Factors affecting maternal and perinatal outcomes in HELLP syndrome: evaluation of 126 cases

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Summary

Objectives: To ascertain the characteristics, clinical features, and maternal fetal outcome in HELLP (hemolysis elevated liver enzymes, low platelets) syndrome at a tertiary referral center. *Material and Methods:* This was a cross-sectional study carried out at Dicle University between January 2004 and December 2008 in which the charts of 126 cases were retrieved retrospectively and data analyzed descriptively. *Results:* Of all deliveries 0.9% were complicated by HELLP syndrome. Of the cases with HELLP syndrome 79 (62.6%) had preeclampsia, 28 (22.2%) had eclampsia and 19 (15.2%) had a diagnosis of HELLP syndrome. The values of significant biochemical parameters (mean ± SD) were documented as ALT (alanin aminotransferase) 224 ± 42 IU/l and ALT[1] (after birth) 140 ± 22, AST 379 ± 23 IU/l and AST[1] 215 ± 51, LDH (lactate dehydrogenase) 1418 ± 67 IU/l and LDH[1] 875 ± 16, together with the hematological parameters as platelet count (86 ± 12 K/Ul), urine protein (3 + in urine test stick) and albumin levels (2 ± 0.9 g/dl). Eighty-six (68.25%) of the patients required albumin replacement. Thirty-one (24.6%) cases were nullipara and 95 (75.4%) multipara; of which 32 women (25.4%) were in Class I, and 94 (74.6 %) in Class II of complete HELLP syndrome. Regular antenatal examination was accomplished in a very small number of patients (12.25%). Fifty-eight (46.03%) patients required transfusions with blood or blood products and 12 (9.5%) underwent laparotomy due to major intraabdominal bleeding. Magnesium sulphate to prevent convulsions and corticosteroids (12 mg betametazone) to enhance fetal lung maturity were administered. Forty-four (34.9%) cases had vaginal delivery and 82 (65.1%) cesarean section; another 18 (14.2%) were with in utero stillbirth. Fifteen babies (11.9%) died, 26 (20.63%) developed placental abruption, 14 (11.11%) acute renal insufficiency, and 13 (10.31%) postoperative subcutaneous hematomas. Maternal mortality occurred in ten cases (7.93%). *Conclusion:* HELLP syndrome is a pathology associated with a high incidence of maternal and perinatal complications. Laboratory parameters in cases with HELLP syndrome are not efficient in detecting perinatal results, but can be used as risk denominators in evaluating maternal complications. Therefore, for patients with HELLP syndrome, standard antenatal follow-up protocols should be applied in order to obtain early diagnosis and improve the speed of transfer to obstetric departments with expertise in this field.

Key words: HELLP; Preeclampsia; Eclampsia; High-risk pregnancy.

Introduction

Hypertensive disorders represent the most common medical complication of pregnancy, affecting 6-8% of gestations in the United States [1]. HELLP (elevated liver enzymes, low platelets) syndrome represents a severe form of preeclampsia/eclampsia characterized by hemolysis, elevated liver enzymes, and low platelets [2] and was described in 1982 by Weinstein [3]. The reported maternal mortality rates from HELLP syndrome range from 1% in the United States [3] to 30% in Turkey [4]. The reported incidence of HELLP syndrome in association with eclampsia ranges from 10.8% to 32.1% [5, 6]. HELLP syndrome, a serious condition in its complete form, is associated with substantial risk for the mother and fetus [7, 8]. Two classifications for the HELLP syndrome are commonly used [9, 10]. The Tennessee System classification is based on the assessment of the following parameters: AST > 70 UI/L, LDH > 600 UI/l, thrombocytes < 100,000/ mm^3. Accordingly, there are two forms: complete (all elements present) and partial HELLP syndrome (one or two elements present). The Mississippi classification relies on the thrombocyte count: class I (< 50,000/mm^3), class II (50,000-100,000/mm^3) and class III (100,000-150,000/mm^3). Martin *et al*., found higher maternal morbidity rates in Class 1 HELLP syndrome [11]. A wide range of complications may arise and the condition represents diagnostic and therapeutic problems; timing and method of delivery are important.

In this study we report the maternal and perinatal outcomes in HELLP syndrome cases at our clinic.

Material and Methods

This retrospective study was performed at Dicle University, School of Medicine, Obstetric and Gynecology Department between January 2004 and December 2008. HELLP syndrome was determined by the presence of all three of the following criteria: hemolysis (characteristic appearance of peripheral blood smear and serum lactate dehydrogenase [LDH] level ≥ 600 U/l or serum total bilirubin level ≥ 1.2 mg/dl), elevated liver enzymes (serum aspartate aminotransferase concentration ≥ 70 U/l), and low platelet count (< 100,000 cells/μl) [10]. Maternal outcomes analyzed included eclampsia, placental abruption, acute renal failure, need for transfusion of blood products, cesarean delivery and maternal death. For each woman, categoric data were collected concerning age, parity, gestational age at diagnosis, mean arterial blood pressure, blood platelet count, peak serum levels of aspartate aminotransferase (AST), alanin aminotransferase (ALT), lactate dehydrogenase (LDH) and adverse maternal outcomes. Reported laboratory results and symptoms, such as headache, visual changes, nausea/vomiting

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and epigastric pain were present on admission. Gestational age was determined according to either last menstrual period or ultrasonography (US) examination.

