

Liver Disease in Pregnancy: A Comprehensive Clinical Analysis

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ABSTRACT: Introduction : Liver disease in pregnancy represents a spectrum of conditions that pose significant risks to both maternal and fetal health. For the cross-sectional study purpose, major pregnancy-related liver disorders- HELLP syndrome, Pre-eclampsia with hepatic involvement, Intrahepatic Cholestasis of Pregnancy (ICP), Acute Fatty Liver of Pregnancy (AFLP) and Hyperemesis Gravidarum (HG), patients from first affiliated hospital of Xinjiang Medical University, Xinjiang, China was taken. By comparing demographic characteristics, clinical presentation, laboratory parameters, management approaches, and maternal-fetal outcomes across these conditions, we aim to provide clinicians with enhanced understanding of their distinct pathophysiologies and optimal management strategies.

Method: A cross-sectional study examined 80 pregnant women with liver disorders treated from November 2023 to November 2024. Demographic data, clinical presentation, laboratory parameters, management approaches, and maternal-fetal outcomes were taken from the day of diagnosis from outpatient and administration department till the delivery of the patient. Statistical analysis was performed. Reference were taken from the PUBMED.

Result: HELLP syndrome (n=12) presented with hemolysis, severe thrombocytopenia and hepatic enzyme elevation, resulting in 33.33% perinatal mortality; Pre-eclampsia (n=23) demonstrated significant proteinuria with preserved liver function, showing 8.7% perinatal mortality; ICP (n=45) exhibited pruritus with bile acid elevation, resulting in 13.33% perinatal mortality; AFLP (n=0) and HG (n=0) overall perinatal mortality 15% (n=12).

Conclusion: Multiparity and elevated BMI were common risk factors across all study. This analysis underscores the necessity for early recognition, multidisciplinary management, and tailored therapeutic approaches to optimize outcomes in these complex obstetric scenarios.

Keywords: HELLP syndrome: Intrahepatic Cholestasis of Pregnancy: Liver disease in pregnancy: Pre-eclampsia.

1.INTRODUCTION: Normally pregnancy have direct physiological relation to the liver which adversely affect the outcome of pregnancy. In pregnancy about 3% pregnant women are affected by liver disease in developed countries. Pregnancy related liver disease are HELLP syndrome, Pre-eclampsia, Intrahepatic Cholestasis of Pregnancy (ICP), Acute Fatty Liver of Pregnancy (AFLP) and Hyperemesis Gravidarum (HG) [1]. There is rising proportion of preexisting liver disease in childbearing age, having different prevalence in the pregnant population across the world[2]. Liver function is done by the liver function biomarker levels (LFBs), including γ glutamyl transferase (GGT), alanine aminotransferase (ALT), alkaline phosphatase (ALP), and aspartate aminotransferase (AST) [3].

This comprehensive analysis was done because of increasing penenatal mortality nowadays, for which examines three major pregnancy-related liver conditions—HELLP syndrome, Pre-eclampsia with hepatic involvement, and Intrahepatic Cholestasis of Pregnancy—through detailed evaluation of 80 number of patients from first affiliated hospital of Xinjiang Medical University, Xinjiang, China.

METHODS

2.1 Study Design and Population

This cross-sectional analysis examined 80 pregnant women with liver disorders treated between November 2023 and November 2024. The study included 12 patients with HELLP syndrome, 23 with Pre-eclampsia with hepatic involvement, and 45 with Intrahepatic Cholestasis of Pregnancy (ICP). Diagnosis was confirmed using established clinical criteria and laboratory parameters for each condition.

2.2 Diagnostic Criteria

HELLP syndrome was diagnosed based on the presence of hemolysis (LDH >600 U/L or bilirubin ≥ 20.5 $\mu\text{mol/L}$), elevated liver enzymes (AST (SGOT)/ALT (SGPT) >70 U/L), and low platelets (<100,000/ μL) [4]. Pre-eclampsia was defined as new-onset hypertension ($\geq 140/90$ mmHg) after 20 weeks gestation with proteinuria (≥ 300 mg/24 hours or protein:creatinine ratio ≥ 0.3) [5]. ICP was diagnosed when pruritus typical of the condition occurred in pregnancy with elevated serum bile acids (>10 $\mu\text{mol/L}$) and no other explanation for liver test abnormalities or pruritus [6].

2.3 Inclusion criteria

Pregnant women attending antenatal clinic suspected to have Liver Disease on the basis of clinical or investigation data as follows were included: (a) history suggestive of Liver Disease : itching, yellowish discoloration of eye/skin/urine; (b) deranged liver function tests: AST (SGOT)/ALT (SGPT) : >70 U/L, hemolysis (LDH >600 U/L or bilirubin ≥ 20.5 $\mu\text{mol/L}$), platelets (<100,000/ μL), serum bile acid >10 $\mu\text{mol/L}$; (c) blood pressure ($\geq 140/90$ mmHg) after 20 weeks gestation, proteinuria (≥ 300 mg/24 hours or protein:creatinine ratio ≥ 0.3) (d) sonographic changes in liver during pregnancy.

2.4 Exclusion criteria

Women who didn't come for delivery after diagnosis of liver disease, women with fetuses diagnosed with structural/chromosomal anomaly (such as triploid, trisomy 13, trisomy 18, hydatidiform mole, fetal hydrops, severe structural cardiac malformations causing fetal compromise, and others), and those not willing to consent for the study were excluded.

2.5 Data Collection and Analysis

Demographic data, clinical presentation, laboratory parameters, management approaches, and maternal-fetal outcomes were taken from the day of diagnosis from outpatient and administration department till the delivery of the patient. Statistical analysis was performed, with continuous variables expressed as means and categorical variables as percentages. Correlation analysis was conducted using Pearson's correlation coefficient for normally distributed data. Reference were taken from the PUBMED.

RESULTS

3.1 HELLP Syndrome Study Analysis

HELLP syndrome known as Hemolysis, elevated liver enzymes, and low platelet count [7], is a rare, but serious condition arising during pregnancy that occurs in 0.2–0.8% of all pregnancies [8], but the rate is 10-20% in women with pre-eclampsia [9]. At first it was described by Weinstein in 1982. It is an acronym that represents a combination of clinical manifestations. HELLP syndrome is a significant cause of maternal and perinatal morbidity and mortality worldwide [10]. HELLP Syndrome is diagnosed with Mississippi Classifications which divides HELLP syndrome into 3 classes based on platelet count, AST or ALT levels, and LDH levels [11]. Although HELLP syndrome has been distinguished from PE as a separate disease, still viewed as a form of severe PE [12]. HELLP syndrome typically present with the patients between 28 and 37 weeks of pregnancy or postpartum, within seven days of delivery. In contrast, pre-eclampsia begins after 20 weeks of gestation [13].

