Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/mfrm8v65

ADVERSE FETOMATERNAL OUTCOMES IN WOMEN WITH HELLP SYNDROME

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ABSTRACT

Background: HELLP syndrome complicates 0.5 to 0.9% of all pregnancies and 10-20 % cases of severe preeclampsia. Maternal mortality in women with HELLP syndrome has been reported as 1 to 25%. 70% of cases of HELLP syndrome occur antenatally with highest incidence between 27th – 37th weeks of gestation while 10 % occurs before 27th week and 20 % after 37th week of gestation.

Objective: To determine the different adverse fetomaternal outcomes in women with HELLP syndrome.

Material and Methods: This descriptive study was conducted in the Gynae & Obstetrics Unit at LRH MTI Peshawar in collaboration with technical help of Karachi Metropolitan University from 10th October 2020 to 30th April 2021. A total of 114 antenatal women in reproductive age group of any parity with HELLP syndrome were included in the study. Adverse maternal outcomes were analyzed in terms of: DIC, acute renal failure, placental abruption, eclampsia, blood or blood products transfusion, pulmonary edema and maternal death. Adverse fetal outcomes were analyzed in terms of intrauterine fetal demise, preterm delivery, NICU admission and early neonatal death.

Results: Adverse fetomaternal outcomes were disseminated intravascular coagulation 17.5%, acute renal failure 28.1%, placental abruption 12.3%, eclampsia 14%, blood products transfusion 61.4%, pulmonary edema 11.4%, maternal death 7%, intrauterine fetal demise 25.4%, preterm delivery 24.6%, NICU admission 33.3% and neonatal death was 7.9%.

Conclusion: The result of present study shows that HELLP syndrome considerably affects the maternal and perinatal outcome in pregnancy.

Keywords: Pregnancy, HELLP syndrome, Adverse fetomaternal outcomes

INTRODUCTION

HELLP syndrome, a term described by Weinstein in 1982 is an acronym for hemolysis, elevated liver enzymes and low platelet count.[1] It mostly co-exists with severe Pre-Eclampsia (70-80%) but it may occur even in its absence. It is a serious problem, predisposing mother and her fetus to many adverse outcomes.[1,2] HELLP syndrome complicates 0.5 to 0.9% of all pregnancies and 10-20 % cases of severe preeclampsia. Maternal mortality in women with HELLP syndrome has been reported as 1 to 25%. 70% of cases of HELLP syndrome occur antenatally with highest incidence between 27th – 37th weeks of gestation while 10 % occurs before 27th week and 20 % after 37th week of gestation[3]. Postnatally 30% cases occur most often up to 48 hours but may take up to 7 days.[2] Clinical symptoms include pain right upper quadrant of abdomen or pain epigastrium, nausea, vomiting, headache, visual symptoms or just flu-like viral symptoms.[4,5] Hypertension, edema and proteinuria are present; hepatomegaly and easy bruising may also occur in some women. Diagnoses of HELLP syndrome requires triad of hemolysis, liver changes characterized by raised AST and ALT levels and thrombocytopenia.2 Diagnosis is based upon Tennessee classification.

A study published in the Journal of maternal, fetal and neonatal medicine in 2017 studied maternal complications of HELLP syndrome in terms of transfusion requirement (38%), DIC (7%), eclampsia (11.1%), placental abruption (11.1%), ARF (6.4%), pulmonary edema (1.9%) and maternal death (0.6%).[6] A study published in International Journal of Reproduction, Contraception, Obstetrics and Gynaecology showed that severe maternal complications in patients with HELLP syndrome included eclampsia (23.3%), acute kidney injury (6.67%), placental abruption (10%), DIC (3.34%). In the study live birth rate was recorded as 70%, intrauterine fetal demise as 11.7%, NICU admission rate was 36.6% and early neonatal death rate was 8.3%. Majority of the patients (68%) had preterm deliveries either induced or underwent caesarean section.[7] International Journal of Reproduction, Contraception, Obstetrics and Gynaecology includes another study on HELLP syndrome - Maternal and Perinatal Outcome showing the incidence of HELLP syndrome as 14.7%, 60% maternal morbidity, 6.6% maternal mortality and 46.6% of perinatal morbidity and mortality each. In the study live birth rate was 53.3% and still birth rate (IUFD) was13.3%. The major cause of perinatal mortality was prematurity (86.6%).[8] A study published in 2011 in the journal of "Pregnancy Hypertension: An International Journal of Women's cardiovascular health" showed that the rate of maternal complications in patients with HELLP syndrome was 43% and perinatal mortality was 14.1%.[9] The study highlights that the patients who presented with HELLP syndrome in early puerperium had higher number of maternal complications.[10] HELLP syndrome is a serious obstetrical complication which can lead to different adverse maternal and fetal outcomes, even death of the mother and her baby[11]. There are few studies conducted on HELLP syndrome in our country. A very limited data is available on the complications of HELLP syndrome in our local population, while we observe many especially pulmonary edema. Surprisingly, pulmonary edema has been reported very less in previous studies. We aim to study the different adverse maternal and adverse fetal outcomes in patients who present with HELLP syndrome in our local area and compare their incidences with previous studies (especially pulmonary edema) and thus to report their burden in our local population. This will also highlight the most frequent adverse outcome and may help us in adopting proper measures to prevent the patient from further complications, presenting with HELLP syndrome.

