HEMOLYSIS, ELEVATED LIVER ENZYMES AND LOW PLATELET (HELLP) SYNDROME: A DREADED COMPLICATION OF PRE-ECLAMPSIA IN A YOUNG NIGERIAN WOMAN

ABSTRACT

HELLP Syndrome is a fatal rare pregnancy-related syndrome characterised by hemolysis, elevated liver enzymes and low platelet count; occurring in 0.5-0.9% of all pregnancies and in 10-20% of pregnancies with severe pre-eclampsia.

HELLP Syndrome is a complication of severe pre-eclampsia; seventy percent of the cases are developed during the antepartum period, mainly between the 27th and 37th gestational weeks. Thirty percent are diagnosed postpartum often within 48hrs post-delivery. It is a dreaded obstetric catastrophe that is associated with both maternal and perinatal morbidity and mortality such as maternal disseminated intravascular coagulopathy, thrombocytopenia, intracranial hemorrhage, eclampsia, paralysis, liver rupture, maternal collapse and death as well as utero-placental insufficiency, intrauterine fetal death and stillbirth.

This obstetric complication is commonly diagnosed in pregnant women with poorly controlled pre-eclampsia, diabetes mellitus, renal disease and those who are not compliant with routine antenatal clinic visits thus, periconceptional care, adequate management of medical conditions of pregnancy and strict compliance to antenatal care services play vital roles in the prevention of HELLP Syndrome.

This case report presents the timely diagnosis and prompt management of a 35-year-old gravida 2 para 1 woman diagnosed with HELLP syndrome at 32weeks gestational age at the obstetrics and gynecology department in Nigerian Navy Reference Hospital Calabar, Nigeria.

KEYWORDS: HELLP syndrome, Pre-eclampsia, Gestation, Antepartum, Postpartum, Gravida, Complication.

INTRODUCTION

"Weinstein in 1982 named the condition HELLP (Hemolysis, Elevated liver enzymes and Low platelet) Syndrome"[1]. "The onset of HELLP syndrome before 28 weeks gestation account for about 20-30% of the cases and is associated with severe disease with rapid onset of clinical manifestation that often co-exist with fetal growth restriction"[3,12,13,14]. "The aetiology is unclear and it is thought to be a systemic inflammatory disorder mediated by a complicated cascade"[1,4]. "It is proposed that there may be an overlap with similar pathogenesis as in pre-eclampsia with

poor placentation, but for unknown reasons it can lead to exaggerated activation of the complement system and greater hepatic inflammation in patient with HELLP syndrome"[4-6]. "The typical presenting symptoms are right upper quadrant abdominal pain or epigastric pain, nausea and vomitting"[6].

"HELLP syndrome is associated with both maternal and neonatal morbidity and mortality especially when it arises in the postpartum period"[6,7]. "Severe maternal complications are cerebral haemorrhage, disseminated intravascular coagulopathy(DIC) and severe postpartum bleeding"[7]. "Women with postpartum HELLP syndrome have significant increased risk of renal failure and pulmonary edema compared with those of antenatal onset"[8].

She is a 35yr old gravida 2 para 1 woman with a live female child who booked for antenatal care in our facility at 11weeks gestational age and was regular with antenatal visits. Elevated blood pressure was noticed at 20 weeks gestational age but no proteinuria and she was commenced on oral antihypertensive medications (Methyldopa and Nifedipine).

Case presentation

She presented at 32 weeks with complaints of headache which was severe and throbbing in nature, nil blurred vision, dizziness, photophobia, vomitting, upper abdominal pain, nor epigastric pain. She had past history of severe pre-eclampsia that resulted in preterm delivery via an emergency ceaserean section at 30 weeks gestational age.

General examination revealed a middle age woman in no obvious painful or respiratory distress, afebrile to touch (Temperature: 36.6^0C), not pale, anecteric, acynosed, not dehydrated, nil peripheral lymphadenopathy but there was bilateral pitting pedal edema upto one-third of the legs.

