Turkish Journal of Clinics and Laboratory

To cite this article: Yesiler FI, Kosovalı DB, Peker TT, Ozcelik M, Unal MN, Bayar MK. Our experience about HELLP syndrome in intensive care unit. Turk J Clin Lab 2022; 4: 518-524.

Original Article

Our experience about HELLP syndrome in intensive care unit

Yoğun bakım ünitemizde HELLP sendromu deneyimlerimiz

Fatma Irem Yesiler*[1], Behiye Deniz Kosovali[2], Tulay Tuncer Peker[3], Menekse Ozcelik[4], Mustafa Necmettin Unal[4], Mustafa Kemal Bayar[4]

[1]Department of Anesthesiology and Critical Care Unit, Baskent University Faculty of Medicine, Ankara, Turkey
[2]Department of Critical Care, Ankara City Hospital, Ankara, Turkey
[3]Department of Anesthesiology and Critical Care Unit, Gülhane Training and Research Hospital, Ankara, Turkey
[4]Department of Anesthesiology, Ankara University Faculty of Medicine, Ankara, Turkey

Abstract

Aim: HELLP syndrome is a life-threatening condition frequently associated with severe preeclampsia-eclampsia and is characterized by hemolysis, elevated liver enzymes and low plateletes. The aim of our study was to evaluate retrospectively the patients with HELLP syndrome admitted to the intensive care unit (ICU).

Material and Methods: We retrospectively reviewed the medical records of 19 patients with HELLP syndrome admitted to ICU between January 2011 and December 2015.

Results: The mean maternal age was 30.0 ± 5.1 years and the mean gestational age was 32.2 ± 4.8 weeks of 19 patients with HELLP syndrome admitted to the ICU. The mean Acute Physiology and Chronic Health Evaluation System (APACHE II) score, Sequential Organ Failure Assessment (SOFA) score, Glasgow Coma Scale (GCS) were 25.9 ± 4.0, 14.2 ± 2.8 and 5.2 ± 2.7 at ICU admission, respectively. Mechanical ventilation was required for 12 patients (63.6%). Eight patients (42.1%) had acute kidney injury and only 1 patient was required renal replacement therapy. Therapeutic plasma exchange was performed to 11 patients (57.9%). Three patients (15.8%) had dissemine intravascular coagulation (DIC), 5 patients (26.3%) acute respiratory distress syndrome (ARDS), 3 patients (15.8%) septic shock, and 1 patient (5.3%) cardiogenic shock. The mean length of ICU stay was 8.1 ± 4.7 days. Both of maternal and fetal mortality rate was 10.5%.

Conclusion: Maternal/fetal morbidity and mortality are high in HELLP syndrome. Early diagnosis, close follow-up in intensive care unit, appropriate treatment and management by multidisciplinary team may prevent complications and improve prognosis of HELLP syndrome.

Key words: HELLP syndrome, preeclampsia, eclampsia, pregnancy, intensive care unit

Corresponding Author*: Fatma Irem Yesiler, Department of Anesthesiology and Critical Care, Başkent University Faculty of Medicine, Ankara, Turkey.
E-mail: fatmairem84@hotmail.com
ORCİD: 0000-0002-0612-8481
Doi: 10.18663/tjcl.1173744
Recevied: 11.09.2022 Accepted: 11.10.2022

Öz

Amaç: HELLP sendromu, hemoliz, yükselmiş karaciğer enzimleri ve trombosit sayısında azalma ile karakterize, ağır preeklampsi ve eklampsiyle ilişkili hayatı tehdit eden bir durumdur. Çalışmamızın amacı, yoğun bakım ünitesine (YBÜ) kabul edilen HELLP sendromlu hastaları retrospektif olarak değerlendirmektir.

Gereç ve Yöntemler: Ocak 2011 ile Aralık 2015 arasında yoğun bakım ünitesine kabul edilen 19 HELLP sendromlu hastanın medikal kayıtlarını retrospektif inceledik.