MATERIALS AND METHODS

This descriptive study was conducted at the Department of Gynecology & Obstetrics, Unit Lady Reading Hospital (LRH), MTI Peshawar in collaboration with technical help of Karachi Metropolitan University. The sample size consisted of 114 participants, calculated using the WHO sample size calculator V.2 (1.1), with a 4.5% margin of error and a 95% confidence level, based on an anticipated proportion of 6.4% for the incidence of acute renal failure (ARF) as an adverse maternal outcome. The study was conducted over a period from October 10, 2020, to April 30, 2021. Inclusion criteria included antenatal women in the reproductive age group (15 to 49 years, as per WHO guidelines), of any parity, with a gestational period between 24 and 42 weeks, diagnosed with HELLP syndrome based on the Tennessee classification. The exclusion criteria involved women with a gestational

period of fewer than 24 weeks, as well as those with conditions such as viral hepatitis, cholecystitis, pancreatitis, systemic lupus erythematosus, immune thrombocytopenic purpura, chronic liver disease, cholestasis of pregnancy, thrombocytopenia of pregnancy, hemolytic uremic syndrome, or renal disease.

Data Collection and Procedure:
The study was conducted in Gynae Obstetrics Unit Lady Reading Hospital Peshawar after approval from hospital ethical and research committee. Patients with hypertensive disorders of pregnancy were admitted. After taking history, blood for baseline and specific investigations were sent. Those who fall into the inclusion criteria developing HELLP syndrome diagnosed on the basis of Tennessee classification were entered into the study after verbal and written consent. Basic demographics like age, gestational age, parity, weight were recorded. Patients included in the study were followed for developing maternal and fetal complications. Adverse maternal outcomes were analyzed in terms of: DIC, acute renal failure, placental abruption, eclampsia, blood or blood products transfusion, pulmonary edema and maternal death. Adverse fetal outcomes were analyzed in terms of intrauterine fetal demise, preterm delivery, NICU admission and early neonatal death. Data was noted as per operational definition on especially designed proforma.

Data Analysis Procedure:
Data was collected on pre-design proforma. Data was analyzed using SPSS version 20. Descriptive statistics were computed for quantitative variables and qualitative variables, mean and standard deviation was calculated for quantitative variables like age, gestational age, BMI, parity, birthweight. Frequency and percentages were calculated for qualitative variables like maternal and fetal outcomes. Effect modifiers like age, parity, gestational age were controlled through stratification, post stratification chi square test was applied keeping p value $\leq$0.05 as significant.

RESULTS
In this study population of 114 participants, the mean maternal age was 27.6 years (±4.31). The average gestational age at delivery was 34.3 weeks (±5.94), with a mean BMI of 25.1 kg/m² (±1.32). The mean parity was 1.46 (±1.58), indicating that on average, the participants had slightly more than one previous pregnancy.
Adverse maternal outcomes were notable, with 32 cases (28.1%) of renal failure and 14 cases (12.3%) of placental abruption. Eclampsia was observed in 16 participants (14%), and a significant number of patients, 70 (61.4%), required blood products transfusion. Pulmonary edema occurred in 13 cases (11.4%), and maternal death was recorded in 8 cases (7%).
Neonatal outcomes also raised concerns. There were 29 cases (25.4%) of intrauterine fetal demise, and 28 cases (24.6%) of preterm delivery. Additionally, 38 newborns (33.3%) required NICU admission. Birth weight averaged 2.24 kg (±1.02), with 20 newborns (17.5%) having a low birth weight. Unfortunately, neonatal death occurred in 9 cases (7.9%). **Table 1**
Among younger women aged 15-30 years, the incidence of Disseminated Intravascular Coagulation (DIC) was 17% (16 cases), compared to 20% (4 cases) in those aged 31-49 years. However, gestational age had a more profound impact, with 32.8% (19 cases) of DIC occurring in women delivering at 37-42 weeks (p=0.000). Acute Renal Failure was more common in the 31-49 age group at 40% (8 cases) versus 25.5% (24 cases) in the younger group, but was most prevalent in those delivering at 37-42 weeks (51.7%, 30 cases, p=0.000). Placental abruption was similarly distributed across age and parity, with around 12% occurrence in both groups, while eclampsia was significantly more common in younger women (17%, 16 cases, p=0.047) and those delivering preterm at 24-36 weeks (28.6%, 16 cases, p=0.000). Blood product transfusion was required in 61.4% (70 cases) overall, with no significant difference between age groups, though younger women experienced slightly lower rates of pulmonary edema (11.7%, 11 cases) compared to older women (10%, 2 cases). Maternal deaths were only observed in the younger group (8.5%, 8 cases), while Intrauterine Fetal Demise (IUFD) was higher in the younger group at 25.5% (24 cases), and gestational age again played