Cardiovascular examination; Pulse rate: 72b/m, Blood pressure: 180/120mm/hg. Urgent urinalysis showed significant proteinuria. Respiratory system, neurological and cranial nerve examinations were normal. Abdominal examination showed gravidly enlarged, symphyso-fundal height of 27cm which was not compatible with gestational age of 32 weeks.

A diagnosis of severe pre-eclampsia was made and the following laboratory investigations conducted (full blood count, serum electrolytes, urea, creatinine and liver function test). Results of the investigations as shown in figures 1-3 below. She was managed with antihypertensives (hydralazine, methyldopa and nifedipine), Magnesium sulphate to prevent seizure and corticosteroid to enhance fetal lung maturation.

With worsening clinical state, she had a preterm delivery of a live female baby that weighed 1kg via emergency caeserean section. Patient's clinical examination on day 5th postpartum observed respiratory distress (respiratory rate of 38 cycles/minutes), severe jaundice, abdominal ascites, bleeding from punctured sites and poor urine output. Chest auscultation revealed bi-basal crepitation. The above laboratory investigations were repeated as shown in figures (4-6) and the

results showed deranged serum electrolytes, urea, creatinine and liver function test. There were markedly reduced platelet count and prolonged clotting time. D-Dimer test that was conducted was elevated as shown in figure 7.

A diagnosis of HELLPS syndrome was made and a multidisciplinary approach involving the obstetricians, medical physicians, hematologists, nephrologists, anaestetists and intensive care unit team was instituted in her management. She was nursed in an intensive care unit. She was transfused with 5 units of fresh whole blood and had 4 sections of haemodialysis. She responded positively to the treatment and all the signs and symptoms resolved. She was subsequently discharged home and at follow up visits she was clinically stable.

Test Name : EUCR

Remark/Result

	RESULT	REFERENCE
Sodium	144	(135-155)mmol/L
Potassium	3.8	(3.5-5.5)mmol/L
Chloride	99	(96-110)mmol/L
Bicarbonate	20	(22-28)mmol/L
Urea	2.2	(2.1-7.1)mmol/L
Creatinine	68	(53-115)mmol/L
Creatinine Children (1 - 3)Years		(27-62)mmol/L
Urea Children (1 - 3) Years		(1.8-6.0)mmol/L

FIGURE 1: SERUM ELECTROLYTES, UREA AND CREATININE

Test Name : LFT

Remark/Result

	RESULT	REFERENCE
Total Bilirubin	23	(UP TO 20)umol/L
Direct Bilirubin	8	(UP TO 7)umol/L
AST	20	(UP TO 40)u/L
ALT	24	(UP TO 40)u/L
Alkaline Phosphatase	150	(UP TP 270)u/L

COMMENT:

FIGURE 2: LIVER FUNCTION TEST

WBC	11.5	ADULT: 2.6 - 11.0 x $10^{9/L}$ CHILDREN AT 1YEAR: 4.0 - 15.0 x $10^{9/L}$ NEWBORN : 10 - 25.0 x $10^{9/L}$
NEU%	71	ADULTS (40-75), <7 YRS (25-45)
LYM%	28	ADULTS (20-45), <7 YRS (45-75)
MON%	00	(2 - 8)
EOS%	01	(1 - 6)
BAS%	00	(0- 1)
RBC		MALE (4.5-5.9), FEMALE (4.1-5.1), CHILDREN AT BIRTH (4.0-5.6)
HCT%	27%	MALE (38-52)%, FEMALE (37-47)%, CHILDREN AT BIRTH (44-54)%
MCV		(80.0 - 100.0)
MCHC		(32 - 36)
MCH		(27 - 32)
PLT	180	(150 - 400)

FIGURE 3: FULL BLOOD COUNT

Test Name : EUCR

Remark/Result

	RESULT	REFERENCE
Sodium	128	(135-155)mmol/L
Potassium	2.9	(3.5-5.5)mmol/L
Chloride	92	(96-110)mmol/L
Bicarbonate	18	(22-28)mmol/L
Urea	39.8	(2.1-7.1)mmol/L
Creatinine	1779	(53-115)mmol/L
Creatinine Children (1 - 3)Years		(27-62)mmol/L
Urea Children (1 - 3) Years		(1.8-6.0)mmol/L