Bulgular: Yoğun bakım ünitesine kabul edilen 19 HELLP sendromlu hastanın ortalama yaşı 30.0 ± 5.1 yıl ve ortalama gebelik yaşı 32.2 ± 4.8 hafta idi. YBÜ kabuldeki ortalama Akut Fizyoloji ve Kronik Sağlık Değerlendirme Sistemi (APACHE II) skoru, Sıralı Organ Yetmezliği Değerlendirmesi (SOFA) skoru, Glasgow Koma Skalası (GCS) sırasıyla 25.9 ± 4.0, 14.2 ± 2.8 ve 5.2 ± 2.7 idi. On iki hastanın (%63,6) mekanik ventilasyon gereksinimi oldu. Sekiz hastanın (%42.1) akut böbrek hasarı varken sadece 1 hastaya renal replasman tedavisi gerekti. On bir hastaya (%57.9) terapötik plazma değişimi yapıldı. Üç hastada (%15.8) yaygın damar içi pıhtılaşma (DIC), 5 hastada (%26.3) akut solunum sıkıntısı sendromu (ARDS), 3 hastada (%15.8) septik şok ve 1 hastada (%5.3) kardiyojenik şok vardı. Ortalama YBÜ kalış süresi 8.1 ± 4.7 gündü. Hem anne hem de fetal mortalite oranı %10,5 idi.

Sonuç: HELLP sendromunda, maternal/fetal morbidite ve mortalite riski yüksektir. Erken tanı, yoğun bakım ünitesinde yakın takip, multidisipliner ekip tarafından yönetim HELLP sendromunun komplikasyonlarını önleyebilir ve prognozu iyileştirebilir.

Anahtar kelimeler: HELLP sendromu, preeklampsi, eklampsi, gebelik, yoğun bakım ünitesi

Introduction

HELLP syndrome is a life threatening disease that is characterized by hemolysis, elevated liver enzymes, low platelet count and associated with a serious complication of severe preeclampsia and/or eclampsia [1,2]. In 1954 the syndrome was described firstly by Prichard and in 1982 the acronmy was coined by Weinstein [3]. The HELLP syndrome occurs in about 0.5–0.9% of all pregnancies and in 10–20% of pregnancies complicated by severe preeclampsia [1,2,4].

The pathogenesis of HELLP remains unclear and it probably represents a severe form of preeclampsia but the relationship between the two disorders remains controversial. If it is a form of severe preeclampsia, abnormal remodeling of spiral arteries, defective trophoblast differantitiation, systemic endothelial dysfunction, hypoperfusion, hypoxia, ischemia, immunological and genetic factors may play a role. HELLP syndrome has been associated to abnormal placentation similar to preeclampsia, but it has greater hepatic inflammation and activation of the coagulation system than preeclampsia [1,2,3]. In the differential diagnosis of HELLP syndrome, disease such as acute fatty liver of pregnancy, thrombotic thrombocytopenic purpura (TTP), gestational thrombositopenia, hemolytic-uremic syndrome (HUS) should be considered. Several complications such as acute kidney injury (AKI), assite, pleural effusion, dissemine intravasculer coagulopathy (DIC), liver haematoma, endometritis, prolong wound healing, vision loss may occure hence it can be life-therating situation for both mother and fetus [1,2,4]. These patients may need ventilatory and vasopressor support, monitoring of volume status, and advanced hemodynamic monitoring. Approximately 10% of patients may need critical care management. For these reasons, it may be better to follow up and treat these patients in ICU of tertiary care centers [1,2].

In the present study, we aimed to retrospectively evaluate clinical courses and outcomes of the patients with HELLP syndrome admitted to ICU of a tertiary university hospital.

Material and Methods

We retrospectively analyzed the medical records of 19 patients with HELLP syndrome who were admitted to the ICU between January 2011 and December 2015. This study was approved by Ankara University Faculty of Medicine Clinical Research Ethics Committee (ethics committee date 10.10.2016, No: 15-770-16).