a significant role, with 48.2% (27 cases) of IUFD occurring in those delivering preterm (p=0.000). Preterm delivery itself was more common in the younger group at 26.6% (25 cases), while NICU admissions were notably higher among older women at 50% (10 cases) and those with higher parity (53.3%, 8 cases). Neonatal death rates were low across all groups, with the highest incidence in younger women (8.5%, 8 cases), and again gestational age played a significant role, with deaths occurring primarily in those born at 37-42 weeks (15.5%, 9 cases, p=0.002). **Table 2**

Table – 1: Maternal and Neonatal Outcomes in the Study Population, Including Mean Age, Gestational Age, BMI, Parity, and Adverse Events (n=114)

Variables	Frequency	Percentage	Mean±SD
Age(years)	-	-	27.614±4.31
Gestational age (weeks)			34.307±5.94
BMI (Kg/m^2)			25.114±1.32
Parity			1.456±1.58
Birth Weight (Kg)	20	17.5%	2.236±1.02
Renal Failure	32	28.1%	-
Placental Abruption	14	12.3%	-
Eclampsia	16	14%	-
Blood Products Transfusion	70	61.4%	-
Pulmonary Edema	13	11.4%	-
Maternal Death	08	07%	-
Intrauterine Fetal Demise	29	25.4%	-
Preterm Delivery	28	24.6%	-
NICU Admission	38	33.3%	-
Neonatal Death	09	7.9%	-

Table- 2: The relationship between age, parity, and gestational age with various maternal and neonatal outcomes, including Disseminated Intravascular Coagulation, Acute Renal Failure, Placental Abruption, Eclampsia, Blood Product Transfusion, Pulmonary Edema, Maternal Death, Intrauterine Fetal Demise, Preterm Delivery, NICU Admission, and Neonatal Death

Age (years)	**Disseminated Intravascular Coagulation**		**p-value**
	Yes	No	
15-30	16(17%)	78(83%)	0.750
31-49	4(20%)	16(80%)	
Total	20(17.5%)	94(82.5%)	
Parity			**p-value**
	Yes	No	
0-3	16(16.2%)	83(83.3%)	0.319
>3	4(26.7%)	11(73.3%)	
Total	20(17.5%)	94(82.5%)	
Gestational age (weeks)			**p-value**
	Yes	No	
24-36	1(1.8%)	55(98.2%)	0.000
37-42	19(32.8%)	39(67.q%)	
Total	20(17.5%)	94(82.5%)	
Age (years)	**Acute Renal Failure**		**p-value**
	Yes	No	
15-30	24(25.5%)	70(74.5%)	0.191
31-49	8(40%)	12(60%)	
Total	32(28.1%)	82(71.9%)	
Parity			**p-value**
	Yes	No	

