Scientific Research Publishing

Open Journal of Obstetrics and Gynecology, 2023, 13, 1432-1451
https://www.scirp.org/journal/ojog
ISSN Online: 2160-8806
ISSN Print: 2160-8792

Clinical Presentation, Management and Materno-Fetal Outcome of Patients with HELLP Syndrome at the Yaoundé Gyneco-Obstetrics and Pediatric Hospital

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How to cite this paper: Nzometia, C., Pascal, F., Dohbit, S., Kenn, C., Daniel, T., Mbia, C. and Mbu, E. (2023) Clinical Presentation, Management and Materno-Fetal Outcome of Patients with HELLP Syndrome at the Yaoundé Gyneco-Obstetrics and Pediatric Hospital. *Open Journal of Obstetrics and Gynecology*, **13**, 1432-1451.
https://doi.org/10.4236/ojog.2023.138119

Received: July 18, 2023
Accepted: August 27, 2023
Published: August 30, 2023

Abstract

Background: HELLP (Hemolysis, Elevated Liver enzymes and Low Platelets) syndrome is a common complication of severe preeclampsia, with a high maternal and perinatal mortality rate. Data on HELLP syndrome is scanty in our setting. We sought to study the clinical presentation, management, and materno-fetal outcome of patients with HELLP syndrome at the Yaoundé Gyneco-Obstetrics and Pediatric Hospital (YGOPH). **Methods:** This was a cross-sectional, analytical study with a retrospective data collection of patients, diagnosed with HELLP syndrome at the YGOPH between 1st January 2020 and 31st July 2021. Data were analyzed using the software R version 4.0.2. Results are presented as mean ±standard deviation, frequencies and percentages. P values < 0.05 were considered statistically significant. **Results:** Of 254 cases of severe preeclampsia, 17 developed HELLP syndrome, giving us a frequency of 6.7%. One patient who presented with hepatitis B was excluded. The mean age was 27.19 ± 6.44 years. Most patients (56.3%) had poor follow up during antenatal contacts. The most common symptom was headache (93.8%). Most cases (56.3%) were diagnosed during post-partum, pre-partum (25.0%), and per partum (18.8%). Obstetrical management was done by cesarean section (62.5%) and vaginal delivery (37.5%). Post-partum management of HELLP syndrome consisted of antihypertensive medication, anticonvulsants, sedatives, transfusion of blood and blood products, and fluid resuscitation. Of the 50% of patients who presented with acute kidney injury, only 12.5% (1) were referred for dialysis. Over 50% of our study participants presented severe complications after delivery, but 43.8% recovered, while 56.2% finally died. The fetal outcome was: still birth (31.2%), intra-uterine

growth restriction/low birth weight (12.5%), term delivery (≥37 weeks) (31.3%), and preterm deliveries (<37 weeks) (68.7%). Three (18.8%) of the neonates delivered alive presented with a poor Apgar score at the 5th minute. **Conclusion:** Although rare, HELLP syndrome exists in our setting. Proper management in appropriate centers is key to improving maternal and fetal outcomes.

Keywords

HELLP Syndrome, Clinical Presentation, Management, Maternal and Fetal Outcomes

1. Introduction

The acronym HELLP (Hemolysis, Elevated Liver enzymes and Low Platelets) was coined by Weinstein in 1982 to describe a syndrome consisting of Hemolysis, Elevated Liver enzymes and Low Platelet count [1]. It is a variant of severe pre-eclampsia or a complication of it. It is a syndrome, characterized by: preeclampsia, hepatic endothelial disruption, platelet activation, aggregation and consumption, resulting in microangiopathic hemolysis, ischemia and hepatocyte death [1]. HELLP syndrome has a prevalence of 0.5% to 0.9%. About 70% of cases occur in the third trimester of pregnancy, and the remainder occurs within 48 hours of delivery [2]. The mortality rate of women with HELLP syndrome is 0 to 24%, with a perinatal death rate of up to 37%. Class 1 (Mississippi Classification) or complete HELLP (Tennessee Classification) is associated with the highest incidence of perinatal morbidity and mortality. Sixty percent of deaths occur in patients with class 1 disease; cerebral hemorrhage is the most common autopsy finding. Morbidity includes the following: disseminated intravascular coagulation (DIC) (20%), placental abruption (16%), acute renal failure (7%), and pulmonary edema (6%) [3]. HELLP syndrome has been associated with 15% to 20% incidence of perinatal mortality, attributable to premature delivery [4]. The prevalence of HELLP syndrome was reported to be 2.2% in Africa [5]. In Cameroon, the prevalence of hypertensive disorders in pregnancy is 8.2% [6], and HELLP syndrome was found to be the most common maternal complication [7] [8]. In a study in Cameroon, 45.5% of patients with eclampsia and preeclampsia developed HELLP syndrome [9]. Patients with HELLP syndrome are at increased risk of preeclampsia or pregnancy-induced hypertension, in addition to preterm delivery, intra uterine growth restriction, and placental abruption in future pregnancies, and are also at increased risk of developing hypertension and cardiovascular disease [10]. Fetal morbidity and mortality rates range from 9% - 24% and usually result from placental abruption, intra uterine fetal asphyxia, or prematurity [2].