FIGURE 4: SERUM ELECTROLYTES, UREA AND CREATININE

Test Name : LFT

Remark/Result

	RESULT	REFERENCE
Total Bilirubin	19	(UP TO 20)umol/L
Direct Bilirubin	6	(UP TO 7)umol/L
AST	69	(UP TO 40)u/L
ALT	39	(UP TO 40)u/L
Alkaline Phosphatase	309	(UP TP 270)u/L

COMMENT:

FIGURE 5: LIVER FUNCTION TEST

WBC	40.1	ADULT: 2.6 - 11.0 x $10^{9/L}$ CHILDREN AT 1YEAR: 4.0 - 15.0 x $10^{9/L}$ NEWBORN : 10 - 25.0 x $10^{9/L}$
NEU%	94	ADULTS (40-75), <7 YRS (25-45)
LYM%	06	ADULTS (20-45), <7 YRS (45-75)
MON%	0	(2 - 8)
EOS%	0	(1 - 6)
BAS%	0	(0 - 1)
RBC		MALE (4.5-5.9), FEMALE (4.1-5.1), CHILDREN AT BIRTH (4.0-5.6)
HCT%	30	MALE (38-52)%, FEMALE (37-47)%, CHILDREN AT BIRTH (44-54)%
MCV		(80.0 - 100.0)
MCHC		(32 - 36)
MCH		(27 - 32)
PLT	45	(150 - 400)

FIGURE 6: FULL BLOOD COUNT

TEST	RESULT	REFERENCE
D DIMER	> 10000.0	(0 - 500ng/ml

FIGURE 7: D-DIMER

DISCUSSION

"HELLP syndrome is a dreaded complication in pregnancy characterised by hemolysis,elevated liver enzymes and low platelet occuring in 0.5 to 0.9% of all pregnancies and 10-20% of all cases with severe pre-eclampsia"[1]. It usually occurs from age of viability or within seven days of delivery[2].

"The diagnosis of HELLP syndrome is based on different criteria; two commonly used classification for HELLP syndrome are the tennessee and mississippi classification however, it can also be diagnosed based on biochemical evidence"[9]. "The tennessee classification is widely used for diagnosis; it requires the presence of microangiopathic hemolytic anemia with abnormal blood smear and low serum haptoglobin, elevated lactate dehydrogenase hormone level above 600IU/L and Aspatate transaminase above 70IU/L or bilirubin more than 1.2mg/dl and a platelet count below 100 x 10^9L"[9]. "The mississippi classification underlies the severity of the disorder according to the nadir of the platelet count"[9].

"The first step in managing this condition is stabilization of the patient, assessessment of fetal status with a non stress test and ultrasound examination for a biophysical profile"[10]. "Medical management is mainly supportive and requires a multidisciplinary approach involving the intensive care unit team, nephrologist, hematologist, hepatologist, obstetrician and neonatologist"[10].

Management options depends on the gestational age of the pregnancy and should be done in a tertiary institution[4,5,10]. Prompt delivery is the only effective treatment, betamethazone administration is recommended for fetal lung maturity when the patient present <34weeks of gestation[5]. Magnesium sulphate should be initiated at the time of admission to prevent maternal seizures and for its neuroprotective effects on the fetus[5]. Patients with hypertension should be started on intravenous labetalol, hydralazine or nifedipine[4].

Blood transfusion is recommended for patients with haemoglobin <7g/dl, ecchymosis, severe haematuria, or suspected placental abruptio[3,7]. All actively bleeding patient with thrombocytopenia should be transfused with platelet[3]. Fresh frozen plasma and cryoprecipitate is needed in patients with DIC[3,7].

The maternal complication of HELLPS include; placental abruptio, DIC,acute renal failure,severe ascites, pulmonary edema, cerebral edema, liver rupture, wound hematoma, subcapsular heamatoma, hepatic infarction, cerebral infarction, cerebral heamorrhage, retinal detachment and maternal mortality while fetal and neonatal complication include; preterm delivery, intrauterine growth restriction, neonatal thrombocytopenia, respiratory distress syndrome and perinatal death[6-8,11].