0-3	27(27.3%)	72(72.7%)	0.626
>3	5(33.3%)	10(66.7%)	
Total	32(28.1%)	82(71.9%)	
Gestational age (weeks)			**p-value**
	Yes	No	
24-36	2(3.6%)	54(96.4%)	0.000
37-42	30(51.7%)	28(48.3%)	
Total	32(28.1%)	82(71.9%)	
Age (years)	**Placental Abruption**		**p-value**
	Yes	No	
15-30	12(12.8%)	82(87.2%)	0.732
31-49	2(10%)	18(90%)	
Total	14(12.3%)	100(87.7%)	
Parity			
0-3	12(12.1%)	87(87.9%)	0.894
>3	2(13.3%)	13(86.7%)	
Total	14(12.3%)	100(87.7%)	
Gestational age (weeks)			
24-36	7(12.5%)	49(87.5%)	0.944
37-42	7(12.1%)	51(87.9%)	
Total	14(12.3%)	100(87.7%)	
Age (years)	**Eclampsia**		**p-value**
	Yes	No	
15-30	16(17%)	78(83%)	0.047
31-49	0(0%)	20(100%)	
Total	16(14%)	98(86%)	
Parity			
0-3	16(16.2%)	83(83.8%)	0.093
>3	0(0%)	15(100%)	
Total	16(14%)	98(86%)	
Gestational age (weeks)			
24-36	16(28.6%)	40(71.4%)	0.000
37-42	0(0%)	58(100%)	
Total	16(14%)	98(86%)	
Age (years)	**Blood Product Transfusion**		**p-value**
	Yes	No	
15-30	57(60.6%)	37(39.4%)	0.179
31-49	13(65%)	7(35%)	
Total	70(61.4%)	44(38.6%)	
Parity			
0-3	61(61.6%)	38(38.4%)	0.905
>3	9(60%)	6(40%)	
Total	70(61.4%)	44(38.6%)	
Gestational age (weeks)			
24-36	33(58.9%)	23(41.1%)	0.594
37-42	37(63.8%)	21(36.2%)	
Total	70(61.4%)	44(38.6%)	
Age (years)	**Pulmonary Edema**		**p-value**
	Yes	No	
15-30	11(11.7%)	83(88.3%)	0.828
31-49	2(10%)	18(90%)	
Total	13(11.4%)	101(88.6%)	
Parity			
0-3	12(12.1%)	87(87.9%)	0.536
>3	1(6.7%)	14(93.2%)	

Total	13(11.4%)	101(88.6%)	
Gestational age (weeks)			
24-36	3(5.4%)	53(94.6%)	0.046
37-42	10(17.2%)	48(82.8%)	
Total	13(11.4%)	101(88.6%)	
Age (years)	**Maternal Death**		**p-value**
	Yes	No	
15-30	8(8.5%)	86(91.5%)	0.176
31-49	0(0%)	20(100%)	
Total	8(7%)	106(93%)	
Parity			
0-3	8(8.1%)	91(91.9%)	0.254
>3	0(0%)	15(100%)	
Total	8(7%)	106(93%)	
Gestational age (weeks)			
24-36	6(10.7%)	50(89.3%)	0.129
37-42	2(3.4%)	56(96.6%)	
Total	8(7%)	106(93%)	
Age (years)	**Intrauterine Fetal Demise**		**p-value**
	Yes	No	
15-30	24(25.5%)	20(74.5%)	0.960
31-49	5(25%)	15(75%)	
Total	29(25.4%)	85(74.6%)	
Parity			
0-3	26(26.3%)	73(73.7%)	0.604
>3	3(20%)	12(80%)	
Total	29(25.4%)	85(74.6%)	
Gestational age (weeks)			
24-36	27(48.2%)	29(51.8%)	0.000
37-42	2(3.4%)	56(96.6%)	
Total	29(29.4%)	85(74.6%)	
Age (years)	**Preterm Delivery**		**p-value**
	Yes	No	
15-30	25(26.6%)	69(73.4%)	0.274
31-49	3(15%)	17(85%)	
Total	28(24.6%)	86(75.4%)	
Parity			
0-3	26(26.3%)	73(73.7%)	0.278
>3	2(13.3%)	13(86.7%)	
Total	28(24.6%)	86(75.4%)	
Gestational age (weeks)			
24-36	28(50%)	28(50%)	0.000
37-42	0(0%)	58(100%)	
Total	28(24.6%)	86(75.4%)	
Age (years)	**NICU Admission**		**p-value**
	Yes	No	
15-30	28(29.8%)	66(70.2%)	0.082
31-49	10(50%)	10(50%)	
Total	38(33.3%)	76(66.7%)	
Parity			
0-3	30(30.3%)	69(69.7%)	0.078
>3	8(53.3%)	7(46.7%)	
Total	38(33.3%)	76(66.7%)	
Gestational age (weeks)			
24-36	8(14.3%)	48(85.7%)	0.000

37-42	30(51.7%)	28(48.3%)	
Total	38(33.3%)	76(66.7%)	
Age (years)	**Neonatal Death**		**p-value**
	Yes	No	
15-30	8(8.5%)	86(91.5%)	0.597
31-49	1(5%)	19(95%)	
Total	9(7.9%)	105(92.1%)	
Parity			
0-3	8(8.1%)	91(91.9%)	0.850
>3	1(6.7%)	14(93.3%)	
Total	9(7.9%)	105(92.1%)	
Gestational age (weeks)			
24-36	0(0%)	56(100%)	0.002
37-42	9(15.5%)	49(84.5%)	
Total	9(7.9%)	105(92.1%)	

