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St. Paul's Hospital Millennium Medical College

ST PAUL'S HOSPITAL MILLENNIUM MEDICAL COLLEGE
DEPARTMENT OF OBSTETRICS AND GYNECOLOGY

RESEARCH THESIS FOR SUMBMISSION

PREGNANCY OUTCOME OF HEMOLYSIS ELEVATED LIVER
ENZYMES AND LOW PLATELETE COUNT SYNDROME AT
TEACHING HOSPITAL, ADDIS ABABA, ETHIOPIA.

INVESTIGATOR: MUHUDIN ARUSI (MD, OBGYN RESIDENT)

ADVISORS: WONDIMU GUDU (MD, MPH, FM FELLOW)
KNIFE HAILE (MPH)

MAY, 2020 G.C.

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List of abbreviations

A.A-Addis Ababa

ACS-antenatal corticosteroids

ACOG-American College of Obstetrics and Gynecology

ANC- antenatal care

AOR-adjusted odd ratio

APGAR- Appearance, pulse, grimace, activity, respiration

CBC-complete blood count

CI- confidence interval

DIC- disseminated intravascular coagulation

END-early neonatal death

FHB-fetal heart beat

HEELP- **H** = Hemolysis, **EL** = Elevated Liver enzymes and **LP** = Low Platelets

IRB-institutional review board

IUGR-intrauterine growth restriction

IUFD-intrauterine fetal death

IVH-intraventricular hemorrhage

LBW- Low birth weight

LDH-lactate dehydrogenase

NICU -Neonatal intensive care unit.

RDS-respiratory distress syndrome

SGPT- serum glutamic pyruvic transaminase

SGOT- serum glutamic oxaloacetic transaminase

SPHMMC-Saint Paulo's Hospital Millennium Medical College.

SPSS-Statistical package of social science.

U/A- urine analysis

Abstract

Background: HELLP syndrome is a life-threatening complication in pregnancy that occur in 0.5 to 0.9% of all pregnancies and in 10–20% of cases with severe preeclampsia/eclampsia. It is associated with increased rate of both maternal and perinatal complications.

Objectives: The aim of this study was to assess maternal and perinatal outcome of HELLP syndrome at teaching Hospital in Ethiopia.

Methods: This was a 2-year retrospective based chart review of all women diagnosed with HELLP syndrome and delivered at Saint Paul's Hospital Millennium Medical College in obstetrics and gynecology department in A.A, Ethiopia. Data entry and analysis was made using SPSS version 23 software. Frequency and percentages were calculated and presented in tables. Bivariate and multivariate analysis were used to see association and control confounding variables. Ethical clearance was obtained from the IRB of SPHMMC.

Results: There were 20,111 deliveries during the study period, of which 0.57% (115) of the mothers developed HELLP Syndrome. Among these ,101 women fulfilling the inclusion criteria were included and their records were analyzed retrospectively. 36.6% of the cases were in the age group of 27-31 years. Majority 60.4% of the cases were primiparous while 39.6% of them were multiparous. Most of the mothers,92% were referred cases and 63.4% were from Addis Ababa. 89.1% cases occurred during antepartum and 10.9% after delivery. The mean gestational age was 33.40 ± 4.474 wks. 68% had Partial and 32% of them had complete HELLP syndrome. Caesarean and vaginal delivery rate were 47.5% and 52.5% respectively. There was no maternal death. 30.7% (31/101) of the mothers developed maternal complications. Acute kidney injury was the most frequent maternal complication 24.8%, followed by pulmonary Oedema 11.9%. Mothers with complete HELLP syndrome and when it arises in postpartum period were found to have significant influence on maternal morbidity with p -value of 0.03 for both, AOR= 0.223 (95% CI= 0.018-0.863) and AOR =0.360 (95% CI= 0.144-0.901) respectively. The were 108 infants delivered :70.4% were preterm while 29.6% were term deliveries. Twenty-three (21.3%) babies were IUGR. 78.7 % were born alive,12% were intrapartum deaths and 9.3% were still births. 9.3% were ENDs making over all overall perinatal mortality of 30.6%(33/108).

Conclusion: The incidence of HELLP syndrome in this study was low with significant maternal morbidity and perinatal complications. It needs further prospective study with large sample size in country level.

Keywords: HELLP syndrome, Maternal morbidity, Perinatal morbidity, perinatal mortality

Introduction

Background

HELLP syndrome was first described in 1982 by Weinstein and the term HELLP refers to an acronym used to describe the clinical condition that leads to H = hemolysis, EL = elevated liver enzymes and LP = low platelets (1). It occurs in about 0.5-0.9% of all pregnancies and in 10- 20% of cases with severe Preeclampsia and Eclampsia. In about 70% of the cases this syndrome develops before delivery with, average onset often occurs between 27 and 37 gestational weeks, while in about 30% of the cases develops after delivery with a peak frequency within the first 48 hours after birth(2, 3).