3.1.1 Demographic Characteristics

In the study of HELLP syndrome (n=12) detail in **Table 1**, about parity concern 66.7% (n=8) being multiparous and 33.3% (n=4) primiparous, it means as pregnancy number increases chance of HELLP syndrome increase. Age distribution analysis, shows that 66.7% of cases occurred in the women aged over 30 years or older with the peak age group between 30-39 years old, having the mean maternal age of 32.75 years (range:24-43). The mean Body Mass Index (BMI) was 29.6 kg/m² (range: 23-33) indicating the average patient in the overweight category. Advance maternal age with increase BMI are the potent risk factor.

3.1.2 Temporal Patterns and Diagnostic Approach

Diagnosis of HELLP syndrome occurred at a mean gestational age of 30 weeks, with 16.7% (n=2) of cases diagnosed postpartum (4th and 7th postoperative days). In all cases pregnancy were confirmed using Urine Pregnancy Test (UPT) and Obstetric Ultrasound, HELLP syndrome were confirmed with laboratory finding of the diagnostic triad.

3.1.3 Laboratory Profile

The classical laboratory triad of HELLP (H-Hemolysis, EL-Elevated Liver Enzyme, LP-Low Platelet Count), syndrome was strongly evident in our study. Platelet counts averaged 85.92x 10⁹/L, with 91.66% (n=11) of patients demonstrating thrombocytopenia (<150 x 10⁹/L) and 8.34% (n=1) patient have normal platelet count. In which 33.33% (n=4) exhibiting mild thrombocytopenia, 33.33%(n=4) exhibiting moderate thrombocytopenia and 25% (n=3) exhibiting severe thrombocytopenia (<50 x 10⁹/L), having the mean haemoglobin (HB) 10.12(gm%). Hepatic transaminases were significantly elevated, with mean AST of 201.64IU/L and ALT of 131.4 IU/L. Normal Bilirubin levels with a mean of 6.08 $\mu\text{mol/L}$.

3.1.4 Clinical Presentation and Complications

Hypertension was a prominent feature, with 50% (n=6) of patients. Presenting symptoms were diverse, including increased blood pressure, edema, headache, decreased urine output, chest tightness/palpitations, postoperative bleeding, and

abdominal bloating. Maternal complications were severe and multi systemic, including severe pre-eclampsia, renal failure, cardiac failure, placental abruption, and pulmonary hypertension. In the study shows increase blood pressure causing pre-eclampsia play a potent risk factor causing HELLP syndrome.

| Variable | HELLP syndrome |
|--|---------------------------|
| Parity | |
| Primipara | 4 (33.3%) |
| Multipara | 8 (66.7%) |
| Mean Gestation age of diagnosis | 30 weeks |
| Mean maternal age | 32.75years |
| Range of maternal age | 22-43 |
| Body Mass Index (BMI) | 29.6 kg/m ² |
| | |
| Presenting Complaints | Number of Patients |
| Increase BP | 6 |
| Edema | 3 |
| Post-Operative bleeding | 1 |
| Per Vaginal discharge | 1 |
| Decrease urine output | 1 |
| | |
| Investigations (Mean Values) | Values |
| Haemoglobin (Hb) (gm%) | 10.12 |
| Bilirubin (µmol/L) | 6.08 |
| AST (IU/L) | 201.64 |
| ALT (IU/L) | 131.4 |
| Platelet (x10 ⁹ /L) | 85.92 |
| Sever thrombocytopenia | 25% |
| Moderate thrombocytopenia | 33.33% |
| Mild Thrombocytopenia | 33.33% |
| Normal | 8.3% |
| | |
| Complications | Number of Patients |
| Pre eclampsia | 7 |
| Renal failure | 1 |
| Hyperproteinemia | 3 |
| Pulmonary hypertension | 1 |

Table 1: Profile of Patients having HELLP syndrome in Liver disease.

3.1.5 Management and Outcomes

All HELLP syndrome patients (100%) underwent cesarean section, with delivery occurring at a mean gestational age of 30 weeks. The preterm delivery rate was 83.33% (n=10) and term delivery rate was 16.67% (n=2), Concerning with a 33.33% (n=4) perinatal mortality rate (including 1 stillbirth and 3 IUFD), 50% (n=6) NICU admission rate and 16.66%(n=2) live without NICU admission as shown in **Table 2**. Intrauterine growth restriction (IUGR) was present in 50% (n=6) of cases. Notably, there were no maternal deaths in this study.

| S.N. | Variables | Number | Percentage |
|------|-------------------------------------|--------|------------|
| 1 | Cesarean section (mode of delivery) | 12 | 100% |
| 2 | Preterm | 10 | 83.33% |
| 3 | Term | 2 | 16.67% |
| 4 | IUGR present | 6 | 50% |
| 5 | NICU admission | 6 | 50% |
| 6 | Neonatal Death | 4 | 33.33% |

Table 2: Management and Neonatal outcomes in HELLP syndrome in liver disease.

3.2 Pre-eclampsia with Hepatic Involvement Study Analysis

Pre-eclampsia (PE) global incidence at 4.6%, which varies greatly among different countries and regions, it represents one of the four major reasons for maternal mortality, even in developed countries [14]. Pre-eclampsia, characterized by hypertension and proteinuria, is a multisystemic disorder [15] affects 3-4% of pregnancies with adverse effects for both mother and child. It is increasingly recognized that the pathophysiology of preeclampsia is heterogeneous

and may differ depending on the subtype, symptom in question and the severity and organ involvement[16]. The condition usually implicates previously healthy normotensive women, after 20 weeks of gestation, most commonly in the third trimester, without known risk factors or past deliveries[17]. If not treated, it could progress to eclampsia, which is characterized by seizures and can be fatal to the mother and fetus. Pre-eclampsia is difficult to diagnose since it can present in numerous different ways and there is not a consistent diagnostic test [18]. Hypertension was recognized as a feature of eclampsia in 1885 by John William Ballantyne at the University of Edinburgh, who reported hypertension by using sphygmographic tracings in three cases of pregnant women with “Bright’s disease” [19]. Symptoms range from mild hypertension and proteinuria to severe life-threatening multi-organ dysfunction, including hemolysis, elevated liver enzymes, and low platelet count (HELLP) syndrome and other hepatic complications. Pre-eclampsia is associated with functional changes in the liver that are thought to resolve after pregnancy, but the long-term risk of developing chronic liver disease has not been studied [20]. Apart from maternal mortality, these hypertensive disorders of pregnancy can lead to an increased risk for future metabolic and cardiovascular disease for both mother and offspring [21].