Despite all these, the efforts to predict which patients may suffer from HELLP syndrome have not yet resulted in a meaningful method of prevention. Under-

standing the clinical presentation and predisposing factors will help in prevention of HELLP syndrome, early diagnosis, and the prevention of adverse materno-fetal outcomes. We sought to study the clinical presentation, management and materno-fetal outcome of patients with HELLP syndrome at the Yaoundé Gyneco-Obstetrics and Pediatric Hospital (YGOPH).

2. Methods

This was a cross-sectional, analytical study with a retrospective data collection of patients, diagnosed with HELLP syndrome at the YGOPH between 1st January 2020 and 31st July 2021. The study was carried out at the YGOPH. This is a tertiary hospital, located in Ngousso in Yaoundé, Cameroon. On average, about 200 to 250 deliveries are conducted at the maternity of HGOPH monthly, while the intensive care unit receives and manages an average of 10 to 20 cases of severe preeclamptic cases per month. The files of all patients diagnosed with HELLP syndrome at the YGOPH who were referred or delivered at the YGOPH between 1st January 2020 and 31st July 2021 were explored. We excluded files of patients diagnosed with: epilepsy, encephalopathy, tetanus, meningitis, hypoglycemia, ketoacidosis pyrexia, hepatitis, kidney failure and suspected drug toxicity or with incomplete information for the diagnosis to be confirmed.

When the protocol and the questionnaire form were completed, the data collection tools were pretested and validated. Ethical approval was obtained from the Ethical Committee of the Faculty of Medicine and Biomedical Sciences of the University of Yaoundé I. Moreover, administrative authorizations were obtained from the director of the YGOPH and the Obstetrics and Gynecological unit in this hospital. The identity and personal details of the study participants were encoded and kept strictly confidential. Only the investigator was able to decipher these codes.

A thorough analysis of the registers of the said units was done, and a list was established of patients diagnosed with or hospitalized for HELLP syndrome in the context of severe preeclampsia confirmed by the chief of service from 1st January 1, 2020 to 31st July 31, 2021. Using this list, medical records were searched for and obtained at the archives of the units. We retrieved the medical records of all patients diagnosed with HELLP syndrome in the period between 1st January 2020 and 31st July 2021. The diagnosis of HELLP syndrome was based on: elevated liver enzymes: ASAT or ALAT > 70 IU/L, for Mississippi class 1 and 2 and ASAT or ALAT > 40 IU/L for class 3; low platelets count, with values less than 150,000/μL; and clinical evidence of hemolysis: Hemoglobinuria, ecchymosis, bleeding or petechia.

Cases were classified into three groups using the Mississippi classification (**Supplementary** Table S1). We collected data on socio-demographics, history of pregnancy, clinical presentation, paraclinical investigations, medical treatment received, method and outcome of delivery, maternal and perinatal outcome and discharge data from the files. Information concerning the outcome/

complications of the newborns were equally obtained from the files. Demographic factors included: maternal age, marital and employment status, parity, and residence. Pregnancy factors included gestational hypertension, gestational diabetes, new sexual partner during pregnancy, congenital anomaly, placental disorders (e.g., placenta accreta) and premature rupture of membranes. We recorded information on treatment prescribed and compared with the treatment actually received, both before and after delivery.

Maternal variables were categorized into the following subtypes: eclampsia/altered consciousness, disseminated intravascular coagulation, suspected stroke, suspected acute pulmonary edema, acute kidney injury, suspected hepatic hematoma/rupture, normalized blood pressure, stroke, maternal death, and recovery. Stillbirth was defined as fetal death before or during labor, neonatal death as death before hospital discharge, and perinatal mortality as stillbirth and neonatal death. Severe neonatal morbidity was defined as a composite of bronchopulmonary dysplasia, respiratory distress syndrome, intracranial non-traumatic hemorrhage (not including intraventricular hemorrhage [IVH]), IVH grade 3 and 4, periventricular leukomalacia, retinopathy of prematurity, neonatal sepsis, convulsions, necrotizing enterocolitis or severe birth trauma. Data was filled in data collection sheets anonymously and analyzed.

Data of completed and validated questionnaires were entered and analyzed using the software R version 4.0.2. Using a confidence interval of 95%, the major descriptive analysis involved were the calculation of frequency (for qualitative variables such as diagnosis), and means (for quantitative variables such as age). Pearson's chi square test and Fisher's exact test were used for comparison between categorical data and Mann Whitney U test for numerical data. For the statistical tests, the significant threshold was set at 0.05. The results were presented in figures and tables.