HELLP syndrome has variable clinical presentation causing delayed in diagnosis. The typical clinical symptoms are right upper quadrant abdomen or epigastric pain, nausea and vomiting. Majority of women with this syndrome have hypertension and proteinuria, which may be absent in 10-20% of the cases and in more than 50% of cases, excessive weight gain and the presence of generalized edema are signs of HELLP development. Patients may also have a general malaise or viral-like symptoms, which makes the HELLP syndrome clinical diagnosis a challenge. Although variable, the manifestation of this syndrome is fast. Pregnant women with such nonspecific complaints in second half of pregnancy should be considered as HELLP syndrome until proven otherwise with immediate work up (2-4).

The diagnosis of HELLP syndrome requires the presence of symptomatic triad, hemolysis, hepatic changes with increased enzymes and thrombocytopenia, as well as severe symptoms, as general malaise, with or without vomiting, pain in the right upper quadrant of the abdomen, excessive weight gain and the presence of generalized edema. Diagnosis of the complete form of the HELLP syndrome requires the presence of all 3 major components, while partial or incomplete HELLP syndrome consists of only 1 or 2 elements of the triad (H or EL or LP) (2,3). This syndrome, mainly in complete form, is associated with severe clinical complications that may lead to both maternal and fetal death, thus it is necessary to have a faster diagnosis and appropriate clinical intervention. Questions however, remain regarding its management; timing and method of delivery are important. There is a consensus of opinion that prompt delivery is indicated if such syndrome develops beyond 34 weeks' gestation or earlier if obvious multiorgan dysfunctions, DIC, liver infarction or hemorrhage, renal failure, suspected abruption, uncontrollable hypertension or nonreassuring fetal status are apparent. All other cases require administration of magnesium

sulfate, steroids and delivery within 24 hours after the last steroid dose for lung maturity. Mode of deliver is based on maternal and fetal condition, gestational age and bishops score (9).

Statement of the problem

Despite the development of tertiary care facilities, growth of the field of maternal-fetal medicine, advanced blood banking techniques, and sophisticated intensive care capabilities for both maternal and neonatal patients, maternal, perinatal morbidity and mortality continue to occur in association with HELLP syndrome throughout world.

In settings where continuum of preeclampsia /eclampsia is common and expectant management of early-onset pre-eclampsia is not the norm the opportunity for pre-eclampsia to evolve into HELLP syndrome, important predictors of further organ dysfunctions (morbidity) and mortality, is abbreviated (10). However, due to absence of epidemiological information in many developing countries; lack of effort and capacity for data collection and reporting of vital statistics, the exact incidence and associated morbidity and mortality from HELLP syndrome is unknown. Moreover, at present there are few published studies with an adequate sample size to describe maternal and perinatal outcomes in HELLP syndrome. Most of these studies are based on either cross-sectional or, retrospective analyses cohorts collected in hospital(single-institution) after a diagnosis of pre-eclampsia has been made and may not be representative of the HELLP syndrome population as a whole.

HELLP syndrome is the most frequent cited complication of sever preeclampsia in Africa including Ethiopia(17,18) . Although there are no representative community based data on its magnitude, preeclampsia/ eclampsia is one of the major maternal health problems in Ethiopia. The relative contribution of eclampsia for maternal deaths in hospital studies has progressively increased from 6.5 % in 1983 to 35.7% in 2008(22). In the most recent national survey (2016), preeclampsia was the third leading cause of death accounting for 11% of all direct maternal deaths (23). The continuum of preeclampsia /eclampsia is the most common contributing factor for high maternal mortality and perinatal loss. HELLP syndrome, important predictors of further organ dysfunctions (morbidity) and mortality, is the most reported common complication of sever preeclampsia / eclampsia in Ethiopia (21,22). Despite this, there has been no studies that addressed the magnitude of maternal

and perinatal outcomes pregnancies complicated by this syndrome in Ethiopia. Hence, this study will contribute to the knowledge gap on HELLP syndrome.

Significance of the study

This study will have great significance concerning the way and role to improve maternal and prenatal mortality by increasing awareness and knowledge of health professionals. Moreover, this study will be helpful for estimating the burden of disease and associated adverse outcomes so that it can pave the way for further study in order to minimize adverse pregnancy outcomes in country level.

Literature review

A prospective cohort study, which represent the largest well-defined group of patients with the HELLP syndrome in the medical literature, comprising 442 pregnancies complicated by the HELLP syndrome, in a tertiary care facility in Memphis U.S.A (Aug 1977 through Jul 1992)(5). The primary objective of the study is to describe the incidence and effects of serious obstetric complications on maternal outcome in pregnancies complicated by HELLP syndrome. Four hundred thirty-seven women had 442 pregnancies complicated by HELLP syndrome, of which 407(20%) had severe preeclampsia and 35(10%) had eclampsia. Maternal mortality was 1.1 % (five patients). Serious maternal morbidity included DIC (21%), abruptio placentae (16%). Acute renal failure (7.7%), pulmonary edema (6%), subcapsular liver hematoma (0.9%), and retinal detachment (0.9%). In addition, 55% of patients required transfusions with blood or blood products and 2% required laparotomies for major intraabdominal bleeding. The presence of HELLP syndrome in this study is associated with an increased rate of serious maternal morbidity especially when it arises in the postpartum period.