3.2.1 Demographic Characteristics

In the study of Pre-eclampsia (n=23) detail in **Table 3**, about parity concern 87% (n=20) being multiparous and 13% (n=3) primiparous, it means as pregnancy number increases chance of Pre-eclampsia increases. Age distribution analysis, shows that 73.91% of cases occurred in the women aged over 30 years or older with the peak age group between 30-39 years old, having the mean maternal age of 31 years (range: 25-37). The mean Body Mass Index (BMI) was 30.4 kg/m² (range: 20-38) indicating the average patient in the overweight category. This demographic profile challenges traditional teaching that pre-eclampsia predominantly affects multiparous women having higher BMI.

3.2.2 Temporal Patterns and Diagnostic Approach

Diagnosis occurred at a mean gestational age of 33.2 weeks, with most frequent on 31 weeks having range of 25-37 +6 weeks. All patients were diagnosed using UPT and Obstetric Ultrasound, with 24-hour urine protein quantification and liver function tests providing essential diagnostic confirmation.

| Variable | Pre-eclampsia |
|--|---------------------------|
| Parity | |
| Primipara | 3(13%) |
| Multipara | 20(87%) |
| Mean Gestation age of diagnosis | 33.2weeks |
| Mean Maternal age | 31 years |
| Range of Maternal age | 25-37 |
| Body Mass Index (BMI) | 30.4 kg\m ² |
| Presenting Complaints | Number of Patients |
| Increased BP | 21 |
| Increase 24hours Urinary protein | 9 |
| Edema | 4 |
| Per Vaginal discharge | 2 |
| Abnormal Umbilical blood flow | 1 |
| Oligohydramnios | 1 |
| Investigations | Mean Values |
| Bilirubin | 5.86 µmol/L |
| 24-hour urine protein | 3.04 gm/24hr |
| Urine protein | 2456 mg/dl |
| AST (IU/L) | 25.57U/L |
| ALT (IU/L) | 18.11 U/L |
| ALP(IU/L) | 169.39 U/L |
| Parameter | Abnormal Cases |
| Hypertension | 17(73.9%) |
| Proteinuria | 23(100%) |
| Edema | 2(8.7%) |
| Hypertension + Proteinuria | 17(73.9%) |
| Complications | Number of Patients |
| Eclampsia | 1 |
| Heart failure | 1 |

| | |
|-------------------------|---|
| Hyperproteinemia | 3 |
| GDM | 4 |
| Pulmonary HTN | 2 |
| Anemia | 1 |

Table 3: Profile of Patients having Pre-eclampsia in Liver disease.

3.2.3 Clinical Presentation

The study of (n=23) patients exhibiting symptoms consistent the predominant finding is elevated blood pressure, observed in 91.3% of cases. This is frequently accompanied by laboratory evidence of renal impairment, specifically proteinuria, which is present in 39.13% of patients. Additional clinical manifestations include edema (33.33%), vaginal discharge (8.6%) and, in a few instances (4.3%), more severe signs such as chest tightness, abdominal pain, umbilical abnormal blood flow, and oligohydramnios, suggesting a spectrum of symptoms present on it.

3.2.4 Complications

This study reveals that within this specific group of patients (primarily multiparous, obese women with GDM), there is a **high burden of co-morbid medical conditions**. While just over half had no any complication, the other half presented with a serious and diverse range of issues affecting the cardiovascular, pulmonary, and hematological systems. This underscores the critical need for comprehensive screening and multidisciplinary care for pregnant individuals diagnosed with GDM, as they are at significant risk for other concurrent, serious health challenges.

3.2.5 Laboratory Profile

The laboratory hallmark of pre-eclampsia in our study was significant proteinuria 100% (n=23), with a mean 24-hour urine protein of 3.04 gm/24hr (normal: <0.3 gm/24hr) and mean urine protein of 2456 mg/dl (normal: <150 mg/dl); hypertension 73.9% (n=17); edema 8.75% (n=2) and hypertension with proteinuria 73.9% (n=17). Unlike HELLP syndrome, liver enzymes remained relatively preserved (mean AST 25.57 U/L, mean ALT 18.11 U/L), and ALP was elevated (mean 169.39 U/L), within normal bilirubin level of mean 5.86µmol/L. The dissociation between significant proteinuria and relatively preserved liver function helps distinguish pre-eclampsia from HELLP syndrome. The data reveals a critical relationship between Liver Function Test (LFT) results and disease severity in this patient population, with proteinuria being a universal finding across all groups.

3.2.6 Management and Outcomes

Cesarean section was performed in 91.3% (n=21) of cases, with delivery at a mean gestational age of 35.1 weeks. The preterm delivery rate was 73.9% (n=17). Pre-eclampsia leads to severe fetal and newborn complications, this results in poor fetal growth 39.1% (n=9), necessitating early delivery (73.9% preterm births) to save the mother and neonate. Consequently, many newborns require intensive care 34.8% (n=8), and the condition carries a significant stillbirth rate 8.7% (n=2) as shown in **Table 4**. Hence early diagnosis and management prevent both maternal and neonatal death rate. Notably, there were no maternal deaths in this study.

| S.N. | Variables | Number | Percentage |
|------|---|-----------|--------------|
| 1 | Cesarean section (Mode of delivery) | 21 | 91.3% |
| 2 | Normal delivery | 2 | 8.7% |
| 3 | Preterm | 17 | 73.9% |
| 4 | Term | 6 | 26.1% |
| 5 | IUGR present | 9 | 39.1% |
| 6 | NICU admission | 8 | 34.8% |
| 7 | Stillbirth\Intra Uterine Fetal Death | 2 | 8.7% |