3. Results

3.1. Sociodemographic and Diagnostic Characteristics

A total of 254 cases of severe preeclampsia were received and managed at the YGOPH, from 1 January 2020 to 31 July 2021. Seventeen of them presented with HELLP syndrome (frequency: 6.7%), amongst which one patient who presented with hepatitis B was excluded; 16 patients were retained. The mean age was 27.19 ± 6.44 years, while the most represented age group in our study were those between 20 and 24 years (31.3%) (**Figure 1**). Of these participants, 41.7% were employed, 50% were unemployed, and 8.3% were students. In addition, 33.3% were single and 66.7% were married, while 50% had only primary education, and those that had no education, secondary and higher level of education each consisted of 16.7% of the study population.

The 16 cases retained were divided into: 6 (37.5%) class 1, 9 (56.2%) class 2, and 1 (6.3%) class 3, according to the Mississippi's classification of HELLP syndrome [11]. Following the Mississippi classification, 37.5% of our study participants had severe HELLP syndrome, 56.2% had moderate HELLP syndrome,

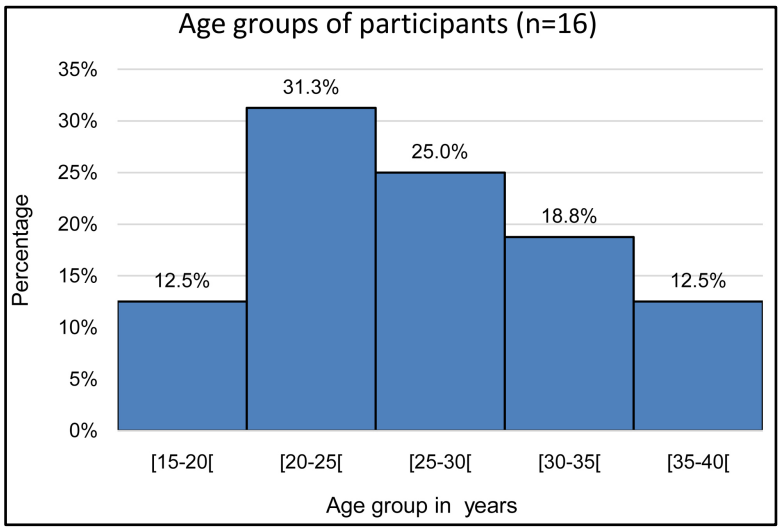

Figure 1. Distribution of participants according to their age groups.

6.3% participants had mild HELLP syndrome.

In the course of treatment, 9 patients died while 7 survived. The majority of our study participants have had no delivery (33.3%), alongside those who have had two deliveries at term (33.3%). Similarly, the majority, 56.3% of our study participants had antenatal contacts of poor quality, while three (18.8%) of the participants had no contacts. Only two (12.5%) participants had good quality antenatal contacts, according to WHO's recommendations. All the study participants who were referred, did their antenatal contacts in the different category hospitals in Cameroon, including specialized clinics, with the majority coming from integrated health centers and specialized clinics respectively (31.3% each).

Concerning preeclampsia, the diagnosis was missed during antenatal contacts in up to 25% of cases, meanwhile the diagnosis was made in 18.8% of our study participants, but 12.5% of their health providers did not put on treatment and closely follow-up their patients, while 6.3% initiated antihypertensive treatment. The rest were revealed either as HELLP syndrome or eclampsia, which are all complications of preeclampsia.

Concerning HELLP Syndrome, the majority of cases were diagnosed during post-partum (56.3%), three cases (18.8%) were diagnosed during labor, while the rest were either diagnosed during antenatal contacts or brought in emergency to the hospital.

Contrary to the literature, where HELLP syndrome usually manifests within the first 48 hours post-partum, two cases (22.2%), were diagnosed beyond 48 hours (**Figure 2**).

3.2. Clinical Presentation of HELLP Syndrome

As seen in **Table 1** below, our study participants manifested common clinical features, amongst which were: elevated blood pressure, headache, epigastric pain, convulsions, nausea and dizziness, which were remarkable at: 100%, 93.8%,

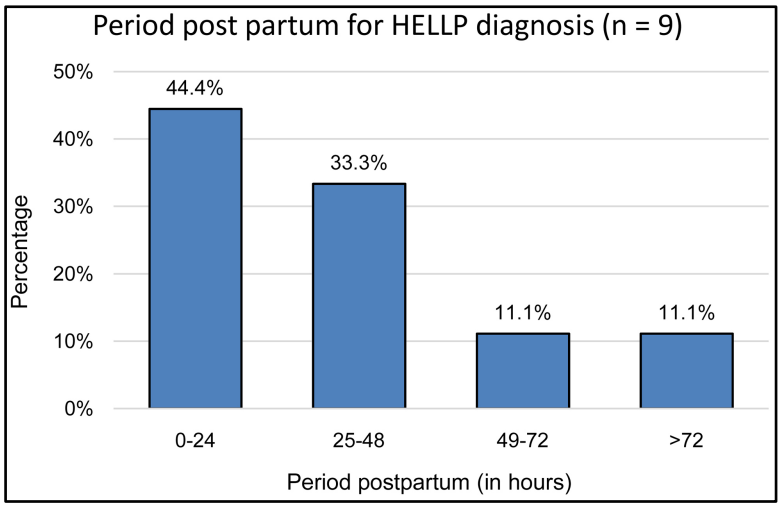

Figure 2. Distribution of participants according to the post-partum diagnosis period.

