



Retrospective Analysis of Maternal and Neonatal Outcomes in Pregnant Women with HELLP Syndrome Under General and Spinal Anesthesia

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Abstract

We aimed to document anesthetic techniques for cesarean section in cases of HELLP (hemolysis, elevated liver enzymes and low platelets) syndrome. A retrospective study was carried out in a tertiary center including all patients who underwent emergency cesarean section for HELLP syndrome. The immediate preoperative maternal laboratory results including complete blood count, D-dimer, ALT, AST, LDH, bilirubin, and uric acid), the method of anesthesia, and complications were recorded. Fetal and neonatal outcomes were reviewed. HELLP class of the patients according to Mississippi classification were made to compare demographics, laboratory results and perinatal outcomes.

A total number of 193 charts were reviewed and 25 ASA IV HELLP syndrome was identified and 22 of these parturients underwent cesarean delivery while the remaining 3 parturients had vaginal delivery. The mean maternal age and gestational age of all patients were 31.2±2.77 weeks and 32.08±3.95, respectively. General anesthesia was selected in 14 out of 22 patients (63.63%), while 8 out of 22 (36.36%) received single-shot spinal anesthesia. Preoperative platelet count was significantly higher ($p<0.01$) in the spinal anesthesia group. All patients with a lower platelet count than 50,000/ μ L received general anesthesia. Regarding the classification of parturients, there were 5, 7 and 10 patients in HELLP Class 1, 2 and 3, respectively. In conclusion although spinal anesthesia was used in selected HELLP patients in the literature, our data demonstrated that general anesthesia was the most commonly performed technique than spinal anesthesia in parturients with HELLP syndrome

1. Introduction

In 1982, Weinstein (Weinstein, 1982) described an advanced stage of preeclampsia, characterized by a triad who names the disease; intravascular hemolysis (H), elevated liver enzymes (EL), and low platelets (LP). The pathophysiology of HELLP syndrome is still unclear but endothelial damage and activation of the coagulation cascade are considered to be underlying mechanism. Microangiopathic hemolytic anemia causes hemolysis by vascular damage and fibrin deposits (Wilke, Rath, Schutz, Armstrong, & Kuhn, 1992). As the liver appears to be the main site of this process, downstream liver cells suffer ischemia leading to periportal necrosis (Audibert, Friedman, Frangieh, & Sibai 1996). Elevated liver enzymes may reflect both liver damage and a hemolytic process. A drop in platelet count is mostly due to increased platelet consumption by adhesion to endothelium damage with a short half-life (D'Anna, 1996).

Typical clinical symptoms include abdominal pain in the right upper quadrant or epigastric area, nausea, and vomiting. These nonspecific symptoms can delay the diagnosis for a long time (Thiagarajah, Bourgeois, Harbert, & Caudle, 1984; Weinstein, 1985; Sibai et al., 1986). Up to 30–60% of women complain from headache and up to 20% suffer from visual disturbances (Sibai, 2004). Another common feature of HELLP is severe coagulopathy before, during, and after birth, which requires a close, continuous clinical evaluation. Diagnostic laboratory values from Tennessee Classification System are lactate dehydrogenase (LDH) ≥ 600 IU/l, AST ≥ 70 IU/l, and platelet count $\leq 100000/\mu\text{L}$ (Audibert et al., 1996).

HELLP syndrome may result in life-threatening complications, such as placental abruption, pulmonary edema followed by acute respiratory distress, disseminated intravascular coagulation (DIC), cerebral hemorrhage, septic shock, acute renal failure, and hepatic hemorrhage due to hepatic rupture (Barton & Sibai, 2009; Zeeman, 2009). Maternal mortality ranges from 1%-3%, with a perinatal mortality rate of 20% (Roelofsen, 2003). Hence, efforts to enhance the management of these disorders are vital to reduce both maternal and fetal morbidity and mortality, safe and evidence-based anesthetic management of patients with HELLP syndrome in the peripartum period is of critical importance. The choice of the anesthetic method for the patients is highly dependent on preeclampsia, their platelet counts, and their coagulation statuses.

In the present retrospective study, we aimed to report the anesthetic method during cesarean delivery and maternal and neonatal outcomes in parturients with HELLP Syndrome and to compare them within the classes of HELLP.