Table 4: Management and Neonatal outcomes of Pre-eclampsia in liver disease

3.3 Intrahepatic Cholestasis of Pregnancy (ICP)

Intrahepatic cholestasis of pregnancy (ICP) is the most common pregnancy-specific liver disease, typically occurring in the second and third trimesters of pregnancy [22] affecting 0.5–2% of pregnancies [23]. ICP is also known as cholestasis gravidarum. It was first described as a “jaundice in pregnancy” by Ahlfeld in 1883 [24]. Case reports in the 1950s described pregnancy having severe itching, with or without jaundice, resolve after childbirth, with high recurrence rates. Over the time, now it is globally known as ICP, it has been described as: jaundice of pregnancy, obstetric hepatitis, hepatitis gestationalis, or obstetric cholestasis [25]. The etiology of ICP is thought to be multi factorial and includes environmental and hormonal contributions in genetically susceptible women. The prevalence of ICP in twin pregnancies is higher compared to singletons pregnancy [26]. ICP is clinically characterized by pruritus and increased bile acids, symptoms usually disappear after labor. Although it is non-threatening from a maternal perspective, ICP is associated with an elevated risk for fetal

outcomes, including spontaneous preterm labor, meconium staining of the amniotic fluid, birth asphyxia, and sudden intrauterine death [27]. Increased total serum bile acid (TSBA) concentration is biomarker for ICP in the most studied, initially it may not be present but, in its absence, should be rechecked if symptoms are present, in particular in combination with increased serum ALT [28]. Various countries have issued guidelines over the years, for the diagnosis and management of ICP to mitigate adverse perinatal outcomes caused by TBA [29]. Patients with ICP frequently have premature labour and delivery. This happens because bile acids increase the uterus' sensitivity to oxytocin, which stimulate the uterine contractions. About 20 to 40 percent of ICP pregnancies end in preterm labour Spontaneously [30].

Ursodeoxycolic acid, which has a significantly lower bile acid hydrophobicity index, is widely used to treat ICP [31]. Ursodeoxycolic acid improves biliary flow, enhances the protective bicarbonate environment on the surface of cholangiocytes, and protects the liver from bile acid-induced apoptosis. This therapy has anti-inflammatory actions, and can reduce the elevation of serum bile acid concentration in the fetus, probably by upregulating placental bile acid export [32].

3.3.1 Demographic Characteristics

The ICP study (n=45) detail in **Table 5**, demonstrated a predominance of multiparous women (77.8%, n=35) with a compared to primiparous women (22.2%, n=10) with a mean age of 32.42 years range (25-42years). The mean BMI was

| Variable | ICP |
|--|-------------------------|
| Parity | |
| Primipara | 10(22.2%) |
| Multipara | 35(77.8%) |
| Mean Gestation age of diagnosis | |
| Mean gestation age | 31 weeks |
| Mean maternal age | 32.42 yrs |
| Range of maternal age | 25-42 |
| BMI | 28.07 kg/m ² |
| Presenting Complaints | |
| Number of patients | |
| Pruritus only | 12 |
| Pruritus + jaundice | 5 |
| Decrease fetal movement | 9 |
| Increase Blood Pressure | 8 |
| Increase Bile acid | 6 |
| Per Vaginal discharge | 4 |
| Asymptomatic | 5 |
| Investigations | |
| Mean Values | |
| ALT (IU/L) | 125.49U/L |
| AST (IU/L) | 120.39U/L |
| ALP(IU/L) | 235.32U/L |
| Serum Bilirubin | 8.83µmol/L |
| Serum Bile Acid(SBA) | 50.78µmol/L |
| Mild ICP | 21(46.7%) |
| Moderate ICP | 18(40%) |
| Severe ICP | 6(13.3%) |
| Complications | |
| Number of Patients | |
| Pre-Eclampsia | 12 |
| Abortion | 1 |
| Hyperproteinemia | 1 |
| Hysterectomy | 1 |
| HELLP syndrome | 1 |
| Anemia | 1 |
| Pleural effusion | 1 |
| Epilepsy | 1 |

28.07 kg/m², which is in the overweight range.

Table 5: Profile of Patients having ICP in Liver disease.

3.3.2 Temporal Patterns and Diagnostic Approach

In all cases pregnancy were confirmed using Urine Pregnancy Test (UPT) and Obstetric Ultrasound, ICP were confirmed with laboratory finding in the late second to third trimester (≥ 21 weeks) with a Mean Gestation age of 31 weeks. This timing corresponds with the typical presentation of pruritus in the late second or third trimester.

3.3.3 Clinical Presentation

Itching was the most frequent complaint, present in over a quarter of cases, strongly pointing to Intrahepatic Cholestasis of Pregnancy (ICP) as a key concern. However, a significant number of patients presented with other serious issues, including reduced fetal movement and high blood pressure, suggesting the patient population was dealing with a variety of obstetric complications beyond just ICP. The presence of jaundice alongside pruritus indicates a more severe form of liver disease compared to pruritus alone.

3.3.4 Complication

An overwhelming majority of cases complicated for **Pre-eclampsia**. Other conditions were much less frequent, including: **HELLP syndrome**, Serious obstetric procedures/outcomes (e.g., **Hysterectomy, Abortion**).

3.3.5 Laboratory Profile and Correlations

In the study of ICP (n=45) shows in **Table:6** laboratory abnormalities including elevated serum bile acids 91% mean value 50.87 $\mu\text{mol/L}$, categorized as 46.7% (n=21) mild ICP ($\text{SBA} \geq 10\text{--}39 \mu\text{mol/L}$), 40% (n=18) moderate ICP ($\text{SBA} \geq 40\text{--}99 \mu\text{mol/L}$) and 13.4% (n=6) severe ICP ($\text{SBA} \geq 100 \mu\text{mol/L}$), ALT 69% mean value 125.49 U/L, AST 78% mean value 120.39 U/L, ALP 73% mean value 235.32 U/L, and bilirubin 18% mean value 8.83 $\mu\text{mol/L}$, **the average patient shows laboratory evidence of significant liver dysfunction, predominantly characterized by cholestasis with accompanying hepatocellular damage.**

3.3.6 Management and Outcomes

In the study of ICP most of the delivery done by cesarean section (95.5%), with a mean gestational age at delivery of 34.2 weeks with 93% have laboratory abnormalities having 71.11% preterm-delivery following 33.3% NICU admission to neonates. The neonatal mortality rate was 13.33% (n=6), while no maternal deaths occurred as describe in **Table 6**. This is clearly illustrating the profound impact of **prematurity** and **Intrauterine Growth Restriction (IUGR)** on newborn health. These two conditions are the primary drivers for the need for intensive care (NICU admission) and are the most significant risk factors for the tragic outcome of neonatal death. The study is highly valuable for identifying at-risk pregnancies and improving neonatal care protocols.

| S.N. | Variables | Number | Percentage |
|------|-------------------------------------|--------|------------|
| 1 | Cesarean section (Mode of delivery) | 43 | 95.5% |
| 2 | Preterm | 32 | 71.11% |
| 3 | Term | 7 | 15.56% |
| 4 | IUGR present | 17 | 37.8% |
| 5 | NICU admission | 15 | 33.3% |
| 6 | Neonatal death | 6 | 13.33% |

Table 6: Management and Neonatal outcomes of ICP in Liver disease

3.4 Comparative Analysis Across Disorders

A comparative analysis of the study reveals both shared characteristics and important distinctions. All three conditions showed a predominance of multiparous women (HELLP: 66.7%, Pre-eclampsia: 87%, ICP: 77.8%) and elevated BMI (HELLP: 29.5 kg/m^2 , Pre-eclampsia: 30.4 kg/m^2 , ICP: 28 kg/m^2). However, laboratory profiles differed significantly: HELLP syndrome was characterized by thrombocytopenia and markedly elevated liver enzymes; Pre-eclampsia by significant proteinuria with relatively preserved liver function; and ICP by elevated bile acids with variable liver enzyme elevation and pruritus symptoms better controlled by early treatment.