We obtained the following data from ICU follow-up records and hospital medical records: age, gestational age (week), medical history, comorbidities, presence of proteinuria, Acute Physiology and Chronic Health Evaluation System (APACHE II) score, Sequential Organ Failure Assessment (SOFA) score, Glasgow Coma Scale (GCS), vital signs of ICU admission, complications, need for mechanical ventilation (MV), presence of AKI, AKI stage, and need for RRT, presence and type of

shock, the length of stay (LOS) in MV, ICU and maternal-fetal mortality rate. Laboratory parameters were analyzed; liver and kidney function tests, serum electrolytes (sodium, potassium, chloride), complete blood count, prothrombin time (PT).

In Missisippi classification HELLP syndrome was classified according to platelet (Plt) count, lactate dehydrogenase (LDH), asparate aminotransferase (AST) or alanine aminotransferase (ALT) levels. In Mississippi Classification, LDH ≥ 600IU/L, AST or ALT≥70IU/L in all stage, but Plt count ≤ 50.10 ^{9}/L in class I, ≥50.10 ^{9}/L ≤100. 10 ^{9}/L in class II and ≥100. 10 ^{9}/L in class III [1,2,5].

AKI was identified on the basis of the Kidney Disease Improving Global Outcomes (KDIGO) clinical practice guidelines [6], ARDS was diagnosed according to the Berlin Definition [7] and septic shock were defined according to the 2021 Surviving Sepsis Campaign [8]. DIC was defined and scored according to International Society of Thrombosis and Haemostasis (ISTH) Scientific and Standardization Committee criteria which are thrombocytopenia, prolonged PT and activated partial thromboplastin time (aPTT), increased international normalized ratio (INR) and D-dimer level, hypofibrinogenemia, microangiopathic hemolytic anemia (MAHA), with schistocytes and helmet cells seen on the peripheral blood smear [9].

Those whose gestational age was less than 20 weeks, chronic liver disease, TTP, HUS, acute fatty liver disease, and gestational cholestasis and those without available data were excluded from the study.

Statistical Analyses

Statistical analyses were performed with SPSS software (SPSS: An IBM Company, version 22.0, IBM Corporation). In summary statistics, the mean±standard deviation (minimum to maximum) was used for continuous variables, and frequency distributions and percentages were used for categorical variables. We generated graphs using percentages and frequencies to summarize the results. P < .05 indicated statistical significance.

Results

During this period, 19 patients were admitted to the ICU with a mean age of 30.0 ± 5.1 years (range, 21-41 years) and the mean gestational age was 32.2 ± 4.8 weeks (range, 21-38 weeks). HELLP syndrome was the most common in the third trimester of pregnancy (94.7%) and in patients wtih multigravida (68.4%) (Table 1). Three patients (15.8%) had chronic hypertension and 1 patient had mitral stenosis. None of the patients had a history of preeclampsia, eclampsia and/or HELLP, diabetes mellitus, or renal disease. All of the patients underwent cesarean section by the team of gynecology and obstetrics.

Ten patients (52.6%) were class I HELLP syndrome, 5 patients (26.3%) class II and 4 patients (21.1%) class III according to The Mississippi-Triple Class System (Table 1). Seven patients (36.8%) had peripheral blood smear with hemolysis (cystocytes, fragmented erythrocytes).

Table 1. Clinical Features of Patients with HELLP syndrome

Characteristics	Mean± SD	Minimum-Maximum
Age (year)	30 ± 5.1	21- 41
Gestational age (week)	32.2 ± 4.8	21- 38
	Number (n)	Percent (%)
Trimester		
Second	1	5.3
Third	18	94.7
Gravida		
Primigravida	6	31.6
Multigravida	13	68.4
The Mississippi-Triple Class System		
Class I	10	52.6
Class II	5	26.3
Class III	4	21.1

SD: Standart Deviation

On ICU admission, 12 patients (63.2%) had respiratory failure, 12 patients (63.2%) elevated liver function tests, 11 patients (57.9%) hyperbilirubinemia, 5 patients (26.3%) AKI, 4 patients (21.1%) convulsion, 1 patient arrhythmia, 1 patient visual impairment.