DISCUSSION

HELLP syndrome is a serious complication of pregnancy associated with increased maternal morbidity and mortality. The purpose of screening and management of HELLP syndrome is to prevent intrauterine death, eclampsia, acute renal failure, DIC, and decrease incidence of maternal and perinatal morbidity and mortality. The result of the present study shows that 62.5% of patients were unregistered and HELLP was more common in 15-30 years age group accounting 82.5%.

In our study, Adverse fetomaternal outcomes were disseminated intravascular coagulation 17.5%, acute renal failure 28.1%, placental abruption 12.3%, eclampsia 14%, blood products transfusion 61.4%, pulmonary edema 11.4%, maternal death 7%, intrauterine fetal demise 25.4%, preterm delivery 24.6%, NICU admission 33.3% and neonatal death was 7.9%. A study published in the Journal of maternal, fetal and neonatal medicine in 2017 studied maternal complications of HELLP syndrome in terms of transfusion requirement (38%), DIC (7%), eclampsia (11.1%), placental abruption (11.1%), ARF (6.4%), pulmonary edema (1.9%) and maternal death (0.6%).[6]

A study published in International Journal of Reproduction, Contraception, Obstetrics and Gynaecology showed that severe maternal complications in patients with HELLP syndrome included eclampsia (23.3%), acute kidney injury (6.67%), placental abruption (10%), DIC (3.34%). In the study live birth rate was recorded as 70%, intrauterine fetal demise as 11.7%, NICU admission rate was 36.6% and early neonatal death rate was 8.3%. Majority of the patients (68%) had preterm deliveries either induced or underwent caesarean section.[7]

International Journal of Reproduction, Contraception, Obstetrics and
Gynaecology includes another study on HELLP syndrome - Maternal and Perinatal Outcome showing the incidence of HELLP syndrome as 14.7%, 60% maternal morbidity, 6.6% maternal mortality and 46.6% of perinatal morbidity and mortality each. In the study live birth rate was 53.3% and still birth rate (IUFD) was13.3%. The major cause of perinatal mortality was prematurity (86.6%).[8]

A study published in 2011 inthe journal of "Pregnancy Hypertension: An International Journal of Women's cardiovascular health" showed that the rate of maternal complications in patients with HELLP syndrome was 43% and perinatal mortality was 14.1%. The study highlights that the patients who presented with HELLP syndrome in early puerperium had higher number of maternal complications.[10]

Intrauterine death and prematurity were most common complications associated with this study whereas study by Kaur AP et al, had IUGR (35.2%) and prematurity (61.5%) as the most common neonatal complications subsequently.[12]

Most common complication in this study were acute renal failure (28.1%) and DIC (17.5%). Study by Durugkar K et al and Kaur AP et al showed most common complications to be of DIC (14.1%) and eclampsia (21.1%) subsequently.[12]

Patients with DIC required PCV, FFP, PRC, cryoprecipitate transfusions. All the patients with PPH were managed conservatively with uterotonics and blood transfusions. As 67.5% patients in this study

were belonged to lower socio-economic class and anemic and 87.5% patients had platelet count less than 1, 00,000 so blood and blood component requirements is higher in this study (61.4%).
All the patients with eclampsia were given full dose MgSO4 and after stabilization they had undergone induction of labour. Patients with pulmonary edema and MODS required ICU admission and ventilator support. Maternal mortality occurred in 7% cases showing HELLP syndrome to be a very fatal disease in pregnancy.

CONCLUSION

The result of present study shows that HELLP syndrome considerably affects the maternal and perinatal outcome in pregnancy. It has a very unpredictable course and outcome. It needs to be diagnosed as early as possible. The study suggests that all patients with hypertension should be screened and should have a complete blood count, platelet count and liver function tests.
Once diagnosis of HELLP syndrome has been made, it warrants aggressive intervention with control of blood pressure, anti-seizure prophylaxis, corticosteroid treatment for fetal lung maturity and expeditious delivery. In this study most of the patients required blood component transfusions and patients with organ failure required ICU support and/or haemodialysis. So, patients diagnosed with HELLP syndrome should be managed at a tertiary care centre where all medical facilities are available. Thus, an early diagnosis and early initiation of treatment significantly helps in improving maternal morbidity and mortality of patients with HELLP syndrome.

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