Results

During the study period 126 women met the strict criteria for HELLP syndrome and there were 21,487 deliveries totally; 0.9% of all deliveries were complicated by HELLP syndrome. Demographic and clinical characteristics of the cases are presented in Table 1. Fifteen cases had severe preeclampsia, four had chronic hypertension and 18 had eclampsia. Gestational ages at diagnosis were ≤ 28, 28 to 32, and > 32 weeks of gestation in 13.5%, 31.7%, and 54.8% of cases, respectively. Nadir blood platelet count < 50,000 cells/μl, peak AST concentration > 150 U/l, and peak LDH concentration > 1400 U/l were present in 25.4%, 62.7%, and 27.7% of the cases, respectively. There was no correlation between gestational age at onset of HELLP syndrome and either nadir platelet count (r = 0.05), peak serum AST concentration (r = 0.06), or peak serum LDH concentration (r = 0.04). Adverse maternal outcomes studied included eclampsia, placental abruption, acute renal failure, the need for transfusion, and death. Acute renal failure was diagnosed in the presence of oliguria or anuria in association with a creatinine clearance of ≤ 20 ml/min or an elevated serum creatinine level of ≥ 2 mg/dl. Fourteen (11.11%) cases had acute renal failure, and seven (50%) were transferred to the nephrology clinic. In 58 (46.03%) cases blood products were transfused. Magnesium sulphate was administered routinely to prevent and control convulsions (a loading dose of 6 g given over 20 min, followed by a maintenance dose of 2 g/h as continuous intravenous solution for at least 24 h postpartum). Corticosteroids (12 mg betametazone intramuscularly every 12 h/2 times) were administered to enhance fetal lung maturity at ≤ 34 weeks' gestation. The cesarean delivery rate was 65.1% and spontaneous vaginal delivery rate was 34.9% (Table 2). Maternal mortality occurred in ten cases (7.93%). Table 3 presents the clinical characteristics of those maternal death cases. The mean birth weight of the cases was 1991.89 ± 957.77 g and 91 (72.22%) fetuses had a fetal weight of < 2500 g. The mean 0-min Apgar score was 4.77 ± 2.28 and the 5-min Apgar score was 7.05 ± 2.03. Sixty-four (55.65%) of these infants had low 5-min Apgar scores and 15 (11.90%) of the fetuses died.

Discussion

Although the term HELLP syndrome was not coined until 1982, its pathological features have been recognized for at least 100 years [12]. However, controversies persist regarding the diagnosis, management, and prognosis of this enigmatic disease. This uncertainty exists partly because the pathophysiological mechanism remains obscure and partly because of disagreement about the criteria used to define this syndrome. Sibai defined standardized strict laboratory criteria for disease diagnosis

Table 1. — *Demographic and clinical characteristics of the cases (n = 126).*

	Mean (SD)	Range
Maternal age (years)	30.32 ± 8,76	18-48
Gestational age (weeks)	32.63 ± 5,87	25-39
Gravidity	4.58	1-16
Parity	3.27	0-13
Blood pressure (systole/diastole) (mm/hg)	144.96/97.61	220-70
Platelets (K/UL)	86.88	142-424
Albumin (g/dl)	2.09	3.5-5.0
Blood urea nitrogen (mg/dl)	39.071	10-45
Creatinin (mg/dl)	0.99	0.6-1.30
Alanin aminotransferase (IU/l)	224.42	0-55
Alanin aminotransferase[1] (IU/l)*	140.22	0-55
Aspartate aminotransferase (IU/l)	379.23	5-40
Aspartate aminotransferase[1] (IU/l)*	215.51	5-40
Total bilirubin (mg/dl)	1.76	0.2-1.2
Lactic dehydrogenase (IU/l)	1418.67	125-243
Lactic dehydrogenase[1] (IU/l)*	875.16	125-243

*: ALT , AST and LDH values after birth.