Table 1. Clinical features of patients with HELLP Syndrome.

Clinical characteristic	N = 16	Frequency
Elevated blood pressure	16	100
Headaches	15	93.8
Epigastric pain	14	87.5
Convulsions	12	75.0
Nausea	11	68.8
Dizziness	10	62.5
Vomiting	9	56.2
Blurred vision	9	56.2
Dyspnoea	2	12.5
Placenta Abruptio	2	12.5

87.5%, 75.0%, 68.8%, and 62.5% respectively.

3.3. Treatment Modalities

Concerning delivery, 62.5% (10) of our study participants delivered by cesarean section, while 37.5% (6) delivered vaginally. Though all referred cases, 56.2% delivered at the YGOPH, while 43.8% delivered at the health centers where follow-up was done. The majority of our study participants received Magnesium sulphate (81.2%) and Nicardipine (87.5%). However, few participants received Alpha Methyl Dopa (31.2%) and Labetalol (18.8%).Thirteen (81.2%) of our study participants received anti-convulsant; diazepam and phenobarbital, while 4 each (25.0%) further received Midazolam and Fentanyl (Table 2).

All our study participants were rehydrated with crystalloids; the mean volume of crystalloids administered was 2938 ± 310 ml. Concerning transfusions, 60%

Table 2. Treatment modalities: Rehydration and transfusions.

Rehydration/transfusion modalities	N = 16	Frequency	Quantity in cc: Mean (SD*)
Rehydration with crystalloids	16	100	2938 (310)
Whole blood	9	60.0	1333 (661)
Platelet concentrate	7	46.7	1143 (476)
Fresh frozen plasma	5	31.2	800 (274)

*SD: Standard deviation.

(9) participants received whole blood, 31.2% (5) received fresh frozen plasma, while 46.7% (7) received platelets concentrate. Of the 16 participants with HELLP syndrome, 50.0% (8) received the LMWH enoxaparin (Lovenox®) during their management, while only 4 out of 11 who delivered preterm received corticosteroids, with the aim of maturing fetal lungs.

3.4. Outcome Assessment

As seen in Table 3 below, over 50% of our study participants presented severe complications after delivery, some of which were suspected without paraclinical confirmation, albeit with strong clinical suspicion. Regarding the type of complications, a majority had altered consciousness (87.5%), followed by disseminated intravascular coagulation (68.8%), and suspected stroke and acute pulmonary edema at 56.2% each. It is important to note that stroke was confirmed in 12.5% of our participants. However, 43.8% (7) cases recovered with blood pressure normalization occurring in 6 (37.5%) participants, while 56.2% (9) finally died.

Table 4 below presents the gestational ages of all participants at delivery, foetal birthweights, and the Apgar score at fifth minute.

Table 4 below shows the gestational ages, birthweights and the Apgar score at the 5th minute of the neonates delivered during the study period. Birthweights were missing for 4 neonates. So, we could not ascertain whether there was low birth weight or IUGR.

Concerning fetal outcome assessment, the majority, 68.7% (11) neonates were delivered preterm, while 31.3% (5) were delivered at term. Amongst them, 31.2% (5) were still births, 12.5% (2) had intrauterine growth restriction or low birth weight. Three (18.8%) of the neonates presented with a poor Apgar score at the 5th minute, while 50% finally had a good Apgar score. Placenta abruptio was identified in one case of still birth (Table 5).

3.5. Comparative Assessment of Participants Who Survived and Those Who Died

Compared to those who survived (43.8%), participants who died (56.2%) presented more severe complications (suspected stroke, $P < 0.001$; suspected hepatic hematoma/rupture, $P = 0.001$; disseminated intravascular coagulation, $P = 0.005$;

Table 3. Maternal outcome among participants.

Outcome	N = 16	Frequency
Eclampsia/altered consciousness	14	87.5
Disseminated intravascular coagulation**	11	68.8
Suspected stroke*	9	56.2
Suspected acute pulmonary edema*	9	56.2
Acute kidney injury	8	50.0
Suspected hepatic hematoma/rupture*	7	43.8
Normalized blood pressure	6	37.5
Stroke	2	12.5
Maternal death	9	56.2
Recovery	7	43.8

*Suspected: Strong clinical suspicion in patient's file, but without paraclinical confirmation. **Disseminated intravascular coagulation: based on excessive bleeding, ecchymosis and/or petechia.

Table 4. Foetal outcomes at individual level (n = 17 neonates).