A prospective hospital based study from Tertiary Centre in India, 1.83%(55) of patients developed HELLP syndrome from 122,702 patients admitted for delivery during 2015 October to 2016 October (19). Maternal morbidity was 34.54%. No Maternal deaths were there. Perinatal morbidity was 14.4%. Prematurity (76.36%) and IUGR (14.5%) accounted for most common neonatal complications. The reported perinatal death rate in this study was 9%, and this high perinatal death rate is mainly experienced at early gestational age (preterm) in association with IUGR. As a result, these infants have a high rate of acute neonatal complications.

Another study done in India Guntur District for a period of 16 months i.e., Jan 2015 to Apr 2016, including 102 cases of severe preeclampsia and Eclampsia, which were analyzed retrospectively(18). The aim of the study was to describe the incidence, different clinical presentations and diagnosis of HELLP syndrome in Pre-eclampsia and Eclampsia and to analyze the severity, complications, maternal and perinatal outcome. Out 102 cases, 91 were preeclampsia and 11 were eclampsia and 15 cases were diagnosed as HELLP Syndrome of which 12 cases were from preeclampsia and 3 cases were from Eclampsia. Majority of the cases belonged to 21-25years age group and were mostly from lower Socio economic status. The presence of HELLP syndrome is associated with an increased rate of maternal morbidities (60%) such as DIC, renal failure, pulmonary edema, pleural effusion, PRES retinal detachment,

abruption, multi organ failure, PPH, eclampsia. The rate of these complications in this study depends on the severity, timely intervention, availability of tertiary care facilities like ICU, dialysis, ventilator support and equipment and availability of blood and blood products. In all these cases studied, 2(13.3%) were delivered vaginally and in 13 cases (86.6%), active management was taken in the form of termination of pregnancy by caesarean section irrespective of gestational age as delivery is the definitive management to prevent further complications and to save the mother. In this study, 9 cases (60%) needed intensive care management; of which 8 cases were discharged home healthy and 1(6.66%) case death occurred because of late referral in bad condition. All 9 cases (60%) admitted to ICU were treated with FFP, platelet transfusion and other blood products. The perinatal morbidity and mortality was 46.6% each. The main cause for perinatal deaths in the study was prematurity (86.6%) followed by birth Asphyxia. This study concluded that HELLP Syndrome is a severe variant and a dreadful complication of Preeclampsia and Eclampsia, it needs early diagnosis and timely intervention in the form of termination of pregnancy to arrest further progress of pathophysiology leading to complications.

A prospective study conducted in 1559 patients hospitalized at the Intensive Care Unit in Mali to evaluate the diagnostic and therapeutic problems of HELLP Syndrome and related to the immediate postpartum period for pre-eclampsia from January 1999 to January 2002. Of 1559 patients, nine cases (0.58 %) were complicated with HELLP Syndrome: seven multiparas and two primiparas (8). This corresponded to 6.2 % of obstetrical emergencies and 18.0% of pre-eclampsia. The clinical signs were convulsive crises (eclampsia), high blood pressure, icterus, nausea and vomiting, epigastric with or without hypochondriac pain. The biological signs were anemia: six of nine cases, obvious low platelet count (between 56,000 and 150,000/mm³) and elevated liver enzymes (2 to 17 times higher than the normal). Six fetuses were alive, but hypoxic and three died in utero. The maternal complications were eclampsia (7 cases), severe renal insufficiency (6 cases) and disseminated intravascular coagulation (3 cases). In three cases with positive checks for malaria, situation was worsened. In six cases of severe anemia, transfusion was indicated. The most frightening complication was the acute renal insufficiency, but hemodialysis was helpful for four of patients (44.4%) after failure of diuretic administration. The evolution was favorable in six cases, unfavorable in three (33.3 % with maternal deaths). Mortality rate seemed high and mainly attributed by the quality of the care available to and especially the delay by our patients in seeking consultation and care in Sub-Saharan Africa. This study concluded that HELLP Syndrome

remained a serious complication of pregnancy. It must be suspected for all patients with preeclampsia; but also among the pregnant women with normal blood pressure, presenting with digestive symptomatology. Moreover, in this study the coexistence with serious malaria darkened the maternal prospects. Therefore, to decrease in maternal mortality related to HELLP Syndrome, Sub-Saharan countries would require training of practitioners and awareness of the risks, suspicious factors and alarm signs at the antenatal consultations.

A prospective hospital-based study was conducted involving 34 consecutive cases of severe pre-eclampsia (12), imminent eclampsia (10) and eclampsia (12) who were admitted at tertiary hospital in Nigeria during study period between 1 January and 31 December, 2006 (18). The objective of this study is to determine the incidence, severity, symptomatology, complications, length of hospital stay, mode of delivery, modalities of treatment and pregnancy outcome in cases of HELLP syndrome seen in Nigerian women. The duration of stay in the hospital of the 34 cases ranged from 2 to 20 days (mean 8.8 days). The syndrome was identified in (33%) cases of eclampsia, 1/10 (10%) cases of imminent eclampsia and 1/12 (8.3%) cases of severe pre-eclampsia with over all prevalence of 17.6%. All of the four eclamptic cases with HELLP syndrome died giving a 100% fatality rate while none of the imminent eclamptic and severe pre-eclamptic patients with the syndrome died. All the cases of HELLP syndrome that died and all the perinatal deaths recorded were all among unbooked patients. The study emphasized the role of Substandard care that have contributed to the progression of the disease state and consequently, to maternal mortality. This study concluded that in an environment like this, Prevention of incidence and complications of preeclampsia and eclampsia, the precursors of HELLP syndrome, and its complications is always better. This study stressed important of ANC especially after 20 weeks' gestation and at every assessment, the following signs and symptoms should be identified and prompt and appropriate action taken: hypertension and proteinuria developing for the first time, symptoms of headache, visual disturbances or both, reduced fetal movement and a small for gestational age fetus.