The mean APACHE II score was 25.9 ± 4.0, SOFA score was 5.2 ± 2.7, and GCS was 14.2 ± 2.8 at ICU admission. The mean arterial pressure was 105.2 ± 21.8 mmHg (Table 2).

Table 2. Severity Scores and Vital Signs of Patients with HELLP syndrome at ICU Admisson

Characteristics	Mean ± SD	Minimum	Maximum
APACHE II	25.9 ± 4.0	21	35
SOFA	5.2 ± 2.7	2	10
GCS	14.2 ± 2.8	3	15
Systolic blood pressure (mmHg)	147.5 ± 37	42	210
Diastolic blood pressure (mmHg)	82.4 ± 17.3	32	110
Mean arterial pressure (mmHg)	105.2 ± 21.8	35	140

ICU: Intensive Care Unit; APACHE II: Acute Physiology and Chronic Health Evaluation II; SOFA: Sequential Organ Failure Assessment; GSC: Glasgow coma scale; SD: standard deviation

Methylprednisolone therapy (1mg/kg/day) was initiated intravenously to 4 patients (21.1%). Packed red blood cells (PRBCs) were replaced in 10 patients (52.6%) and platelet suspension in 8 patients (42.1%). Antihypertensive treatment was given to 16 patients (84.2 %) and and 5 patients had visual impairment (26.3%) during ICU follow-up. Eleven patients (57.9%) had pretibial edema, and 17 patients (89.5%) proteinuria.

Six patients (31.6 %) required invasive MV and 6 patients

(31.6%) noninvasive MV. Eight patients (42.1%) had AKI and 1 patient required RRT. Therapeutic plasma exchange (TPE) was performed to 11 patients (57.9%).

Three patients (15.8%) had DIC, 5 patients (26.3%) had ARDS, 3 patients (15.8%) had sepsis and 1 patient (5.3%) had cardiogenic shock. One patient needed vasopressor therapy (Table 3).

Table 3. The Therapies and Complications of Patients with HELLP syndrome

Therapies and Complications	Number (n)	Frequency (%)
Need of Mechanical Ventilation	12	63.2
Invasive	6	31.6
Non-invasive	6	31.6
Acute Kidney Injury	8	42.1
Renal Replacement Therapy	1	5.3
Need of Therapeutic Plasma Exchange	11	57.9
Dissemine Intravascular Co-agulation	3	15.8
Acute Respiratory Distress Syndrome	5	26.3
Sepsis	3	15.8
Cardiogenic Shock	1	5.3
Need of Vasopressor Therapy	1	5.3
Postpartum Cardiomyopathy	1	5.3
Gastrointestinal Bleeding	1	5.3
Retroperitoneal Hematoma	1	5.3
Acute Coronary Syndrome	1	5.3

The mean levels of hemoglobin, platelet, AST, ALT, LDH and total bilirubin were 10.0 ±2.5mg/dL, 67.9 ± 55.5 103/ mm^3, 290 ± 308 IU/L, 147.5 ± 203 IU/L, 1250 ± 862.6 IU/L and 3.2 ± 3.9 mg/ dl, respectively at ICU admission (Table 4).