2. Materials and Methods

After obtaining approval from the local institutional Ethics Committee (Decision number.187. 10.03.2016 version 1, updated 2021), the database of Gazi University Hospital between June 1, 2016 to June 1, 2021 was searched and 193 patients with ICD code for preeclampsia were retrieved. Among them specifically 25 parturients with HELLP were identified; 22 of them had cesarean section and 3 had vaginal delivery.

Diagnostic laboratory values from Tennessee Classification System for HELLP syndrome include lactate dehydrogenase (LDH) ≥ 600 IU/L, AST ≥ 70 IU/L, and platelet count $\leq 100,000/\mu\text{L}$ (Audibert, 1996). In the present study, we classified HELLP syndrome according to Mississippi classification (Magann & Martin, 1999)(Table 1). Patients with severe disease were in class 1, characterized by low platelet count $\leq 50,000/\mu\text{L}$ and AST or ALT ≥ 70 IU/L. If the platelet count was between 50,000/ μL to 100,000/ μL , HELLP was defined as class 2. Those with mild thrombocytopenia ($>100,000/\mu\text{L}$), with mild elevations of AST or ALT were considered class 3. LDH is ≥ 600 IU/L in every class.

Twenty five ASA IV parturients' age, comorbidities, gestational age, parity, and preeclampsia history were recorded. Antenatal follow-up of maternal laboratory results including liver function tests, complete blood count, proteinuria, and D-Dimer were compared among the HELLP classes.

Regarding the perinatal outcomes, the method of anesthesia, need for platelet/RBC/FFP transfusions, and complications were presented and compared among the HELLP classes. Fetal outcomes consisted of stillbirth (death after 20 completed weeks of gestation and before birth), preterm birth (at <37 weeks of gestation), newborn weight, admission to the Neonatal Intensive Care Unit (NICU), and Apgar scores (at 1 and 5 minutes).

3. Results

There were 22 ASA IV women with HELLP syndrome underwent cesarean section during the audit. Demographics and focused maternal history characteristics of these patients were shown in Table

2. The mean maternal age and gestational age were 31.2 ± 2.77 years and 32.08 ± 3.95 weeks, respectively and all deliveries were preterm.

When patients' demographic properties were compared among the HELLP classes they were comparable. Proteinuria was documented in all patients within class 1 HELLP syndrome.

The peripartum morbidity/comorbidities were presented (Table 2).

Laboratory results of parturients included Hb (g/dL), platelet (count/ μL), AST (U/L), ALT (U/L), LDH (U/L), bilirubin (mg/dL), uric acid (mg/dL), and D-dimer (ng/mL) were listed (Table 3). The mean hemoglobin levels were almost acceptable limits according to the trimester of pregnancy in all 3 classes of HELLP. Platelet count was significantly lower ($p=0.001$) and D-Dimer was higher in class 1 HELLP syndrome ($p=0.55$). Liver enzymes (AST/ALT/LDH) were significantly high in all classes of HELLP, which was a diagnostic criteria (Table 3). Bilirubin and uric acid levels were higher than normal limits in class 1 of HELP (Table 3). The type of anesthesia, transfusion need, and perinatal outcomes were shown (Table 4). Approximately 36.36% of the parturients received single-shot spinal anesthesia using 10 mg of hyperbaric bupivacaine with opioids (fentanyl 10 μg and morphine 100 μg). While 63.63% of patients underwent cesarean delivery under general anesthesia, Preoperative platelet count was significantly higher in the spinal anesthesia group ($p<0.01$, Table 5). The majority of patients who received the general anesthesia was belong to class 1 HELLP including patients with platelet count less than 50,000/ μL .

Table 1. Classifications of HELLP (Magann & Martin, 1999, Audibert, 1996).

HELLP	Mississippi Class	Tennessee Class	HELLP
Class 1	Platelet count $\leq 50,000/\mu\text{L}$	Platelet count $\leq 50,000/\mu\text{L}$ AST or ALT ≥ 70 IU/L LDH ≥ 600 IU/L	Complete
	AST or ALT ≥ 70 IU/L		
	LDH ≥ 600 IU/L		
Class 2	Platelet count $50,000-100,000/\mu\text{L}$	Platelet count $\leq 50,000/\mu\text{L}$ AST or ALT ≥ 70 IU/L LDH ≥ 600 IU/L	Complete
	AST or ALT ≥ 70 IU/L		
	LDH ≥ 600 IU/L		
Class 3	Platelet count $>100,000/\mu\text{L}$	Severe preeclampsia with ELLP, EL, or LP	Incomplete
	AST or ALT ≥ 70 IU/L		
	LDH ≥ 600 IU/L		