A cross-sectional study conducted retrospectively by reviewing the five-year medical records of 1,809 cases to identify trends of preeclampsia/eclampsia and maternal and neonatal outcomes among women delivering in Addis Ababa selected government hospitals, Ethiopia(20). HELLP syndrome (a variant of preeclampsia) was the most frequent complication observed in mothers, in 39.5% of cases. As the prevalence of HELLP syndrome

is very high, there is no single published study on maternal and perinatal outcomes of HELLP syndrome in Addis Ababa hospital and Ethiopia in general.

Objectives

General objective:

To assess maternal and perinatal outcomes of pregnancies complicated by HELLP syndrome in women delivering in St. Paul's health medical millennium collage in Addis Ababa, Ethiopia during the period from Jan 1, 2019 to Dec 31, 2019 G.C.

Specific objective:

To determine prevalence of HELLP syndrome.

To assess maternal out comes of affected mothers.

To assess perinatal outcomes affected mothers.

Methods

Study area and period

The study was conducted at Saint Paul's Hospital Millennium Medical College in Addis Ababa, Ethiopia during the period from Oct 11, 2018 to Sep 5, 2019 G.C.

Description of study areas

Saint Paul's Hospital Millennium Medical College is tertiary teaching referral hospitals located in Addis Ababa, Ethiopia and provides the highest maternity service of the country. The hospital handles complicated obstetric cases and referring normal or less complicated pregnant mothers to other hospital and health centers for birth. It gives nearly more than 10,000 antenatal care services and around 9000 deliveries per year.

Study design

A two years' retrospective hospital based chart review study

Source population

All pregnant women who delivered at SPHMMC from Oct 11, 2018 to Sep 5, 2019 G.C.

Study population

All women who delivered at SPHMMC and had diagnosis of HELLP syndrome from Oct 11, 2018 to Sep 5, 2019 G.C.

Inclusion and exclusion criteria

Inclusion criteria

All pregnant women whose Gestational age >20 weeks and meeting the diagnostic criteria of HELLP syndrome as judged by the most senior physician.

Exclusion criteria

Mothers with incomplete data on important variables, or whose cards has been lost

Mothers with other causes of thrombocytopenia and deranged liver function tests like viral hepatitis, acute cholecystitis and gastro enteritis

Study variables

Independent variables

Sociodemographic characteristics (age, place of residence), Obstetric history (Gravidity, Parity, gestational age, number of fetus, ANC visits, mode of delivery), Preexisting medical conditions (chronic hypertension, lupus), laboratory variables (complete blood count (CBC),

U/A(proteinuria), creatinine and BUN, SGPT, SGOT, LDH, bilirubin, peripheral morphology) and management (use of antihypertensive, Magnesium sulfate, corticosteroid and blood and its product transfusion).

Dependent variables

Maternal mortality and morbidity.

perinatal mortality and morbidity.

Sampling and Sample size methods

Purposive sampling was used and all cases with HELLP syndrome in the two years' period were included sequentially.

Data collection technique

Data was collected by BSC Nurses using structured data extraction format prepared in English language. Two-day training on questionnaires was given to data collectors. The group members were discussed on how to collect data and the tool in detail before actual data collection. Patients cards were reviewed to confirm diagnosis from medical and labor records. Data was collected. These data include baseline characteristics, obstetric data, diagnosis, management, maternal outcomes and perinatal outcomes. The primary investigator was continuously supervising the data collection process.

Data analysis and interpretation

After data collection, each questionnaire checked for completeness and coded before data entry in to SPSS version 23 software. Further, data cleaning was performed for outliers, missed values and any inconsistencies before the data analysis. The results were expressed as number and percentage for all the qualitative variables. Mean and standard deviation was used for quantitative variables. Bivariate analysis was used to look at presence and strength of association between explanatory and outcome variables. Multivariate analysis was done for those variables statically significant at bivariate analysis to control confounders. Odds ratio, 95% confidence interval and p-value were used to determine strength of associations.

Ethical considerations

Ethical clearance & permission letter was obtained from the Institutional Review Board (IRB) of SPHMMC. An official letter of cooperation was taken to the medical director of the hospital and respective departments where the study was undertaken. Confidentiality was maintained during data collection, analysis and interpretation by coding variables.

Plans for utilization and dissemination of results

This study is expected to be useful for all concerned bodies. It will be disseminated to the departments, hospital administrators and the scientific community. Publication on journal will be considered.

Possible limitations

Patients data may not be documented completely as well as disappearance of patient's cards may affect representativeness of the study. Various out come in HELLP syndrome is depends on laboratory criteria. However; this study is being done in resources limited set up; laboratory investigations may not be complete.