Table 4. Laboratory Values of the Patients at Intensive Care Unit Admission

	Minimum	Maximum	Mean ± SD
Haemoglobin (mg/dl)	4.8	14.2	10.0 ± 2.5
Platelets (103/ mm^3)	21	244	67.9 ± 55.5
BUN (mg/dl)	5	58	19.7 ± 15.6
Creatinine (mg/dl)	0.39	3.36	1.2 ± 0.8
AST (IU/L)	20	856	290 ± 308
ALT (IU/L)	11	845	147.5 ± 203
LDH (IU/L)	274	2958	1250 ± 862.6
Total bilirubin (mg/dl)	0.5	14.1	3.2 ± 3.9
Albumin (g/dl)	0.8	3.3	2.3 ± 0.5
PT (sn)	9.3	37.2	13.6 ± 6.9
INR (%)	0.84	3.19	1.2 ± 0.6
Fibrinogen (mg/dl)	0.45	4.02	2.6 ± 1
D- dimer (ng/ml)	1741	18432	6541 ± 4952
Lactate (mmol/L)	0.5	12.5	3.2 ± 3.1

SD: Standart Deviation, BUN: blood urea nitrogen AST: aspartate aminotransferase ALT: alanine aminotransferase LDH: lactate dehydrogenase PT: prothrombin time INR: international normalized ratio

The mean LOS in MV and ICU was 4.6 ± 4.8 days (0-18 days) and 8.1 ± 4.7 days (3-18 days). Maternal and fetal mortality rate was 10.5%. Our maternal mortality was lower than the expected mortality rate of 56.9% as calculated from the mean APACHE II score.

Discussion

In our study, there were 19 patients with HELLP, the most common was class I. The mean age of patients was 30.0 ± 5.1 years and the mean gestational age was 32.2 ± 4.8 weeks. HELLP was most common in the third trimester and patietns with multigravida. The most common presentations of patients at ICU admission were respiratory failure, elevated liver function tests, and hyperbilirubinemia. The need for mechanical ventilation, therapeutic plasma exchange and acute kidney injury were observed most frequently among therapies and complications. There were high LDH and increased bilirubin level due to hemolysis. Our maternal mortality was lower than the expected mortality rate as calculated from the mean APACHE II score.

Most of our patients were in HELLP class I. The Mississippi-Triple Class System classifies HELLP syndrome according to platelet value. Platelet count is <50.000/mm3 in class I. If the platelet count is reduced, patients are high risk of bleeding. Thus, this indicates that the patients are serious. Our patients were critically ill patients according to the classification and similar to previous studies [10,11,12].

Patients with HELLP syndrome are usually multiparous and >35 years old. So, multigravida, multiparity and age may contribute to increased risk in HELLP syndrome [1,2,13,14,15,16]. High-risk patients with HELLP syndrome may be followed in ICUs and this may improve outcomes [1,2,10].The mean maternal age in our study was 30 ± 5.1 years and the patients were multigravida, so the patients were high risk similar to clinical trials [1,13,14,15,16].

About 70% of HELLP syndrome happen in the third trimester of pregnancy and between 28 -37 weeks of pregnancy [2,17]. In our cohort study, 94.7% of patients with HELLP syndrome were in the third trimester and the mean gestational age was 32.2 ± 4.8 weeks similar to previous study [2,5,10,17,18]. The etiology and pathophisiolgy of HELLP syndrome is not fully understood. Genetic mutation (both maternal and fetal) and inflammatory process are among the causes. HELLP syndrome should be considered if a pregnant patient in the third trimester of pregnancy or immediately after delivery <7 days has symptoms. The process of the disease is unknown [1,2,3].

The most common presentations of patients at ICU admission

were respiratory failure, elevated liver function tests, and hyperbilirubinemia in our study. A clinical studies in Turkey reported pregnancy-induced hypertensive disorders, haemorrhage, respiratory failure, HELLP syndrome and DIC were major complications requiring to ICU admission [19,20]. Hemorrhage, hypertensive disorders, preeclampsia, sepsis, HELLP syndrome, peripartum cardiomyopathy, embolism of cerebral palsy and acute fatty liver of pregnancy are the most common causes of hospitalized pregnant women [19-21]. Unlike previous studies there were only patients with HELLP syndrome in our cohort. Elevated liver function test and hyperbilirubinemia are expected presentations for HELLP syndrome. We thought that respiratory failure was associated with the severity of HELLP syndrome, pulmonary edema and also tachypnea in liver dysfunction-associated metabolic acidosis.