AST: Aspartate aminotransferase, **ALT:** Alanine aminotransferase, **LDH:** Lactate dehydrogenase, **ELLP:** Elevated Liver enzymes Low Platelets, **EL:** Elevated Liver Enzymes, **LP:** Low Platelet

Table 2. Demographics and focused maternal history (Mean \pm Sd, n or %)

	Total (n=22)	Class 1 (n=5)	Class 2 (n=7)	Class 3 (n=10)
Age (year)	31.2 \pm 2.77	34.4 \pm 3.36	29.1 \pm 4.52	30.3 \pm 6.37
Primiparity (%)	54.5	60.0	57.1	50.0
Gestation (week)	32.08 \pm 3.95	33.6 \pm 2.26	30.6 \pm 4.5	32.15 \pm 4.33
Preeclampsia history (%)	9.1	0.0	14.2	10.0
Hypertension before pregnanc (%)	6.6	0.0	0.0	20.0
Systolic BP (mmHg)	162 \pm 15.67	163.33 \pm 32.14	156.66 \pm 5.77	163.33 \pm 12.24
Diastolic BP (mmHg)	103.75 \pm 19.27	100 \pm 20	107.5 \pm 37.74	103.33 \pm 7.07
Proteinuria (%)	86.36	100.00	85.00	80.00
Maternal comorbidity (%)	31.81	20.00	28.50	80.00

BP: Blood pressure

Table 3. Demographics and focused maternal history (Mean \pm Sd, n or %)

	Total (n=22)	Class 1 (n=5)	Class 2 (n=7)	Class 3 (n=10)
Hb (g/dl)	11.12 \pm 1.48	11.18 \pm 1.43	10.98 \pm 1.70	11.1 \pm 1.49
Platelet (count/ μL)	88.68 \pm 44.23	32.6 \pm 9.96*	67.42 \pm 13.37	131.6 \pm 16.04
AST (U/L)	212.95 \pm 243.36	232.6 \pm 112.67	171.28 \pm 241.77	232.3 \pm 302.65
ALT (U/L)	189.77 \pm 161.32	241 \pm 102.23	135.71 \pm 143.22	202 \pm 196.23
LDH (U/L)	531.13 \pm 224.07	603 \pm 122.38	493.57 \pm 242.61	521.5 \pm 259.21
Bilirubin (mg/dL)	0.74 \pm 0.63	1.57 \pm 1.20	0.62 \pm 0.35	0.34 \pm 0.12
Uric acid (mg/dL)	6.46 \pm 1.43	7.2 \pm 2.26	6.33 \pm 1.91	6.31 \pm 0.61
D-dimer (ng/mL)	5.74 \pm 4.48	8.65 \pm 8.98	5.54 \pm 2.13	3.15 \pm 0.52

Hb: Hemoglobin, **AST:** Aspartate aminotransferase, **ALT:** Alanine aminotransferase, **LDH:** Lactate dehydrogenase,

*:P<0.05 compared to class 2 and 3

General anesthesia protocol consisted of induction using intravenous (IV) 5 mg/kg of thiopental and 1 mg/kg succinylcholine for facilitation of endotracheal intubation using 7.0 mm tube followed by 1 MAC of sevoflurane inhalation in 50% oxygen-air mixture until delivery of the newborn and maintained by adding 0.2 µg/kg/h of IV remifentanyl infusion. There were no postoperative complications associated with either regional or general anesthesia. Mean newborn weight was 1815±808.16 gram (81.81% of newborns with low birth weight and 36.36% of newborns were with very low birth weight). One patient had a stillbirth on the 24th gestational week. Mean Apgar scores at 1 and 5 minute (min) were 7±2.34 and 9±2.27, respectively. One newborn (4.54%) had Apgar score <7 at 1 min and 1 newborn (4.54%) had Apgar score <7 at 5 min. The neonatal intensive care unit (NICU) admission rate was 18.8%. In Class 1 HELLP group, 3 patients received 1 unit of red blood cell (RBC) transfusion and one patient received 1 unit of platelet + FFP (fresh frozen plasma) which was significantly higher than the other classes (p=0.02). In the class 2 HELLP group, one patient received 2 units of platelet and 1 unit of platelet + FFP in one patient. In class 3 HELLP group, only 2 units of RBC was transfused to one patient (Table 4).