Table 2. — *Symptoms, complications, and mode of delivery of the cases.*

	n (%)
Headache	107 (84.92%)
Nausea and/or vomiting	99 (78.57%)
Epigastric pain	77 (61.11%)
Visual symptoms	86 (68.25%)
Eclampsia	28 (22.22%)
Placental abruption	26 (20.63%)
Cerebral ischemia-edema	17 (13.49%)
Cerebral hemorrhage	8 (6.34%)
Acute renal failure	14 (11.11%)
Transfusion of blood products	58 (46.03%)
Laporatomy for major bleeding	12
Albumin transfusion	86 (68.25%)
Cesarean delivery	82 (65.1%)
Spontaneous vaginal delivery	44 (34.9%)
Maternal death	10 (7.93%)
Fetal death	15 (11.90%)

Table 3. — *Clinical characteristics of maternal death cases.*

Case	Maternal age (years)	Gestational age (weeks)	Associated pathologies	Delivery route	Day of death	Complication leading to death
1	26	38	Eclampsia	Cesarean	6th	IHH*
2	30	27	Eclampsia	Vaginal delivery	1st	IHH
3	18	33	Eclampsia	Vaginal delivery	1st	Sepsis
4	38	31	Eclampsia	Cesarean	3rd	IHH
5	42	28	Eclampsia	Cesarean	7th	IHH
6	35	26	Stillbirth	Vaginal delivery	1st	Sepsis
7	43	30	Pulmonary embolism	Vaginal delivery	3rd	Sepsis
8	32	31	Fulminant hepatitis	Cesarean	1st	Fulminant hepatitis
9	38	30	Eclampsia	Cesarean	1st	IHH
10	26	37	Eclampsia	Vaginal delivery	4th	IHH

IHH: intrahemispheric hemorrhage.

[10] which we have used in this study to define HELLP syndrome. HELLP syndrome can be diagnosed in pregnant women whose blood pressure elevation was first detected after mid-pregnancy, either with or without proteinuria. Sibai observed that hypertension and proteinuria may be absent or only slight. Even though HELLP syndrome is considered to be a variant or an atypical variant form of severe preeclampsia, its severity is reflected in the laboratory parameters, and not in the usual clinical parameters of blood pressure and proteinuria that typically reflect preeclampsia disease severity [13]. We observed that 7% of women did not have proteinuria in our study. HELLP syndrome is associated with both maternal and neonatal complications. In the literature, there is controversy regarding adverse maternal outcomes in HELLP syndrome. Martin *et al*. [11] reported a significant maternal and perinatal complication rate in patients with platelet count values ≤ 50,000 cells/mm^3, but Haddad *et al*. [15] found that laboratory parameters of HELLP syndrome are not independent risk factors for adverse maternal outcome. Laboratory thresholds that indicate more than 75% risk of serious maternal morbidity are LDH concentration > 1400 U/l, AST > 150 U/l, ALT > 100 U/l and platelet count ≤ 50,000 cells/mm^3. Thirty-two of the women had these values in our study. A decrease in these parameters after delivery is a good prognostic factor; 116 of the women had lower laboratory values after birth in our study. Interestingly, clinical symptoms, such as headache, visual changes, epigastric pain and nausea/vomiting have been suggested to be better predictors of adverse maternal outcome than laboratory parameters [14]. These clinical symptoms were more predictive than laboratory values in our study. The prognosis of the women who had clinical symtoms was worse than the others. HELLP syndrome carries a significant risk to mother and fetus, with approximately 1-3.5% for the mother, with increased proportion of multi-organ failure (MOF) and acute renal failure (ARF). Sixteen of the cases had MOF and 14 had ARF in our study.

Intensive care management of patients with HELLP syndrome producing multiple organ system failure consists of careful monitoring with active and supportive treatment of any complications. Coagulopathy and hemorrhage require aggressive replacement with blood and clotting factors. We treated our cases with coagulopathy and DIC with blood and clotting factors such as red blood cells, platelets, fresh frozen plasma and albumine. Cerebral hemorrhage is a serious complication and has been shown to be a fatal event in 50% to 65% of cases [17]. We had six such cases. We also had eight cases of pulmonary edema. In previous reports, maternal mortality was calculated to be approximately 1%, which was mostly a result of disseminated intravascular coagulopathy and the complications [18]. We only observed ten maternal fatalities in HELLP. Perinatal mortality and morbidity are considerably higher in HELLP syndrome offspring than for the mothers, and are primarily dependent on the gestational age when the condition develops Kim *et al*. reported that newborns with HELLP syndrome have low 5 min Apgar scores [19]. Sixty-four of the cases had lower 5 min Apgar scores in our study. The perinatal mortality rate related to HELLP syndrome is between 7.4% and 34%. Neonates delivered before completing 32 weeks' of gestation have the highest risk of perinatal death [20, 21]. Fifty-seven of the cases delivered before 32 weeks and 15 of the fetuses died.

In conclusion, devastating effects of a hypertensive disorder associated with pregnancy could be prevented by close antenatal follow-up, timely prediction of risk factors and reasonable management strategies. Early detection of high-risk individuals and mild cases by well- trained primary medical personnel and timely referral to advanced tertiary centers will lead to improved perinatal and maternal outcomes in this critical group of patients.

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