Results

During the study period, Oct 11, 2018 to Sep 5, 2019 G.C, there were a total of 20,111 deliveries in our institution. Of these, 1356 cases had preeclampsia with severe feature and 76 cases had eclampsia. Out of these, 115 patients developed HELLP Syndrome making prevalence of 0.57% among all deliveries and 8 % in cases of preeclampsia with severe feature /eclampsia. Fourteen patients :10 patients who were incompletely investigated and 4 patients their charts lost, were excluded from the study. Among the remainder 101 women fulfilling the inclusion criteria were included and their records were analyzed retrospectively. Ninety -seven cases (96 %) had a prior diagnosis of preeclampsia with severe feature and 4% of the cases had Eclampsia.

Most of the mothers (36.6%) were in the age group of 27-31 years. Majority of them were married and from Addis Ababa, 99% and 63.4% respectively. 92% (93/101) of the mothers were referred from primary hospital, clinics and health centers. Regarding educational levels, 45.5% and 18.9% of the mothers were elementary and secondary school level respectively. 11.9% college level and 22.7 % had no formal education. Only 40(39.6%) were employed.

As for parity, 61(60.4%) cases were primiparous while 40 (39.6%) patients were multiparous. Majority, 96%(97/101) of mothers had ANC follow up. 89.1%(90/101) occurred during antepartum: 55.4% between the 28th and 37th weeks of gestation, 10.9% of the cases before 28th week, 22.8% after 37th week. The mean gestational age was 33.40 ± 4.474 wks. The remaining (10.9%) of the cases develop it after delivery. Majority, 68%(69/101) of the patients had Partial HELLP and 32 %(32/101) of them had complete HELLP syndrome. 18.8% of the mothers had spontaneous onset of labour. Eighty-two cases (81.2%), pregnancy was terminated before the onset of spontaneous labour. Of these (64.4 %) of the cases active management was taken in the form of termination of pregnancy by induction of labor and 16.8% by caesarean delivery. Overall caesarean and vaginal delivery rate in our study were 47.5%(48/101) and 52.5% (53/101) respectively. Majority of complete HELLP cases 53.1% had caesarean delivery whereas the caesarean and vaginal delivery rate of the partial HELLP cases were comparable (50.7% vs 49.3%).

Maternal outcomes are illustrated in table -1. In the present study no maternal death was observed. Around 30.7%(31/101) of the mothers developed maternal complications. Majority of them had more than one complications. Acute kidney injury was the most frequent maternal complication 24.8%(25/31), followed by pulmonary Oedema 11.9%(12/31).

Character	No of cases	Percent (%)
Acute Kidney Injury	25	24.8
Pulmonary Oedema	12	11.9
Disseminated Intravascular Coagulation	9	8.9
Abruptio Placenta	7	6.9
Postpartum haemorrhage	6	5.9
Blood transfusion	18	17.8
Hysterectomy	1	1
ICU stay	3	3
Maternal death	0	0
Total	74	-
Table-1: cases according to maternal out comes in patients with HELLP syndrome*		

***some women had more than one out come**

Table -2 below summarizes maternal morbidity stratified by sociodemographic characteristics of patients. The highest adjusted maternal morbidity, 37.5% (12/32) was seen in the age group of 22-26 years while the lowest adjusted maternal morbidity, was in the age category of 17-21 years which accounting 25% (4/16) of the cases. As for place of residency, mothers from outside of Addis Ababa had highest adjusted maternal morbidity of 40.5%. Multiparous women had the highest adjusted maternal morbidity of 32.5%. In our study also showed that those mothers who were un married, un employed, had no formal education had highest adjusted maternal morbidity of 100, 34.4 and 52.2 percent of the cases respectively.

Character	Cases of HELLP syndrome		Adjusted maternal morbidity	
	No	Percent (%)	No	Percent (%)
Age in years				
17-21	16	15.8	4	25
22-26	32	31.7	12	37.5
27-31	37	36.6	10	27
32-37	13	12.9	4	30.8
38-42	3	3	1	33.3
Total	101	100	31	-
Parity				
Primiparous	61	60.4	18	29.5
Multiparous	40	39.6	13	32.5
Total	101	100	31	-
Referral				
Yes	93	92	30	32.3
No	8	8	1	12.5
total	101	100	31	-
Address				
AA	64	63.4	16	25
out of AA	37	36.6	15	40.5
Total	101	100	31	-
Marital status				
Married	100	99	30	30
Unmarried	1	1	1	100
Total	101	100	31	-
Occupation				
Employed	40	39.6	10	25
Unemployed	61	60.4	21	34.4
Total	101	100	31	-
Education level				
No formal education	23	22.7	12	52.2
Elementary	46	45.5	8	17.4
Secondary	19	18.8	7	10.5
College	12	11.9	2	11.8
Total	101	100	31	-
Table-2 :Maternal morbidity stratified based on sociodemographic factors				

There was no significant association of maternal morbidity and variables such as place of residency, parity, past medical history, number of fetus, ANC and use of Mgso4($p>0.05$). The presence of fetal death during referral was significantly associated maternal morbidity with p -value of 0.0045 (COR =6.25, 95% CI =1.5-26.09). Those mothers who develop this syndrome in postpartum period were 4.81 times more likely to develop maternal complications with p -value of 0.032 (95% CI= 1.29-17.9). Mothers with complete HELLP syndrome 2.92 times

more likely to develop maternal morbidity with p-value of 0.0169 (95% CI =1.2-7.13). (see table-3 below).