Maternal ID	Gestational age at delivery (in weeks)	Birth Weight (in grams)	APGAR 5th minute
1	35	2000	0
2	30	1500	6
3	38	3200	9
4	29	NA	7
5	36	NA	9
6	36	NA	9
7	35	2300	9
8	37	2800	5
9	30	1300	0
10	38	3000	10
11	30	1000	5
12	38	NA	0
13	36	2800	0
14	39	4000	10
15	27	800	0
16*	34	1200	10
16*	34	1100	10

*Multiple pregnancy.

Table 5. Foetal outcomes at group level (n = 16 pregnancies).

Outcome parameters	N	Frequency
Still birth*	5	31.2
Intra-uterine growth restriction/LBW**	2	12.5
Term delivery (≥37 weeks)	5	31.3
Preterm deliveries (<37 weeks)	11	68.7
<28	1	6.7
28 to <32	4	26.7
32 to <34	0	0
34 to <37	5	33.3
≥37	5	33.3
APGAR score at 5th minute		
0	5	31.2
1 to 3	0	0
4 to 6	3	18.8
7 to 10	8	50.0

*Still births included one term and four pre-term deliveries; **Based on birthweights adjusted for gestational age; LBW: Low birth weight.

Table 6. Comparison of clinical features among participants who survived vs died.

	Survived (n = 7)	Died (n = 9)	
Clinical symptom	n (%)	n (%)	P-value[a]
Eclampsia/altered consciousness	5 (71.4)	9 (100)	0.175
Sepsis	0 (0)	4 (44.4)	
Stroke	2 (28.6)	0 (0)	0.097
Suspected stroke*	0 (0)	9 (100)	<0.001
Suspected hepatic hematoma/Rupture*	0 (0)	7 (87.5)	0.001
Suspected acute pulmonary edema*	3 (42.9)	6 (66.7)	0.615
Disseminated intravascular coagulation (DIC)**	2 (28.6)	9 (100)	0.005
Acute kidney injury (AKI)	2 (28.6)	6 (85.7)	0.103
Normalized blood pressure	6 (85.7)	0 (0)	0.001

*Suspected: Strong clinical suspicion in patient's file, but without paraclinical confirmation; **Disseminated intravascular coagulation: based on excessive bleeding, ecchymosis and/or petechia; [a]Chi squared test or Fischer exact test (if counts < 5).

and normalized blood pressure, P = 0.001). Other clinical features like altered consciousness, confirmed stroke, suspected pulmonary edema, and acute kidney injury were also higher in those who died, albeit without statistical significance. The blood pressure took between 11 to 35 days to normalize in survivors. However, there was no blood pressure normalization in those who died (Table 6).

Table 7. Comparison of management received by participants who survived vs died.

Treatment received	Survived (n = 7)	Died (n = 9)	P-value[a]
	n (%)	n (%)	
Rehydration with crystalloids	7 (100)	9 (100)	1.000
Whole blood	4 (66.7)	5 (55.6)	1.000
Fresh frozen plasma	2 (28.6)	3 (33.3)	1.000
Platelet concentrate	2 (33.3)	5 (55.6)	0.608
Quantities received (in cc)	**Mean (SD)**	**Mean (SD)**	**P-value[b]**
Crystalloid's volume	2786 (393)	3056 (167)	0.074
Whole blood volume	1500 (913)	1200 (447)	0.686
Fresh frozen plasma volume	750 (354)	833 (289)	0.739

[a]Chi squared test or Fischer exact test (if counts < 5); [b]Mann-Whitney U test; SD: Standard deviation.

Table 8. Comparison of paraclinical examinations and dialysis care received by participants who survived vs died.

Treatment received	Survived (n = 7)	Died (n = 9)	P-value[a]
	n (%)	n (%)	
Abdominal ultrasound	1 (14.3)	0 (0)	0.438
Chest x-ray	0 (0)	0 (0)	NA
Head CT scan	1 (14.3)	0 (0)	0.438
Dialysis care	1 (14.3)*	0 (0)	0.438

[a]Chi squared test or Fischer (if counts < 5); *Patient was referred to another hospital for dialysis; NA: Not applicable.

More participants who died received fluid resuscitation and blood products than those who survived, but the difference was not statistically significant. All participants were hydrated with crystalloids, and over 50% in each subgroup (survived vs died) received whole blood transfusions. A third of the participants in each group received fresh frozen plasma, while over 50% of those who died received an additional platelet transfusion. Although not statistically significant, those who died received more crystalloid resuscitation volume whereas those who survived received a greater volume of whole blood transfusions on average (Table 7).

As seen in Table 8 above, none of the participants who died did any of the investigations mentioned. Of the survivors, one participant did an abdominal ultrasound, one did a CT scan, which revealed ischemic stroke and she was adequately managed, while 1 participant with AKI was finally sent for dialysis.