Maternal complications were most severe in HELLP syndrome, affecting multiple organ systems, while Pre-eclampsia and ICP demonstrated fewer major maternal complications. Perinatal outcomes were poorest in HELLP syndrome (33.3% mortality), intermediate in ICP (13.33% mortality), and best in Pre-eclampsia (8.7% mortality) as describe in **Table 7**, represents a significant burden of neonatal morbidity.

| Disease (n) | Maternal deaths (%) | Perinatal deaths (%) |
|-------------------|---------------------|----------------------|
| HELLP (12) | 0 | 4(33.33%) |
| Pre-eclampsia(23) | 0 | 2(8.7%) |
| ICP(45) | 0 | 6(13.33%) |
| Total(80) | 0 | 12((15%) |

Table 7.Liver disease in pregnancy mortality outcome

DISCUSSION

4.1 Demographic Risk Factors and Pathophysiological Implications

Our study questions a number of conventional beliefs on liver problems associated with pregnancy. The traditional teaching that pre-eclampsia mostly affects primiparous women is contradicted by the prevalence of multiparity in all three circumstances [33]. This might be a result of shifting demographic trends, such as older mothers and higher obesity rates in contemporary obstetric populations [34]. The increasing understanding of metabolic variables in the pathophysiology of pregnancy-related liver disorders is supported by the consistent finding of higher BMI across all studies [35].

Despite their differences, the pathophysiological mechanisms underlying these disorders are similar in that they include systemic inflammation and placental abnormalities [36]. Endothelial dysfunction is brought on by oxidative stress and the production of anti-angiogenic factors in pre-eclamptic syndromes due to aberrant placentation [37]. Hormonal and genetic variables work together in ICP to reduce biliary production, which causes bile acids to build up and directly harm the placenta and fetal heart [38]. Placental insufficiency plays a crucial role in these situations, as evidenced by the high rate of IUGR across all studies (HELLP: 50%, Pre-eclampsia: 39.1%, ICP: 37.8%).

4.2 Diagnostic Challenges and the Importance of Laboratory Differentiation

Careful laboratory distinction is required due to the similar clinical characteristics of pregnancy-related liver diseases. Our research shows distinct biochemical patterns that can help in diagnosis: HELLP syndrome is defined by the triad of hemolysis, raised liver enzymes, and low platelets; pre-eclampsia is characterized by substantial proteinuria and hypertension; and ICP is diagnosed by elevated bile acids and pruritus [39]. It is especially significant because pre-eclampsia has comparatively maintained liver function as compared to HELLP syndrome, as this difference has significant management and delivery timing implications.

ICP correlation patterns shed light on the causes behind sickness. The intermediate association between bile acids and transaminases ($r=0.65-0.63$) demonstrates that cholestasis and hepatocellular injury are connected but not perfectly coupled processes, whereas the significant correlation between ALT and AST ($r=0.93$) reveals widespread hepatocyte damage. Due to its placental origin during pregnancy, ALP's weak correlation with other measures such as ALT, AST, and serum bile acid ($r=0.55$, $r=0.53$, and $r=0.48$, respectively) limits its usefulness in diagnosing ICP.

4.3 Management Strategies and Timing of Delivery

The frequent need for an accelerated delivery in the event of maternal or fetal impairment is reflected in the high rate of cesarean sections across all studies (HELLP: 100%, Pre-eclampsia: 91.3%, ICP: 95.5%). Regardless of gestational age, birth is the only effective treatment for HELLP syndrome and should not be postponed [40]. Delivery time in pre-eclampsia strikes a balance between fetal maturity and maternal status, with early-onset instances posing unique care issues [41]. Although the dangers of iatrogenic prematurity must be considered, delivery is usually advised in ICP at 36–37 weeks in order to prevent stillbirth [42].

It is significant how differently each of these illnesses responds to medical treatment. Antihypertensive medications help lower blood pressure in pre-eclampsia, but they don't change the underlying cause of the illness [43]. Although UDCA improves ICP biochemistry and symptoms, it might not be able to stop unfavorable perinatal outcomes [44]. Corticosteroids may temporarily improve laboratory values in HELLP syndrome, but they do not eliminate the requirement for delivery [45]. These findings demonstrate that the only proven cure for liver disorders unique to pregnancy is still delivery.

4.4 Maternal and Perinatal Outcomes: Implications for Clinical Practice

The three disorders' differing perinatal mortality rates (HELLP: 33.33%, pre-eclampsia: 8.7%, and ICP: 13.33% newborn mortality) are indicative of their diverse pathophysiologies and onset times. The severity of HELLP syndrome and the necessity of prompt identification and treatment are highlighted by its high fatality rate [46]. Despite decreasing rates of maternal complications, the considerable perinatal loss in pre-eclampsia and ICP emphasizes that fetal susceptibility may continue even when maternal disease appears to be under control.

All studies show a high rate of premature delivery (HELLP: 83.33%, Pre-eclampsia: 73.39%, ICP: 95.5%), which contributes significantly to infant morbidity and long-term neurodevelopmental consequences. This research highlights the necessity of long-term monitoring and specialized newborn care for infants exposed to these conditions during pregnancy. The high rates of NICU admission (HELLP: 50%, pre-eclampsia: 34.8%, and ICP: 13.33% among the study participants) highlight the substantial healthcare use linked to these illnesses.

4.5 Long-term Implications and Future Directions

Recent data raises the possibility that liver problems during pregnancy could affect a mother's long-term health [47]. While women with ICP may experience hepatobiliary diseases in later life [49], those with pre-eclampsia have a higher lifetime cardiovascular risk [48]. These correlations emphasize how crucial risk factor management and postpartum follow-up are for these populations.

Improved prediction models for these illnesses should be the main focus of future research in order to enable focused surveillance and preventive measures. Early diagnosis and more precise tracking of illness progression may be made possible by the creation of disease-specific biomarkers [50].

