Original Article

Iraqi Journal of Gastroenterology

MATERNAL MORBIDITY AND PERINATAL MORTALITY IN HELLP SYNDROME

SINGLE CENTER STUDY

*Anwar Al Bassam C.A.B.O.G
**Laith Alhadad C.A.B.S, F.I.C.M.S.D.S (subspecialty in digestive surgery)
**Riyadh Al-Sharifi (C.A.B.M., F.I.C.M GE&H)

ABSTRACT

OBJECTIVE:
HELLP, a syndrome characterized by haemolysis, elevated liver enzyme levels and low platelet count, is a life -threatening obstetric complication usually considered to be a variant of preeclampsia. The purpose of this study is to describe the incidence and the effect of this serious obstetric complication on maternal and foetal outcome.

MATERIAL AND METHOD:
This is a case series study conducted at Nursing Home, and Baghdad Teaching Hospital from the beginning of January 2006 to the end of June 2007 including nine patients diagnosed as HELLP syndrome. We analyzed the clinical characteristics, complications, maternal and foetal survival of patient suffering from HELLP syndrome during third trimester of pregnancy. Diagnostic criteria were defined on the bases of preeclampsia and the following laboratory abnormalities, platelet count <100000/cubic mm, serum hepatic aminotransferase >70UI/L, serum lactic dehydrogenase >600UI/L, total bilirubin >1.2mg/dl

RESULT:
Nine cases included in the study in their third trimester, the mean maternal age was 28 years ,five of the patient were primigravida and four were multigravida ,average gestational age was 32 weeks ,average blood pressure at time of presentation was (164/104mmHg),proteinuria ranged from score 1+ to 3+ on dipstick test on two separate tests ,average platelet count was 80000 /cubic mm . according to mode of delivery three of the patient had preterm vaginal delivery ,the other six delivered by emergency caesarean section .maternal complication were hepatic subcapsular hematoma which was treated surgically(one patient) , temporary blindness (one patient)pulmonary oedema(one patient) ,acute renal failure (one patient),placental abruption (2 patients), and disseminated intravascular coagulation (2 patients). The neonatal outcome was two stillbirths, and one early neonatal death no maternal death recorded during the studying period

CONCLUSION
: HELLP syndrome is considered as a variant of preeclampsia .the pathogenesis of HELLP syndrome remains unclear. From our study Hellp syndrome found to occur during the third trimester and is associated with high maternal morbidity, preterm and intrauterine foetal death

KEYWARD
HELLP syndrome, maternal morbidity, neonatal outcom.

INTRODUCTION:

The acronym HELLP was coined in 1982 to describe a syndrome consisting of haemolysis elevated liver enzymes, and low platelet count (1). The syndrome has been considered a variant of preeclampsia, but it can occur on its own or in association with preeclampsia .it is associated with an increase risk of adverse outcome for both the mother and the foetus .2 HELLPsyndrome is a rare complication of pregnancy that is associated with pre-eclampsia(hypertension ,and proteinuria)and may result in rupture of the liver.(3)the proteinuria is useful in diagnosing preeclampsia but not HELLP syndrome(4)the platelet count is the best indicator of the later,therefore,HELLP syndrome should be suspected in any patient who shows a significant drop in the platelet count during the antenatal period.(5)

In a primigravida, the gradual development of hypertension and proteinuria in pregnancy is most t

*Department of gynecology and obstetrics Baghdad teaching hospital, Medical city complex
** gastroenterology and hepatology teaching hospital ,medical city complex
*** Gastroenterology and hepatology teaching hospital, medical city complex

often due to preeclampsia. These findings typically become apparent in the third trimester and progress until delivery .in some patients, however, symptoms begin in the latter half of the second trimester, while other women have an onset that is delayed until delivery or even the early postpartum period. Similar symptoms and signs developing in multigravidas are often due to underlying hypertension or renal disease. (6,)

Severe preeclampsia is amulti-system disorder, and the liver is one of the major organs frequently involved (7).the hepatic lesions may be clinically silent but biochemically manifests or clinically overt, where the patient usually presents with epigastric or low sub costal pain which is known as (preeclamptic angina)(7)