4. Discussion

In this study, we sought to study the clinical presentation, management and ma-

terno-fetal outcomes of patients with HELLP syndrome at the Yaoundé Gynaeco-Obstetrics and Paediatric Hospital (YGOPH). This was a descriptive study of all severe preeclamptic patients, who were diagnosed with HELLP syndrome at the YGOPH between 1st January 2020 and 31st July 2021. A total of 254 cases of severe preeclampsia were received and managed at the YGOPH during the study period. Seventeen (6.7%) of them presented with HELLP syndrome, amongst which one patient who presented with hepatitis B was excluded and of the 16 cases retained, the peak age group was 20 - 24 years, and most patients were aged 20 - 30 years, 41.7% were employed, 50% were unemployed, and 8.3% were students. In addition, 33.3% were single and 66.7% were married, while 50% had only primary education, and those that had no education, secondary and higher level of education each consisted of 16.7%. Most participants (56.3%) had poor follow up and were gravida 1 and 2 (33% each). Most (56.3%) participants, presenting with HELLP syndrome were diagnosed in the post-partum period, with the most common symptom being headache (93.8%), followed by epigastric pain (87.5%). Obstetrical management was done by cesarean (62.5%) and vaginal (37.5%) delivery. Though all referred cases, 56.2% delivered at the YGOPH, while 43.8% delivered at the health centres where follow-up was done. Postpartum treatment of HELLP syndrome consisted of: antihypertensives, anticonvulsants, sedatives, fluid resuscitation and transfusion of blood and blood products. Those who died (56.2%) presented more severe complications, amongst which was eclampsia, sepsis, suspected: hepatic hematoma/rupture, acute pulmonary edema, stroke, DIC, and AKI. Those who survived (43.8%) presented some of these complications to a lesser degree, which were resolved. Of the 17 neonates, 5 were still births, while 12 were delivered alive, amongst which three (03) presented with a poor Apgar score at the 5th minute.

4.1. Sociodemographic Charecteristics

The frequency of HELLP syndrome in our setting (6.7%) is different from that stated in the literature (10% - 20%) [11]. African statistics are fairly incomplete regarding the incidence of this syndrome. However, Noubiap *et al.* in their meta-analysis of hypertensive disorders in pregnancy in the African setting found that HELLP syndrome occurred in 2.2% of patients [5]. This prevalence could have been lower if it was assessed amongst only patients with severe preeclampsia as in the present study. In Cameroon, Essiben *et al.* in their study of eclampsia, found that 9.9% of patients with eclampsia developed HELLP syndrome [8]. This result is higher than ours probably because unlike the present study, they studied patients with eclampsia, which are a subset of the patients with severe preeclampsia. Another Cameroonian retrospective study by Kemfang *et al.* in 2015 [12] showed that 1.8% of patients with severe preeclampsia developed HELLP syndrome. Their findings may have differed from ours because their study involved 3 referral hospitals with a larger sample size unlike our single-centre study. The values in our setting are lower than those in the literature

probably due to under-diagnosis and the fact that most women visit health centres for delivery.

We found that the most represented age group was those between 20 and 24 years (31.3%), while the least represented, were those between 15 to 19 years (12.5%) and 35 to 39 years (12.5%) respectively. However, the majority of patients (56.3%) were aged 25 years and above. This corroborates with the literature, where HELLP has been shown to occur in older maternal age groups, with a mean age of 25 years [11] [13]. Essiben *et al.* equally had the 20 to 25 year age group as the most represented at 31.8% in patients with eclampsia [8]. Age is a well-established risk factor of complications during pregnancy, including hypertensive disorders in pregnancy [5].

Most patients (56.3%) had poor follow up and were gravida one and two respectively. Moreover, most of our study participants were nulliparous (33.3%) or have had two deliveries at term (33.3%). This differs from the prevalence of HELLP, which is more frequent amongst multiparous women stated in the literature [13]. However, our findings are similar to those of Essiben *et al.* and Fouedjio *et al.* who studied eclampsia in Cameroon [7] [8]. Tebeu *et al.* equally found that older women had fewer than four antenatal contacts in the north region of Cameroon [14]. This could be because in our setting, most women visit specialized health care facilities during their first delivery, and decrease this tendency with increasing parity. In effect, a systematic review of antenatal consultations in developing countries found a statistically significant negative effect of parity on the adequacy of antenatal consultation [15]. In unspecialized health centres, there is an increased tendency of missed diagnosis as these lack the appropriate diagnostic equipment and trained personnel required for the prompt detection of this fatal disease. The mortality rate can be reduced by regular antenatal contacts, good follow-up and transfer of pregnant women who present with the risk of developing HELLP syndrome to the intensive care unit without delay.