CONCLUSION

HELLP Syndrome is a fatal and dreaded complication of pre-eclampsia however, early diagnosis and prompt intervention avert the fetal and maternal morbidity and mortality associated with it.

Consent

As per international standards or university standards, patient(s) written consent has been collected and preserved by the author(s).

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REFERENCES

1. Pritchard JA, Weinstein R, Ratnoff OD, Vosburgh GJ: Intravascular hemolysis, thrombocytopenia and other hematological abnormalities associated with severe toxemia of pregnancy. N Engl J Med. 1954, 250:89-98.
2. Weinstein L: Syndrome of hemolysis, elevated liver enzymes, and low platelet count: a severe consequence of hypertension in pregnancy.1982. Am J Obst Gynecol.2005,193:859-10.1016/j.ajog.2005.02.113.
3. Thiagarahaj S, Burgeois FJ, Harbert GM, Landle MR. Thrombocytopenia in pre-eclampsia: associated abnormalities and management principles. Am J Obstet Gynecol 1984; 150: 1-7.

4. Ellison J, Sattar N, Greer I: HELLP syndrome: mechanisms and management. Hosp Med.1999, 60;243-249.
5. Martin JN, Rose CH, Briery CM; Understanding and managing HELLP syndrome:the integral role of aggressive glucocorticoids for mother and child. Am J Obstet Gynecol. 2006,195; 914-934.
6. Ertan AK, Wagner S, Hendrik HJ, Tanriverdi HA, Schmidt W: Clinical and biophysical aspects of HELLP-syndrome. J perinat Med.2002,30: 483-489
7. Lopez-Llera M., Espinosa M., Leon MD, Linares UR. Abnormal coagulation and fibrinolysis in eclampsia. A clinical and laboratory correlation study. Am J Obstet Gynecol 1976;124: 681-692.
8. Sibai BM, Taslimi MM, El-Nazer A., Amon E., Mabie BC, Ryan GM. Maternal-perinatal outcome associated with the syndrome of hemolysis, elevated liver enzymes, and low platelets in severe pre-eclampsia/eclampsia. Am J Obstet Gynecol 1986; 155: 501-508.
9. Audibert F, Friedmann SA, Frangieh AY, Sibai BM: Clinical utility of strict diagnostic criteria for HELLP syndrome. Am J Obstet Gynecol. 1996,175: 460-464.
10. Magann EF, Martin JN: Twelve steps to optimal management of HELLP syndrome.Clin Obstet Gynecol.1999,42:532-550.
11. Celik C, Gezginc K, Altintepe L, Tonbul HZ, Yaman ST, Akyurek C, Turk S: Results of the pregnancies with HELLP syndrome. Ren Fail. 2003, 25; 613-618.

12 Vázquez-Rodríguez JG, Salas-Magaña MT, Serrano-Rodríguez J. Incidence and Clinical Manifestations of Posterior Reversible Encephalopathy Syndrome (PRES) in Patients with Eclampsia. 2017-2021 Data from a High Specialty Medical Unit, Mexico City. Int. J. Res. Rep. Gynaecol. [Internet]. 2022 Jul. 28 [cited 2024 Jun. 4];5(1):214-21. Available from: https://journalijrrgy.com/index.php/IJRRGY/article/view/65

13 Gatina K, Barinov E, Sulaieva O, Gnylorybov A, Hushchyna Y, Menzarar A. Sensitivity to Epinephrine Determines Platelet Hyperreactivity in Myocardial Infarction under Antiplatelet Therapy. J. Adv. Med. Med. Res. [Internet]. 2014 Jun. 27 [cited 2024 Jun. 4];4(29):4770-9. Available from: https://www.journaljammr.com/index.php/JAMMR/article/view/1508

14 Abildgaard U, Heimdal K. Pathogenesis of the syndrome of hemolysis, elevated liver enzymes, and low platelet count (HELLP): a review. European Journal of Obstetrics & Gynecology and Reproductive Biology. 2013 Feb 1;166(2):117-23.