In addition, multivariate logistic regression analysis was done for those variables significantly associated with maternal complications with bivariate analysis. And only time of onset and type of HELLP syndrome were found to have significant influence on maternal morbidity with p -value of 0.03 for both and AOR= 0.223 (95% CI= 0.018-0.863) and AOR =0.360 (95% CI= 0.144-0.901) respectively.

Character	Cases		Maternal morbidity		COR(95%CI)	p-value
	No	(%)	Yes	No		
Place of residency						
Out of Addis Ababa	37	39.6	15	22	2.05(0.86-4.87)	0.103
Addis Ababa	64	60.4	16	48		
Total	101	100	31	70		
Parity						
Primiparous	61	60.4	18	43	0.87(0.37-2.06)	0.750
Multiparous	40	39.6	13	27		
Total	101	100	31	70		
Time of on set						
Postpartum	11	10.9	7	4	4.81(1.29-17.9)	0.032
Antepartum	90	89.1	24	66		
Total	101	100	31	70		
ANC						
Yes	97	96	30	67	0.12(0.03-0.47)	1
No	4	4	1	3		
Total	101	100	31	70		
Number of fetus						
Single	94	93.1	27	67	0.3(0.06-1.44)	0.1158
Twin(multiple)	7	6.9	4	3		
Total	101	100	31	70		
Type of HELLP syndrome						
Complete	32	31.7	15	17	2.92(1.2-7.13)	0.016
Partial	69	68.2	16	53		
Total	101	100	31	70		
Past medical history						
Yes	9	8.9	3	6	1.14(0.27-4.9)	0.857
No	92	91.1	28	64		
Total	101	100	31	70		
FHB						
Negative	10	9.3	7	3	6.25(1.5-26.09)	0.0045
Positive	91	90.7	24	67		
Total	101	100	31	70		
Administration of Mgso4						
Yes	99	98	30	69	0.43(0.03-7.18)	0.522
No	2	2	1	1		
total	101	100	31	70		

Table -3: Factors associated with adverse maternal out comes

Table -4 summarized maternal morbidity based on laboratory findings. Most (96.8%) maternal complications occurred in those mothers with platelet count of $\leq 100,000/\text{mm}^3$. Other laboratory findings: SGPT /SGOT levels $\geq 72\text{IU/L}$, LDH $\geq 600\text{ IU/L}$, Bilirubin $\geq 2\text{ mg/dl}$ and creatinine $\geq 1.2\text{ mg /dl}$ indicate more than 60% of sever maternal morbidity.

Character	Maternal morbidity	
	No.	Percent(%)
Platelet count $\leq 1*10^5/\text{mm}^3$	30	96.8
SGPT $\geq 72\text{IU/L}$	26	83.9
SGOT $\geq 72\text{IU/L}$	24	77.4
LDH $\geq 600\text{IU/L}$	19	61.3
Bilirubin $>2\text{mg/dl}$	19	61.3
Uric acid $\geq 6\text{mg/dl}$	26	83.9
Creatinine $\geq 1.2\text{mg/dl}$	25	80.6
Total	—	—
Table- 4: Maternal morbidity according to laboratory findings. *(n=31)		

*some cases may have more than one elevated laboratory findings.

Perinatal out comes are illustrated in table -5. There were 108 infants delivered by the 101 mothers with HELLP syndrome:78.7%(85/108) of the neonates were born alive,11%(13/108) were intrapartum deaths and 9.3%(10/108) were still births. Most of the newborns ,70.4%(76/108) were preterm deliveries, of which 69.7%(23/77) of babies had IUGR, while 29.6% (32/108) were term deliveries. 25 %(27/108) of the neonates admitted to NICU:19 neonates were discharged alive and 8 neonates died. Prematurity was the cause of death in the 5 babies at NICU and 3 newborns due to IUGR. Additionally, two newborns were died before arrival in the hospital: one home delivery and one on the way to health center, all died soon after delivery, possibly due to complications of birth asphyxia making over all proportion of ENDS to be 9.3%(10/108). The overall perinatal morbidity and mortality in our study were 23/108(21.3%) and 33/108(306/1000) respectively.

Character	No of cases	Percent
Preterm	76	70.4
Term	32	29.6
IUGR	23	21.3
Still birth	10	9.3
Intrapartum death	13	12
APGAR score (single)		
1st minute < 5	20	18.5
5th minute <7	8	7.4
NICU admission	27	25
Early ND	10	9.3
Total	-	-
Table-5:Composite perinatal out come		

*Some cases had more than one out come

Place of residency, gestational age and mode of delivery were found to have significant influence on PNM rate ($p < 0.05$) on binary logistic regression analysis. (Table -6)

Variables	Beta	P-value
Place of residency	1.807	0.001
Gestational age	-1.794	0.004
Mode of delivery	-1.692	0.002
Constant	1.994	0.003
Table-6: Binary logistic regression analysis comparing predisposing factors and PNM		

Discussion

HELLP syndrome is a life threatening complication in pregnancy that associated with significant maternal and perinatal morbidity and mortality. No population-based estimates of incidence were identified in the literature. The prevalence of HELLP Syndrome in our study was 0.57 % of all deliveries, which is comparable to a 2015 review of revisiting of HELLP syndrome which quotes a prevalence of 0.5–0.9% of all pregnancies (3). The prevalence was also consistent to a study done in Mali (0.58%) (18). Another study conducted in India found prevalence of 1.83% (7).