Conclusion

Pregnancy-related liver disorders represent a spectrum of conditions with distinct demographic profiles, clinical presentations, laboratory findings, and outcomes. Our analysis of 80 patients with HELLP syndrome, Pre-eclampsia with hepatic involvement, and Intrahepatic Cholestasis of Pregnancy reveals several key findings:

1. Multiparity and elevated BMI are common risk factors across all pregnancy-related liver disorders, challenging traditional epidemiological concepts.
2. Laboratory differentiation is essential for accurate diagnosis and appropriate management, with each condition demonstrating characteristic patterns.
3. Despite differences in maternal complication profiles, all three conditions are associated with high rates of preterm delivery and significant perinatal morbidity.
4. Cesarean section is commonly employed across all severe pregnancy-related liver disorders, reflecting the frequent need for expedited delivery.
5. Long-term follow-up is warranted given the association between these pregnancy complications and future maternal health risks.

These findings underscore the importance of heightened surveillance in high-risk populations, early recognition of abnormal laboratory parameters, multidisciplinary management involving obstetricians, hepatologists, and neonatologists, and careful timing of delivery to optimize both maternal and fetal outcomes. Future research should focus on developing improved predictive models and targeted therapies to reduce the substantial burden of these conditions.

Conflict of Interest: None

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REFERENCES:

1. Lim, E., Mouyis, M., & MacKillop, L. (2021). Liver diseases in pregnancy. *Clinical medicine (London, England)*, 21(5), e441–e445. <https://doi.org/10.7861/clinmed.2021-0497>
2. Nana, M., Medina, V., Maxwell, C., McCormick, C., Taliani, G., Beuers, U., Money, D., Jacobsson, B., Kapur, A., Beyuo, T., Ruiloba, F., Smith, G., Bergman, L., O'Reilly, S., O'Brien, P., Hanson, M., Rosser, M., Sosa, C., Adam, S., Guinto, V., ... FIGO Committee on Impact of Pregnancy on Long-term Health, FIGO Committee on Infections during Pregnancy and the FIGO Division of Maternal and Newborn Health (2025). FIGO guideline on liver disease and pregnancy. *International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics*, 170(1), 28–48. <https://doi.org/10.1002/ijgo.70161>
3. Yang, H., Tang, T., Qian, Q., Zhang, X., Liu, Y., Zhou, X., Zhang, Y., Jin, L., & Chen, X. (2025). Maternal Abnormal Liver Function in Early Pregnancy and Spontaneous Pregnancy Loss: A Retrospective Cohort Study. *Journal of epidemiology*, 35(5), 230–236. <https://doi.org/10.2188/jea.JE20240233>
4. Giannubilo, S. R., Marzioni, D., Tossetta, G., & Ciavattini, A. (2024). HELLP Syndrome and Differential Diagnosis with Other Thrombotic Microangiopathies in Pregnancy. *Diagnostics (Basel, Switzerland)*, 14(4), 352. <https://doi.org/10.3390/diagnostics14040352>
5. Gestational Hypertension and Preeclampsia: ACOG Practice Bulletin, Number 222. (2020). *Obstetrics and gynecology*, 135(6), e237–e260. <https://doi.org/10.1097/AOG.0000000000003891>
6. European Association for the Study of the Liver (2009). EASL Clinical Practice Guidelines: management of cholestatic liver diseases. *Journal of hepatology*, 51(2), 237–267. <https://doi.org/10.1016/j.jhep.2009.04.009>
7. Petca, A., Miron, B. C., Pacu, I., Dumitraşcu, M. C., Mehedintu, C., Şandru, F., Petca, R. C., & Rotar, I. C. (2022). HELLP Syndrome-Holistic Insight into Pathophysiology. *Medicina (Kaunas, Lithuania)*, 58(2), 326. <https://doi.org/10.3390/medicina58020326>
8. Wang, L., Tang, D., Zhao, H., & Lian, M. (2021). Evaluation of Risk and Prognosis Factors of Acute Kidney Injury in Patients With HELLP Syndrome During Pregnancy. *Frontiers in physiology*, 12, 650826. <https://doi.org/10.3389/fphys.2021.650826>
9. Guan, Y., Zhou, Y., Pan, H., Li, X., Lin, L., Yu, S., Teng, H., & Wang, X. (2024). Subcapsular Liver Hematoma Rupture in HELLP Syndrome During Pregnancy: A Case Study and Multidisciplinary Approach. *The American journal of case reports*, 25, e945440. <https://doi.org/10.12659/AJCR.945440>

