obtain robust data, it was observed that hypertensive disorders of pregnancy affect various aspects of women's daily lives, as well as their functioning during and after pregnancy. Given the severity of complications like HELLP syndrome, knowledge of clinical and laboratory patterns is crucial for early recognition and effective management.

4. Conclusion

HELLP syndrome is a potentially life-threatening condition for both mother and baby, particularly occurring in the third trimester of pregnancy, where timely diagnosis and treatment are crucial. Symptoms are often confused with other conditions, such as pre-eclampsia or gastrointestinal problems, making it essential for doctors and healthcare

professionals to study the syndrome thoroughly. HELLP syndrome can lead to several severe complications, such as liver failure and disseminated intravascular coagulation (DIC), both of which significantly increase the risk of maternal death. Fetal complications are also critical, as they contribute to neonatal mortality, including intrauterine growth restriction (IUGR), the risk of premature birth, and fetal death.

Therefore, based on the analysis of the clinical and laboratory profile of the syndrome and its complications, it is evident that early diagnosis and appropriate treatment are paramount. Healthcare professionals must recognize these patterns and respond promptly, given the severity of the syndrome's effects on both the mother and fetus.

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