Maternal complications are frequently observed in patients with HELLP syndrome, and some of these are serious. Maternal death occurs due to DIC, AKI, placental abruption or postpartum hemorrhage. The incidences of DIC, AKI, placental abruption and postpartum hemorrhage occurs are between 15%-62.5%, 36%-50%, 11%-25% and 12.5%-40%, respectively [1,2,12,22-24]. In our cohort study, 42.1% of patients had AKI. In a previous study, patients with Mississippi class I HELLP syndrome had higher rates of serious maternal complications than class II [25]. So, we thought that our incidence of AKI was high because most of our patients were class I HELLP syndrome and they were critically ill patients. Our incidence of DIC was 15.8%. We associated this low DIC rate with emergency cesarean delivery, rapid hemostatic management, and follow-up in the ICU with a multidisciplinary team.

ARDS is a serious complication which affects <1% of the patients with HELLP syndrome [1,2,26]. Mechanical ventilation is required in 30% of the patients with HELLP syndrome admitted in ICU [1,2]. In our cohort study, incidence of ARDS was 26.3 % and, noninvasive and invasive mechanical ventilation were required for 63.2% of our patients. These rates were higher than the previous studies [1,27]. These high rates may be associated with pulmonary edema due to renal dysfunction and diffuse edema and severity of the disorder, lifethreatening complications. Continuing pregnancy poses a risk in HELLP syndrome, so emergency cesarean delivery should be performed. Both risky pregnancy and emergency delivery may be associated with the need for intubation and mechanical ventilation. Previous research has identified emergency cesarean delivery as an independent risk factor for all obstetric patients (ie, patients with HELLP syndrome, eclampsia, preeclampsia, and other problems) that determines the need for admission to the ICU [28].

TPE may remove immune complexes, antibodies, endogenous and exogenous toxins from plasma and replace some plasma proteins and coagulation factors. HELLP syndrome is also an inflammatory and immunological clinical condition together active coagulation cascade and microangiopathic hemolytic anemia [1,2,29,30]. There are clinial studies reporting that the use of TPE within 24-72 hours postpartum was an effective and life-saving treatment option [29,30]. Therefore, we performed TPE to 57.9% of the patients. However, our post-procedure data were incomplete due to the retrospective study.

The definitive treatment is delivery in HELLP syndrome [1,2]. Pregnancies of all patients were terminated with cesarean section in the department of gynecology and obstetrics in our study. Then, the patients were admitted to our ICU. In our center, definitive treatment as delivery was administered urgently to our patients in cooperation with a multidisciplinary approach.

Hemolysis is one of the major features of HELLP syndrome and is associated to a microangiopathic hemolytic anemia. Fragmentation of erythrocytes by hemolysis increases lactic dehydrogenase (LDH) level and decreases hemoglobin level. Thus, high LDH and unconjugated bilirubin levels may support the diagnosis of hemolysis. In our cohort study, LDH and bilirubin levels were high enough to support the diagnosis of HELLP to similar previous study [1,2,10].

The mortality rate of women with HELLP syndrome is 0%-25% [1,2,29,30] and maternal mortality was as high as 66% in early reports [27]. The maternal mortality associated with HELLP syndrome is mainly due to renal failure, coagulopathy, abruptio placentae, hepatic hemorrhage, and hypovolemic shock [1]. HELLP syndrome is associated with a perinatal mortality of 7.7%–60% [2,27]. Our maternal and fetal mortality rate were lower than in other studies althouhg our patients had severe disorder and life-threatening complications. We attribute that our ICU was in a tertiary university hospital center and had an experienced team. Thus, our patients were diagnosed early and emergency cesarean delivery was performed. We think that our mortality rates were lower with close follow-up in the intensive care unit.

This study had some limitations. It was a retrospective study with data obtained from medical records, and it was conducted at a single center, which limits the generalizability of the results. The lack of data for risk factors, prenatal care of the patients and neonates information was another limitation.