4. Discussion

In this retrospective study, we have reported maternal and neonatal outcomes and choice of anesthesia and its management in pregnant women with HELLP syndrome who underwent cesarean section.

The incidence of HELLP syndrome varies between 0.5 to 0.9% of all pregnancies and 4–20% of women with preeclampsia. It develops most commonly

between the 27th and 37th week of gestation (Haram, Svendsen, & Abildgaard 2009). Similarly, we documented 197 preeclamptic parturients and 25 of them were identified as HELLP corresponding to an incidence of 12.69%.

One study showed that maternal complications including the requirement for blood transfusion were significantly higher in class 1 HELLP patients (Miranda et al., 2011). We also found that class 1 patients needed transfusions more than the patients in the other two classes.

As it is well known epidural venous plexus engorgement in delivering women and low count of platelets predispose them to a higher risk of hematoma after regional anesthesia (Makris, Thornton, & Hennessy 2004). However, in one of the retrospective studies reviewed antepartum HELLP cases, the rate of combined spinal-epidural (CSE) block was 52.0%, whereas rate of general anesthesia and single shot spinal anesthesia were 36.3% and 11.8%, respectively (Palit, Palit, Vercauteren, & Jacquemyn, 2009). The authors stated that CSE anesthesia was feasible and safe in selected cases of HELLP syndrome without spinal-epidural hematoma luckily. We did not come across CSE block in our audit in this particular patient group of HELLP.

According to the latest consensus report of society for obstetric anesthesia and perinatology (SOAP) (Bauer et al., 2021) in case of platelet count higher than 70,000/ µL risk of spinal-epidural hematoma is very rare but if platelet count is less than 50,000/µL, there might be an increased risk. In our study, since spinal anesthesia was not chosen for patients with platelet count less than 100,000/µL, no complications associated with spinal anesthesia were encountered

Table 4. Perinatal outcomes and anesthesia method performed (Mean \pm Sd, n or %).

	Total (n=22)	Class 1 (n=5)	Class 2 (n=7)	Class 3 (n=10)
Need for transfusion (n)	7	4	2	1
RBC/Platelet/FFP (unit)	5/4/2	3/1/1*	0/3/1	2/0/0
Newborn weight (g)	1815 \pm 808.16	1979 \pm 747.28	1642 \pm 758.12	1826 \pm 924.47
General anesthesia (%)	63.63	100.00	85.70	30.00
Spinal anesthesia (%)	36.36	0.00	14.20	70.00
1 min APGAR score	7 \pm 2.34	7.6 \pm 0.89	5.7 \pm 3.1	8 \pm 1.88
5 min. APGAR score	9 \pm 2.27	9.4 \pm 0.89	7.57 \pm 3.4	9 \pm 2
Stillbirth (%)	4.54	0.00	14.20	0.00
Admission to NICU (%)	18.18	20.00	14.20	20.00

NICU: Newborn Intensive Care Unit, RBC: Red Blood Cell

Table 5. Preoperative platelet count for spinal and general anesthesia. (Mean \pm Sd)

	Spinal (n=8)	General (n=14)	p value
Platelet Count (/ μ L)	119.25 \pm 28.42*	61.21 \pm 42.69	0.007

NICU: Newborn Intensive Care Unit, RBC: Red Blood Cell

A higher risk of respiratory depression may occur given the increased incidence of premature fetuses; deleterious effects of catecholamine on uterine blood flow after laryngoscopy, drug interactions, and access to difficult airways are the main causes of maternal mortality (Chestnut, 1995). It was reported that (Del-Rio-Vellosillo & Garcia-Medina, 2016) the hemodynamic response to intubation could be blunted with esmolol, fentanyl, remifentanyl, or alfentanil. In our study, we used remifentanyl analgesia only for the maintenance of general anesthesia. Remifentanyl is an opioid that is not metabolized in the plasma not by the kidney or liver, without risk of accumulation in presence of renal or hepatic impairment which could be possible in the HELLP syndrome.

5. Conclusion

In conclusion pregnant women with HELLP evaluated according to HELLP classification, anesthesia method should be selected based on the safe platelet counts stated in the recently published consensus report.

Statistical analysis

Statistical analysis was carried out using SPSS version 21.0. After performing descriptive statistics, data were presented as number (n), rate (%), mean, and standard deviation (sd) or median where appropriate. A p value less than 0.05 was considered as statistically significant.

Conflicts of interest

The authors declare no conflicts of interest.

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