10. Taj, S., Mujtaba, M., Miller, B., Dandu, S., Austin, C. P., Ali Akbar, U., Sanekommu, H., & Hossain, M. A. (2023). Role of Plasmapheresis in Hemolysis, Elevated Liver Enzymes and Low Platelets (HELLP) Syndrome. *Cureus*, *15*(2), e35520. <https://doi.org/10.7759/cureus.35520>
11. Anwar, A. D., Nugrahani, A. D., Amaluna Zahra, T., & Santoso, D. P. J. (2023). How to Differentiate Acute Fatty Liver in Pregnancy (AFLP) with Hemolysis, Elevated Liver Enzymes, and Low Platelets (HELLP) Syndrome in Resource-Limited Settings? - The Importance of Swansea Criteria. *European journal of obstetrics & gynecology and reproductive biology: X*, *17*, 100176. <https://doi.org/10.1016/j.eurox.2023.100176>
12. Wang, L. Q., Bone, J. N., Muraca, G. M., Razaz, N., Joseph, K. S., & Lisonkova, S. (2024). Prepregnancy body mass index and other risk factors for early-onset and late-onset haemolysis, elevated liver enzymes and low platelets (HELLP) syndrome: a population-based retrospective cohort study in British Columbia, Canada. *BMJ open*, *14*(3), e079131. <https://doi.org/10.1136/bmjopen-2023-079131>
13. Jenkins, J., Ferozuddin, A. A., Mourad, J., Abdulla, Z. Z., & Oviedo, A. (2024). Incongruence of Hemolysis, Elevated Liver Enzyme, Low-Platelet Count Syndrome (HELLP) and Preeclampsia Criteria in Pregnancy: Implications for Medical Education and Obstetrics Training. *Cureus*, *16*(8), e67211. <https://doi.org/10.7759/cureus.67211>
14. Gardikioti, A., Venou, T. M., Gavriilaki, E., Vetsiou, E., Mavrikou, I., Dinas, K., Daniilidis, A., & Vlachaki, E. (2022). Molecular Advances in Preeclampsia and HELLP Syndrome. *International journal of molecular sciences*, *23*(7), 3851. <https://doi.org/10.3390/ijms23073851>
15. Lüscher, B. P., Schoeberlein, A., Surbek, D. V., & Baumann, M. U. (2022). Hyperuricemia during Pregnancy Leads to a Preeclampsia-Like Phenotype in Mice. *Cells*, *11*(22), 3703. <https://doi.org/10.3390/cells11223703>
16. Burwick, R. M., Java, A., & Regal, J. F. (2025). The role of complement in normal pregnancy and preeclampsia. *Frontiers in immunology*, *16*, 1643896. <https://doi.org/10.3389/fimmu.2025.1643896>
17. Gardikioti, A., Venou, T. M., Gavriilaki, E., Vetsiou, E., Mavrikou, I., Dinas, K., Daniilidis, A., & Vlachaki, E. (2022). Molecular Advances in Preeclampsia and HELLP Syndrome. *International journal of molecular sciences*, *23*(7), 3851. <https://doi.org/10.3390/ijms23073851>
18. Chawla, N., Shah, H., Huynh, K., Braun, A., Wollocko, H., & Shah, N. C. (2023). The Role of Platelet-Activating Factor and Magnesium in Obstetrics and Gynecology: Is There Crosstalk between Pre-Eclampsia, Clinical Hypertension, and HELLP Syndrome?. *Biomedicines*, *11*(5), 1343. <https://doi.org/10.3390/biomedicines11051343>
19. Erez, O., Romero, R., Jung, E., Chaemsathong, P., Bosco, M., Suksai, M., Gallo, D. M., & Gotsch, F. (2022). Preeclampsia and eclampsia: the conceptual evolution of a syndrome. *American journal of obstetrics and gynecology*, *226*(2S), S786–S803. <https://doi.org/10.1016/j.ajog.2021.12.001>
20. Auger, N., Jutras, G., Paradis, G., Ayoub, A., Lewin, A., Maniraho, A., & Potter, B. J. (2025). Long-term risk of chronic liver disease after pre-eclampsia. *International journal of epidemiology*, *54*(3), dyaf072. <https://doi.org/10.1093/ije/dyaf072>
21. Man, A. W. C., Zhou, Y., Xia, N., & Li, H. (2023). Dietary supplements and vascular function in hypertensive disorders of pregnancy. *Pflugers Archiv : European journal of physiology*, *475*(7), 889–905. <https://doi.org/10.1007/s00424-023-02810-2>
22. Monrose, E., Bui, A., Rosenbluth, E., Dickstein, D., Acheampong, D., Sigel, K., Ferrara, L., & Kushner, T. (2021). Burden of Future Liver Abnormalities in Patients With Intrahepatic Cholestasis of Pregnancy. *The American journal of gastroenterology*, *116*(3), 568–575. <https://doi.org/10.14309/ajg.0000000000001132>
23. Dixon, P. H., Levine, A. P., Cebola, I., Chan, M. M. Y., Amin, A. S., Aich, A., Mozere, M., Maude, H., Mitchell, A. L., Zhang, J., NIHR BioResource, Genomics England Research Consortium Collaborators, Chambers, J., Syngelaki, A., Donnelly, J., Cooley, S., Geary, M., Nicolaidis, K., Thorsell, M., Hague, W. M., ... Williamson, C. (2022). GWAS meta-analysis of intrahepatic cholestasis of pregnancy implicates multiple hepatic genes and regulatory elements. *Nature communications*, *13*(1), 4840. <https://doi.org/10.1038/s41467-022-29931-z>
24. Obiegbusi, C. N., Dong, X. J., & Obiegbusi, S. C. (2023). Pregnancy outcomes following antenatal screening for intrahepatic cholestasis of pregnancy (ICP). *Taiwanese journal of obstetrics & gynecology*, *62*(6), 809–816. <https://doi.org/10.1016/j.tjog.2023.09.001>
25. Briley, A., & Cooper, M. (2024). ICP: A midwifery perspective. *Obstetric medicine*, *17*(3), 152–156. <https://doi.org/10.1177/1753495X241257709>