Conclusion

HELLP syndrome is life-threatening and serious condition encountered by pregnant women. Maternal/fetal morbidity and mortality are high in HELLP syndrome. In this study, the maternal mortality was lower than the expected mortality rate as calculated from the mean APACHE II score. Delivery is considered the ultimate therapeutic approach for the HELLP syndrome. Early diagnosis, close follow-up in intensive care unit, appropriate treatment and management by multidisciplinary team may prevent complications and improve prognosis of HELLP syndrome. And our center had an experienced team in terms of emergency delivery and close intensive care follow-up. It would be appropriate to suggest that more comprehensive studies be conducted on this subject.

Declaration of conflict of interest

The authors have no conflicts of interest to declare. The authors received no funding for this work.

References

1. Lam MT, Dierking E. Intensive Care Unit issues in eclampsia and HELLP syndrome. Int J Crit Illn Inj Sci 2017; 7:136-41.
2. Khalid F, Mahendraker N, Tonismae T. HELLP Syndrome. 2022 Jun 16. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan–. PMID: 32809450.
3. Weinstein L. Syndrome of hemolysis, elevated liver enzymes, and low platelet count: a severe consequence of hypertension in pregnancy. Am J Obstet Gynecol. 2005; 193:859.
4. Abildgaard U, Heimdal K. Pathogenesis of the syndrome of hemolysis, elevated liver enzymes, and low platelet count (HELLP): a review. Eur J Obstet Gynecol Reprod Biol. 2013 Feb; 166(2): 117-23.
5. Ağaçayak E, Bugday R and Peker N, et al. Factors Affecting ICU Stay and Length of Stay in the ICU in Patients with HELLP Syndrome in a Tertiary Referral Hospital. International Journal of Hypertension. Vol. 2022.
6. Kidney Disease: Improving Global Outcomes (KDIGO) Acute Kidney Injury Work Group. KDIGO Clinical Practice Guideline for Acute Kidney Injury; 2012. Available from:https://www.kdigo.org/wp-content/uploads/2016/10/kdigo-2012-aki guidelineenglish.pdf
7. ARDS Definition Task Force, Ranieri VM, Rubenfeld GD, Thompson BT, Fergoson ND, Caldwell E, et al. Acute respiratory distress syndrome: The Berlin definition. JAMA 2012;307(23):2526-33. https://doi.org/10.1001/jama.2012.5669
8. Evans L, Rhodes A, Alhazzani W, et al. Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021. Intensive Care Med. 2021 Nov;47(11):1181-1247.
9. Taylor FB, Toh CH, Hoots WK, Wada H, Levi M. Towards definition, clinical and laboratory criteria, and a scoring system for disseminated intravascular coagulation. Thrombosis and Haemostasis. 2001; 86: 1327–1330.
10. Yosunkaya A, Keçecioğlu A, Erdem TB, Borazan H. Selçuk Tıp Üniv. Dergisi 2011; 27(1): 18-23.
11. Yucesoy G, Cakiroglu Y, Bodur H, Ozkan S, Tan T. An analysis of HELLP syndrome cases: does platelet count predict adverse maternal and fetal outcomes in women with HELLP syndrome? Arch Gynecol Obstet 2011; 283: 941-5.
12. Gedik E, Yücel N, Sahin T, Koca E, Colak YZ, Togal T. Hemolysis, elevated liver enzymes, and low platelet syndrome: Outcomes for patients admitted to intensive care at a tertiary referral hospital. Hypertens Pregnancy. 2017 Feb; 36(1): 21-29.
13. Fitzpatrick KE, Hinshaw K, Kurinczuk JJ, Knight M. Risk factors, management, and outcomes of hemolysis, elevated liver enzymes, and low platelets syndrome and elevated liver enzymes, low platelets syndrome. Obstet Gynecol. 2014 Mar;123(3):618-627.
14. Javier E, Fonseca M, Clandia C. Dexamethasone treatment does not improve the outcome of woman with HELLP syndrome: a double blind, placebo controlled randomized clinical trail. Am J Obstet Gynecol. 2005; 193: 1591-8.
15. Bang NO, Satia MN, Poonia S. Obstetric and neonatal outcome in pregnancies complicated by hemolysis elevated liver enzymes low platelet count syndrome at a tertiary care centre in India. Int J Reprod Contracept Obstet Gynecol 2016; 5: 2407-12.
16. Isler CM, Rinehart BK, Terrone DA, Martin RW, Magann EF, Martin JN Jr. Maternal mortality associated with HELLP syndrome. Am J Obstet Gynecol 1999; 181: 924-8.
17. Kirkpatrick CA. The HELLP syndrome. Acta Clin Belg. 2010 Mar-Apr;65(2):91-7.