4.2. Clinical Presentation

In the present study, the majority of cases of HELLP syndrome were diagnosed during post-partum (56.3%), three cases (18.8%) were diagnosed during labour, while the rest were brought to the hospital in emergency. Conversely, Sibai *et al.* [16] found that 70% of HELLP syndrome cases occur before delivery. The difference may be attributed to the fact that most of the patients visit health centres that lack specialists and adequate diagnostic tools. Those who eventually go to tertiary hospitals are either referred late from the aforementioned health centres or arrived, there is misdiagnosis or their results are made available late due to financial constraints or bureaucracy. Concerning preeclampsia, the diagnosis was missed during antenatal contacts in up to 25% of cases, meanwhile the diagnosis was made in 18.8% of our study participants, but 12.5% of their health providers neglected the treatment and close follow-up, while 6.3% initiated an-

tihypertensive treatment. The rest were revealed either as HELLP syndrome or eclampsia, which are all complications of preeclampsia. None of the patients who died in the present study underwent abdominal ultrasound, chest x-ray, head CT scan, or dialysis care. This mirrors the underdiagnosis due to inappropriate treatment centres.

Our study participants manifested common clinical features, amongst which where: headache, epigastric pain, convulsions, nausea and dizziness, which were remarkable at: 93.8%, 87.5%, 75.0%, 68.8%, and 66.7% respectively. These corroborates with findings from the literature [17] [18]; Sibai *et al.* and Aarnoudse *et al.* reported similar findings in their studies. The only difference between their studies and ours was that epigastric pain was the most common symptom unlike headache in the present study. This may due to the fact that epigastric pain is a common neglected symptom in our setting, which may hide a serious underlying pathology. Physicians should therefore pay attention to this seemingly trivial symptom, especially in pregnant women. Women who present with headache or epigastric pain during contacts should be thoroughly investigated in order to identify the underlying cause and treat accordingly.

4.3. Treatment Modalities

Ten (62.5%) of our study participants delivered by cesarean section, while 6 (37.5%) delivered vaginally. All 6 per-vaginal deliveries had complications; hence, it may be better to proceed to the delivery by caesarien section that is recommended in the literature [13] [19]. Sibai *et al.* recommended that a trial of labor be done only in patients with mild to moderate HELLP syndrome who are stable, have a favorable cervix and are at 32 weeks of gestation or greater [19].

The majority of our study participants received Magnesium sulphate (81.2%) and Nicardipine (87.5%). However, few participants received Alpha Methyl Dopa and Labetalol. This is similar to the findings of the single-centre study of Ahmad *et al.* in Egypt; all patients received Magnesium sulphate and most received antihypertensives (nifedipine; 62%, labetalol; 9.2%) [20]. In our study, no patient who died had a normalisation of blood pressure, whereas 6 (85.7%) of the 7 patients who had attained blood pressure normalisation ($P = 0.001$). This could imply that appropriate antihypertensive treatment could be life-saving in these patient group. However, larger multi-centre studies are required to confirm this finding.

Thirteen (81.2%) of our study participants received anti-convulsant; diazepam and phenobarbital, while 4 (25.0%) further received Midazolam and were also sedated with Fentanyl. Sedatives were mostly given to patients who were comatose, and all eventually died.

The treatment of HELLP syndrome is symptomatic. However, in our setting, we do not always have readily available blood products like fresh frozen plasma and platelets, and most patients also get them late or not at all due to financial constraints. All our study participants were resuscitated with crystalloids; the

mean volume of crystalloids administered was 2938 ± 310 ml. Equally, 9 (60%) participants received whole blood, 5 (31.2%) received fresh frozen plasma, while 7 (46.7%) received platelets concentrate. On average, patients received 4000 ml of fluids per day, which may have predisposed to fluid overload. Compared to patients who survived, those who died received more crystalloids and blood, though the blood products compared to the severity of the disease may not have been sufficient or adapted. A study by Jashmid *et al.* showed that plasmapheresis is a better life-saving treatment in HELLP syndrome patients compared to other blood products [21].

In the present study, corticosteroids (first dose) were administered in only 4 participants, with the aim to mature the foetal lungs. Routine administration of corticosteroids in patients with HELLP syndrome is recommended. The antenatal administration of dexamethasone at a high dosage of 10 mg intravenously every 12 hours has been shown to markedly improve the laboratory abnormalities associated with HELLP syndrome [22]. Patients treated with dexamethasone exhibit longer time to delivery [13]; this facilitates maternal transfer to a tertiary care centre and postnatal maturity of foetal lungs. Therefore, appropriate corticosteroid administration may reduce materno-foetal mortality.

4.4. Outcome Assessments

Concerning outcome assessment, over 50% of our study participants presented severe complications after delivery, ranging from: eclampsia, sepsis, stroke, hepatic rupture, acute pulmonary edema, disseminated intravascular coagulation, and acute kidney injury. Some of these complications were suspected without paraclinical confirmation. However, 43.8% recovered, while 56.2% finally died. This may be due to the fact that there was misdiagnosis, delayed diagnosis, financial constraints, and unadapted treatments. Isler *et al.* found cerebral haemorrhage or stroke to be the primary cause of death in 26% and the most contributing factor in another 45% of the deaths [23]. Dan *et al.* in their study found that maternal and perinatal mortality rate in hepatic rupture ranges from 18 to 86% and 80%, respectively [24]. The onset of acute kidney injury has been associated to increased maternal mortality in HELLP syndrome [25]. In another study, disseminated intravascular coagulation (DIC), sepsis/multi-organ dysfunction, and massive pulmonary embolism were found to be causes of death [26]. In the present study, all comatose patients died, and suspicion of stroke ($P < 0.001$), hepatic rupture ($P = 0.001$), suspected acute pulmonary edema ($P = 0.615$), disseminated intravascular coagulation ($P = 0.005$), and acute kidney injury ($P = 0.103$) were higher in patients who died than in those who survived. Unfortunately, we cannot with certainty say the exact cause of death since the necessary investigations to confirm the diagnosis were not done. However, they were suspected as being possible causes of death. The proper diagnosis of organ dysfunction in patients with HELLP syndrome could enable us to properly manage them and prevent adverse materno-fetal outcomes. In a large retrospec-