In our study HELLP syndrome was found in 60.4% primiparous compared to 39.6% multiparous. Majority of the mothers were unbooked, 80.2% while 19.8% were booked. This is in keeping with studies done in India 20% were booked and 73.3% belonged to Primiparous (14). This also agreed with another study from Nigerian, 24.5 % of cases were booked and 64.7% cases were primiparous (17).

Ninety (89.1%) cases developed HELLP Syndrome during antenatal period which is comparable to a study done in U.S.A about 70 % of the cases developed HELLP Syndrome during antenatal period and majority of cases developed the same gestational age as ours i.e. < 37 week (74.4% vs 80%) (5). A study done India reported maximum number of cases at 32 - 36 week (7). The mean gestational at presentation was 33.40 ± 4.474 week compared to the study conducted in Nigeria ie. 36.1 week (17).

Caesarean delivery rate in our study was 47.5%(48/101) which is comparatively lower than the study done in India that is 86.6%(14). This is might be due to the protocol in our institution is to terminate the pregnancies immediately or after completion of ACS especially in those cases with complete HELLP pregnancy with induction irrespective of gestational age to avoid progression of the disease in order to prevent adverse pregnancy outcomes.

In our study, 31(30.7%) cases developed at least one major morbidity which is comparable to a study done in India i.e. 34.54%(7). Acute kidney injury was the most frequent maternal complication in this study 25(24.8%), Four patients (16%) required dialysis during hospitalization. This finding is similar to the study in turkey study; acute renal failure (ARF) the most frequent maternal complication i.e. 36% and Six of patients (20%) who had ARF were given hemodialysis (16). Another study done in Mali found acute renal insufficiency as the most frightening maternal complication and hemodialysis was helpful for 4 of patients (44.4%) after failure of diuretic administration (18). A study done in U.S. A, which represent the largest

well defined group of patients with the HELLP syndrome in the medical literature. HELLP syndrome was associated with serious maternal morbidity, especially when it arises in the postpartum period. DIC and Abruptio placenta as most frequent maternal complications (5). In our study, it was found in 9(8.9%) and 7(6.9%) of the cases respectively. And, when it arises in postpartum period and complete form were found have significant influence on maternal morbidity with p -value of 0.03 for both and AOR= 0.223 (95% CI= 0.018-0.863) and AOR =0.360 (95% CI= 0.144-0.901) respectively.

In our study there was no maternal deaths which is similar to Indian study (19). In contrast to these studies, the studies done in Nigeria and Mali had reported fatality rate of 11.8% and 33.3 % respectively (7,8). The difference of results with our study could be explained by early recognition, timely and prompt referral from our health centers and primary hospital once they identify the precursors of HELLP syndrome (those with uncomplicated preeclampsia-eclampsia). Moreover, most of the cases 64(63.4%)were referred from health centers in Addis Ababa where there is strong and coordinated referral system.

Still birth and Intrapartum deaths accounts for majority of perinatal deaths, 9.3% (10/108) &12% (13/108) unlike the study conducted in India and Nigeria (7,14). This could be due to large percentage of referred patients to our institute which serves as the main referral center for mothers (preeclamptic and eclamptic patients) that requires extreme premature deliveries as well as with fetal demise. Ten newborns (9.3%) were END making perinatal deaths of 30.6% which is higher than a study done in India, 9%(7) and Nigerian, 15.8%(14). Another study in Mali reported perinatal mortality of 66.7% (6/9) :3 fetal deaths in utero and 3 ENDs due to birth asphyxia (8).

Few studies attempted to investigate the relative influence of gestational versus the severity of HELLP syndrome, however there is general agreement that perinatal mortality is depend on gestational age at deliver as well as presence of IUGR and abruptio placentae (2,28). In present study, place of residency, gestational age and mode of delivery were found to have significant influence on PNM rate (p –value < 0.05) on binary logistic regression analysis. A study conducted in Indian reported prematurity as main cause for perinatal mortality.

Conclusions

The incidence of HELLP syndrome in this study was low with significant maternal morbidity and perinatal complications. It needs further prospective study with large sample size in country level.

Recommendation

Those mothers referred from outside of Addis Ababa had highest adjusted maternal morbidity rate. It implies the need for regular ANC follow up. Moreover, in our study Acute kidney injury is most frequent complication and dialysis was required about 16 % of patients as well as 17.8 % of patients required transfusion of blood and its products, so HELLP syndrome must be managed in tertiary hospitals where blood products and other lifesaving facilities are available. Finally, the need for high number of premature deliver was a major contributing factor for both perinatal morbidity and mortality. Thus, we think that improving intrapartum obstetric and neonatal cares especially for preterm babies as an important instrument to reduce perinatal morbidity and mortality.

Limitations of the study

This study had several limitations. First, this study was based on retrospective data collection, which means that some data might be incomplete so that it needs further large sample sized prospective study. Second, the study population might not represent the general population. Besides, we do not yet have an incidence rate for the overall population in our country, which might limit the generalizability of the results to other settings.