18. Haram K, Svendsen E and Abildgaard U. The HELLP syndrome: Clinical issues and management. A Review. BMC Pregnancy and Childbirth 2009, 9: 8.
19. Togal T, Yucel N, Gedik E, Gulhas N, Toprak HI, Ersoy MO. Obstetric admissions to the intensive care unit in a tertiary referral hospital. J Crit Care 2010; 25: 628-633.
20. Özçelik M, Turhan S, Bermede O, Yılmaz AA, Ünal N, Bayar MK. Outcomes of Antepartum and Postpartum Obstetric Admissions to the Intensive Care Unit of A Tertiary University Hospital: An 8-Year Review. Turk J Anaesthesiol Reanim 2017; 45: 303-9
21. Yi HY, Jeong SY, Kim SH, et al. Indications and characteristics of obstetric patients admitted to the intensive care unit: a 22-year review in a tertiary care center. Obstet Gynecol Sci. 2018 Mar;61(2):209-219.
22. Drakeley AJ, Le Roux PA, Anthony J, Penny J. Acute renal failure complicating severe pre eclampsia requiring admission to an obstetric intensive care unit. Am J Obstet Gynecol 2002; 186: 253-6.
23. Selcuk NY, Odabas AR, Centikaya R, Tonbul HZ, San A. Outcome of pregnancies with HELLP syndrome complicated by acute renal failure (1989-1999). Ren Fail 2000; 22: 319-27.
24. Sadaf N, Haq G, Shukar-ud-Din S. Maternal and foetal outcome in HELLP syndrome at tertiary care hospital. J Pak Med Assoc Vol. 63, No. 12, December 2013, 1500-03.
25. Martin JN Jr, Owens MY, Keiser SD, et al. Standardized Mississippi Protocol treatment of 190 patients with HELLP syndrome: slowing disease progression and preventing new major maternal morbidity. Hipertens Pregnancy 2012;31(1):79–90.
26. Sibai BM. Diagnosis, controversies, and management of the syn¬drome of hemolysis, elevated liver enzymes, and low platelet count. Obstet Gynecol 2004; 103: 981-91.
27. Sibai BM, Ramadan MK, Usta I, et al. Maternal morbidity and mortality in 442 pregnancies with hemolysis, elevated liver enzymes, and low platelets (HELLP syndrome). Am J Obstet Gynecol 1993; 169: 1000.
28. Selo-Ojeme DO, Omosaiye M, Battacharjee P, Kadir RA. Risk factors for obstetric admissions to the intensive care unit in a tertiary hospital: a case-control study. Arch Gynecol Obstet 2005; 272: 207–210.
29. Erkurt MA, Sarici A, Kuku I, et al. The effect of therapeutic plasma exchange on management of HELLP Syndrome: The report of 47 patients. Transfus Apher Sci. 2021 Oct;60(5):103248.
30. Simetka O, Klat J, Gumulec J, Dolezalkova E, Salounova D, Kacerovsky M. Early identification of women with HELLP syndrome who need plasma exchange after delivery. Transfus Apher Sci. 2015 Feb;52(1):54-9.