tive cohort study comprising 442 pregnancies complicated by the HELLP syndrome, maternal mortality was 1.1% [16], which is in accordance with other reports [17] [27]. However, there have been reports of higher maternal mortality, up to 25% [28]. Ideally, unexpected rapid death from HELLP may require forensic expertise and further investigation [29]. The deaths of the 9 (56.3%) mothers and the 5 (31.3%) neonates in the present study could have been prevented if these investigations were done on time to identify the possible complications and give adequate treatment.

Regarding the foetal outcome assessment, the majority (68.7%) neonates were delivered preterm, while (31.3%) were delivered at term. Amongst them, 5 (31.2%) were still births, 2 (12.5%) had intrauterine growth restriction or low birthweight. Eighteen (18) percent of the study participants had a persistent poor Apgar score at the 5th minute, while 50% finally had a good Apgar score. As per the literature, the perinatal mortality rate related to the HELLP syndrome is between 7.4% and 34% [17] [30], similar to that in the present study. Neonates delivered before 32 weeks' gestation have the highest risk of perinatal death. According to Gul *et al*., the perinatal mortality was 34% before 32 weeks' gestation, and 8% after the 32nd gestational week [30]. In the present study, 2 (13.3%) of the 5 neonates delivered before 32 weeks' gestation were still births, alongside 2 (13.3%) delivered after the 32nd week died, and one neonate delivered at term. This differences from the reported data in the literature reflect the misdiagnosis and neglected diagnosis in our setting. Many neonates may have died before 32 weeks' gestation, but may have passed away as still births due to other causes, without the diagnosis of HELLP or preeclampsia ever being made. The lower frequency of HELLP in our context testifies to this. Prematurity, placental insufficiency, with or without intrauterine growth restriction and abruptio placentae, are the leading causes of neonatal death [11]. Early diagnosis and the prompt initiation of appropriate treatment will definitely improve foetal outcome.

5. Limitations

We were able to achieve our objectives but, were confronted with certain important limitations and difficulties. The retrospective nature of our study implied that we could not exercise control over the accuracy with which information concerning the patients were collected and recorded. As a result, a good number of medical records were incomplete and lacked vital information. Most files did not have important laboratory records that were necessary for establishing diagnosis, confirming disease classification, or cause of death. Some cases were recorded in the registers but their medical records were not identified. This led to our sample size being small, thus, limiting its statistical power. However, given the scarcity of data on this subject, the high degree of delayed diagnosis, misdiagnosis, and neglected diagnosis, we believe that this work will help clinicians in their daily practice to increase their index of suspicion of HELLP syndrome in women who present with early or non-specific signs.

6. Conclusion

HELLP syndrome was a common complication in patients with severe preeclampsia, majority of cases were at their first or second pregnancy, and poor antenatal follow-up was common. The most common symptom among patients with HELLP syndrome was headaches, followed by: epigastric pain, convulsions, nausea and dizziness. The required paraclinical investigations to diagnose organ involvement or damage were seldom done. In our setting, the diagnosis of preeclampsia and HELLP syndrome is frequently missed or delayed. Treatment modalities for HELLP syndrome consisted of Obstetrical (cesarean and vaginal delivery) and post-partum management at the intensive care unit consisting of: antihypertensives, anticonvulsants, sedatives, fluid resuscitation and transfusions. Frequent and severe post-partum complications resulted in high mortality (both maternal and fetal), as well as preterm deliveries and IUGR or low birth weight. Compared to HELLP cases that survived, those who died presented more severe complications including eclampsia, sepsis, AKI, DIC, suspected hepatic hematoma/rupture, acute pulmonary edema, and stroke.

Acknowledgements

N.C.Y and K.C.N did the study conception and write up, M.C.H recruited the participants and filled the questionnaires, all authors reviewed the final manuscript.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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Supplementary Material

Table S1. Mississippi triple class classification for severity of HELLP syndrome [31].

Class I	Platelet count ≤50,000/mm^3; AST >70 U/L; LDH >600 U/L; evidence of hemolysis on smear
Class II	50,000 - 100,000/mm^3; AST >70 U/L; LDH >600 U/L; evidence of hemolysis on smear
Class III	100,000 - 150,000/mm^3