In spite of these limitations, this was the first study that evaluated the prevalence, maternal and perinatal outcomes of HELLP syndrome in Ethiopia, and so it might be helpful for estimating the prevalence and burden of disease and pave a way to do further prospective study with large sample size in country level in order to minimize adverse pregnancy outcomes.

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APPENDIX 1.

HOSPITAL NAME:

CARD NUMBER:

IDENTIFICATION NUMBER AND INITIALS:

REFERRAL: 1. Yes, 2. No, If Yes, from?

Questionnaires'

A. SOCIODEMOGRAPHIC STATUS

1. Age: -----years
2. Place of residence: Addis Ababa, Out of Addis Ababa
3. Marital status: Married, unmarried, Divorced, Widow
4. Educational status: No formal education, Elementary, Secondary,
College
5. Occupation: Employed, Unemployed

B. OBSTETRIC HISTORY

7. Current pregnancy: Gravidity ----- Parity----- Abortion -----
8. Onset of HELLP syndrome: antepartum ,post partum
If antepartum ,Gestational age : -----
9. Attended antenatal follow up: Yes No
10. Number of fetus: Single, Twin, higher order
11. Is there any identified hypertension in pregnancy before dx of HELLP syndrome? Yes No
12. If yes, Type of hypertension in pregnancy?
Gestational hypertension, Preeclampsia with severity feature, Preeclampsia without severity feature ,
Eclampsia
13. Drugs given during current pregnancy
Methyldopa Yes No
Nifedipine Yes No
Hydralazine Yes No
Magnesium sulphate Yes No

Diazepam Yes No

Dexamethasone Yes No

 If yes 1D, 2D , 3D, 4D

Blood product Yes No

 If yes Whole blood, Packed RBC, FFP, Platelets

Other (Specify)

C.PAST MEDICAL HISTORY

14. past medical history of pregnant mother

Pregnancy induced hypertension Yes No

Chronic hypertension Yes No

Diabetes mellitus Yes No

Chronic renal disease Yes No

NYHA Class 1-4 heart failure Yes No

TTP-HUS Yes No

HIV/AIDS positive Yes No

Acute fatty liver of pregnancy Yes No

Hepatitis Yes No

Acute cholecystitis Yes No

Acute fatty liver of pregnancy Yes No

Hematologic disorder Yes No

Seizure disorder Yes No

Other(specify) Yes No

15. Family history of preeclampsia

D. CLINICAL FEATURES ON ADMISSION

16. Clinical symptoms (other than labour)

Severe or persistent headache Yes No

Epigastric pain with or without hypochondriac pain Yes No

Visual disturbance Yes No

Nausea and or Vomiting Yes No

Convulsions Yes No

17. Maximum Blood pressure

18. Edema Yes No

19. Weight (Kilogram) -----

E. INVESTIGATIONS

20. Investigation done

Blood group and Rh Yes No

Hematocrit Highest-level ----- lowest level-----

Platelet count /mm³ highest-level ----- lowest level-----

Bilirubin (mg/dl) -----

LDH (iu /ml) -----

SGOT (iu /ml) -----

SGPT (iu /ml) -----

Renal function Urea ----- Creatinine-----

Urine protein Dipstick -ve , 1+, 2+, 3+ Quantitative-----

Peripheral morphology Yes ----- No

G. DELIVERY

21. Onset of labour Spontaneous, Induction, Elective C/S

22. If not spontaneous, Indications-----

23. Mode of delivery vaginal delivery, CD, Instrumental delivery

If caesarean section , Indication-----

H. MATERNAL COMPLICATIONS

24. Is there any maternal complication? Yes No

25. If yes what?

Abruption

DIC

Pulmonary edema

Cerebrovascular Accident

PPH

Hysterectomy

Acute renal failure

Sub capsular Hematoma or liver failure

Wound hematoma

Maternal death if yes, immediate cause of death -----

If other (specify)

26. Intensive Care Unit Admission -----

I. PERINATAL OUT COME: Boy/ Girl, Birth weight (kg) -----,

27. Outcome of delivery: Stillbirth, Live birth

28. GA at delivery -----

29. If live births Apgar score: At 1 minute ----- At 5 minutes-----

29. Birth weight: <1000, 1000-1500, 1500-2500, 2500-4000 >4000

30. Birth Asphyxia: Yes No

31. NICU admission: Yes No

32. RDS: Yes No

33. Necrotizing Enter colitis: Yes No

34. Hypoglycemia: Yes No

35. Jaundice: Yes No

36. IVH: Yes No

37. Early Neonatal death: Yes No If Yes, How old?

ASSURANCE OF PRINCIPAL INVESTIGATOR

The undersigned agrees to accept responsibility for the scientific ethical and technical conduct of the research thesis and for provision of required progress reports as per terms and conditions of the St Paul's Hospital Millennium Medical College in effect at the time of grant is forwarded as the result of this application.

Name of the student: _____

Date. _____ Signature _____

APPROVAL OF THE ADVISORS

Name of the first advisor: _____

Date. _____ Signature _____

Name of the second advisor: _____

Date. _____ Signature _____