26. Axelsen, S. M., Schmidt, M. C., Kampmann, U., Grønbaek, H., & Fuglsang, J. (2024). The effect of twin pregnancy in intrahepatic cholestasis of pregnancy: A case control study. *Acta obstetrica et gynecologica Scandinavica*, 103(10), 1994–2001. <https://doi.org/10.1111/aogs.14928>
27. Yang, Z., Yao, M., Zhang, C., Hu, X., Zhong, Y., Xu, X., & Yin, J. (2022). Application of metabolomics in intrahepatic cholestasis of pregnancy: a systematic review. *European journal of medical research*, 27(1), 178. <https://doi.org/10.1186/s40001-022-00802-z>
28. Hague, W. B., Williamson, C., & Beuers, U. (2024). Intrahepatic cholestasis of pregnancy: Introduction and overview 2024. *Obstetric medicine*, 17(3), 138–143. <https://doi.org/10.1177/1753495X241265772>
29. Zhang, P., Tan, Z., Li, C., Han, Z., Zhou, J., & Yin, Y. (2024). The correlation between serum total bile acid and adverse perinatal outcomes in pregnant women with intrahepatic cholestasis of pregnancy (ICP) and non-ICP hypercholanemia of pregnancy. *Annals of medicine*, 56(1), 2331059. <https://doi.org/10.1080/07853890.2024.2331059>
30. Sahni, A., & Jogdand, S. D. (2022). Effects of Intrahepatic Cholestasis on the Foetus During Pregnancy. *Cureus*, 14(10), e30657. <https://doi.org/10.7759/cureus.30657>
31. Hu, Q., & Yu, H. (2024). Unexplored topics in intrahepatic cholestasis of pregnancy: A review and bibliometric analysis. *Medicine*, 103(42), e39972. <https://doi.org/10.1097/MD.00000000000039972>
32. Ovadia, C., Sajous, J., Seed, P. T., Patel, K., Williamson, N. J., Attilakos, G., Azzaroli, F., Bacq, Y., Batsry, L., Broom, K., Brun-Furrer, R., Bull, L., Chambers, J., Cui, Y., Ding, M., Dixon, P. H., Estiú, M. C., Gardiner, F. W., Geenes, V., Grymowicz, M., ... Williamson, C. (2021). Ursodeoxycholic acid in intrahepatic cholestasis of pregnancy: a systematic review and individual participant data meta-analysis. *The lancet. Gastroenterology & hepatology*, 6(7), 547–558. [https://doi.org/10.1016/S2468-1253\(21\)00074-1](https://doi.org/10.1016/S2468-1253(21)00074-1)
33. Bartsch, E., Medcalf, K. E., Park, A. L., Ray, J. G., & High Risk of Pre-eclampsia Identification Group (2016). Clinical risk factors for pre-eclampsia determined in early pregnancy: systematic review and meta-analysis of large cohort studies. *BMJ (Clinical research ed.)*, 353, i1753. <https://doi.org/10.1136/bmj.i1753>
34. Denison, F. C., Aedla, N. R., Keag, O., Hor, K., Reynolds, R. M., Milne, A., Diamond, A., & Royal College of Obstetricians and Gynaecologists (2019). Care of Women with Obesity in Pregnancy: Green-top Guideline No. 72. *BJOG : an international journal of obstetrics and gynaecology*, 126(3), e62–e106. <https://doi.org/10.1111/1471-0528.15386>
35. Bicocca, M. J., Mendez-Figueroa, H., Chauhan, S. P., & Sibai, B. M. (2020). Maternal Obesity and the Risk of Early-Onset and Late-Onset Hypertensive Disorders of Pregnancy. *Obstetrics and gynecology*, 136(1), 118–127. <https://doi.org/10.1097/AOG.0000000000003901>
36. Rana, S., Lemoine, E., Granger, J. P., & Karumanchi, S. A. (2019). Preeclampsia: Pathophysiology, Challenges, and Perspectives. *Circulation research*, 124(7), 1094–1112. <https://doi.org/10.1161/CIRCRESAHA.118.313276>
37. Phipps, E. A., Thadhani, R., Benzing, T., & Karumanchi, S. A. (2019). Pre-eclampsia: pathogenesis, novel diagnostics and therapies. *Nature reviews. Nephrology*, 15(5), 275–289. <https://doi.org/10.1038/s41581-019-0119-6>
38. Williamson, C., & Geenes, V. (2014). Intrahepatic cholestasis of pregnancy. *Obstetrics and gynecology*, 124(1), 120–133. <https://doi.org/10.1097/AOG.0000000000000346>
39. Wikström Shemer, E., Marschall, H. U., Ludvigsson, J. F., & Stephansson, O. (2013). Intrahepatic cholestasis of pregnancy and associated adverse pregnancy and fetal outcomes: a 12-year population-based cohort study. *BJOG : an international journal of obstetrics and gynaecology*, 120(6), 717–723. <https://doi.org/10.1111/1471-0528.12174>
40. Woudstra, D. M., Chandra, S., Hofmeyr, G. J., & Dowswell, T. (2010). Corticosteroids for HELLP (hemolysis, elevated liver enzymes, low platelets) syndrome in pregnancy. *The Cochrane database of systematic reviews*, (9), CD008148. <https://doi.org/10.1002/14651858.CD008148.pub2>
41. Magee, L. A., Pels, A., Helewa, M., Rey, E., von Dadelszen, P., & Canadian Hypertensive Disorders of Pregnancy (HDP) Working Group (2014). Diagnosis, evaluation, and management of the hypertensive disorders of pregnancy. *Pregnancy hypertension*, 4(2), 105–145. <https://doi.org/10.1016/j.preghy.2014.01.003>
42. Ovadia, C., Seed, P. T., Sklavounos, A., Geenes, V., Di Ilio, C., Chambers, J., Kohari, K., Bacq, Y., Bozkurt, N., Brun-Furrer, R., Bull, L., Estiú, M. C., Grymowicz, M., Gunaydin, B., Hague, W. M., Haslinger, C., Hu, Y., Kawakita, T., Kebapcilar, A. G., Kebapcilar, L., ... Williamson, C. (2019). Association of adverse perinatal outcomes of intrahepatic cholestasis of pregnancy with biochemical markers: results of aggregate and individual patient data meta-analyses. *Lancet (London, England)*, 393(10174), 899–909. [https://doi.org/10.1016/S0140-6736\(18\)31877-4](https://doi.org/10.1016/S0140-6736(18)31877-4)
43. Abalos, E., Duley, L., Steyn, D. W., & Gialdini, C. (2018). Antihypertensive drug therapy for mild to moderate hypertension during pregnancy. *The Cochrane database of systematic reviews*, 10(10), CD002252. <https://doi.org/10.1002/14651858.CD002252.pub4>
44. Chappell, L. C., Bell, J. L., Smith, A., Linsell, L., Juszcak, E., Dixon, P. H., Chambers, J., Hunter, R., Dorling, J., Williamson, C., Thornton, J. G., & PITCHES study group (2019). Ursodeoxycholic acid versus placebo in women

- with intrahepatic cholestasis of pregnancy (PITCHES): a randomised controlled trial. *Lancet (London, England)*, 394(10201), 849–860. [https://doi.org/10.1016/S0140-6736\(19\)31270-X](https://doi.org/10.1016/S0140-6736(19)31270-X)
45. Woudstra, D. M., Chandra, S., Hofmeyr, G. J., & Dowswell, T. (2010). Corticosteroids for HELLP (hemolysis, elevated liver enzymes, low platelets) syndrome in pregnancy. *The Cochrane database of systematic reviews*, (9), CD008148. <https://doi.org/10.1002/14651858.CD008148.pub2>
 46. Haram, K., Svendsen, E., & Abildgaard, U. (2009). The HELLP syndrome: clinical issues and management. A Review. *BMC pregnancy and childbirth*, 9, 8. <https://doi.org/10.1186/1471-2393-9-8>
 47. Bellamy, L., Casas, J. P., Hingorani, A. D., & Williams, D. J. (2007). Pre-eclampsia and risk of cardiovascular disease and cancer in later life: systematic review and meta-analysis. *BMJ (Clinical research ed.)*, 335(7627), 974. <https://doi.org/10.1136/bmj.39335.385301.BE>
 48. Brown, M. C., Best, K. E., Pearce, M. S., Waugh, J., Robson, S. C., & Bell, R. (2013). Cardiovascular disease risk in women with pre-eclampsia: systematic review and meta-analysis. *European journal of epidemiology*, 28(1), 1–19. <https://doi.org/10.1007/s10654-013-9762-6>
 49. Marschall, H. U., Wikström Shemer, E., Ludvigsson, J. F., & Stephansson, O. (2013). Intrahepatic cholestasis of pregnancy and associated hepatobiliary disease: a population-based cohort study. *Hepatology (Baltimore, Md.)*, 58(4), 1385–1391. <https://doi.org/10.1002/hep.26444>
 50. Rana, S., Powe, C. E., Salahuddin, S., Verlohren, S., Perschel, F. H., Levine, R. J., Lim, K. H., Wenger, J. B., Thadhani, R., & Karumanchi, S. A. (2012). Angiogenic factors and the risk of adverse outcomes in women with suspected preeclampsia. *Circulation*, 125(7), 911–919. <https://doi.org/10.1161/CIRCULATIONAHA.111.054361>