When the liver involvement is associated with haemolysis and low platelets, this is known as HELLP syndrome. The haematological abnormality consists of microangiopathic haemolysis, thrombocytopenia and elevated liver transaminase (7) which may occurs in the absence of hypertension (8) the presence of Bur cell and Schistocytes indicates microangiopathic haemolytic anaemia and it may be confirmed by increased lactic dehydrogenase (9)

PATHOGENESIS:

The pathogenesis of HELLP syndrome is not well understood .the findings of this multisystem disease are attributed to abnormal vascular tone, vasospasm and coagulation defects (10)The HELLP syndrome probably represents a severe form of preeclampsia ,but this relationship remains controversial .as many as 15 to 20 percent

of patients do not have antecedent hypertension or proteinuria, leading some experts to believe that HELLP is a separate disorder from preeclampsia (11).one theory is that HELLP syndrome is at least in part caused by placenta -derived proteins (such as CD95,a protein involved in apoptosis) that damage hepatic cells.(12)

Foetuses of some affected women have long -chain 3-hydroxyacyl -coenzyme A dehydrogenase deficiency (LCHAD),which is more commonly a major cause of acute fatty liver of pregnancy (13-14).an association with medium -chain acyl-CoA dehydrogenase deficiency was also reported (15)

MATERIAL AND METHOD:

This is a case series study conducted at Nursing Home and Baghdad teaching hospital from beginning of January 2006 to the end of June 2007 .a total of nine pregnant patients at different gestational age in the third trimester were diagnosed as HELLP syndrome. Diagnostic criteria were defined on the bases of preeclampsia and the following laboratory abnormalities: Platelet count < 100000/cubic mm, serum hepatic aminotransferases >70UI/L, serum lactic dehydrogenase >600UI/L, total serum bilirubin >1.2mg/dl.blood sample were taken from each candidate involved in this study and send for the above investigation, random urine sample was also taken and examined for proteinuria.After the diagnosis is confirmed, the initial steps in management are to stabilize the mother, assess the foetal condition, and then termination of pregnancy.

RESULT:

The maternal age ranged between (16-45 years)with a mean of28 years old , five of them were primigravida (56%) and the other four were multigravida (44%), gestational age ranged between (28-38 weeks)with a mean of (32 weeks),according to the signs and symptoms of the patients are shown in (table one)their blood pressure at presentation ranged from (140/90 to 240/130 mmHg recorded in a semireclining position) with a mean of (164/104mmHg),proteinuria ranged from (score of 1+ to 3+ on dipstick test on two separate tests) platelet count ranged between (<50000 to 100000per cubic mm)with a mean of (86000 per mm) ,total serum bilirubin ranged between 1.2 to4.5 mg/dl with a mean of(2.2 mg/dl)(table 2) .according to mode of delivery 3 out of 9 delivered vaginaly (they are preterm deliveries)the other six patients delivered by emergency caesarean section(four of them were preterm and the other two were term pregnancy.)five patients were admitted to (ICU) intensive care unit (four patient were primigravida, and the other one was multiparous) the maternal complication were subcapsular liver haematoma(one patient), pulmonary oedema (one patient) acute renal failure (one patient) ,temporary blindness (one patient) , placental abruption(two patients), and disseminated intravascular coagulation(two patients) , (table 3)

The neonatal sex distributions were male to female (5:4), six neonates were preterm, and their weights ranged between (900 gm to 2100gm) with a mean of 1950 kg.)All the preterm neonates admitted to neonatal care unite except two (stillbirth weighing 900 gm, 1600gm). (Table 4).no maternal death recorded in the studying sample.

DISCUSSION

HELLP develops in approximately 1 of 1000 pregnancies overall (16). Our study started from 1st of January 2006 lasting for a period of eighteen months, the overall number of admission of pregnant women for labour was 7577 from those nine patients with HELLP syndrome so the incidence of HELLP syndrome was 0.1%. during the period of the study, the majority of cases are diagnosed between 28 and 36 weeks of gestation.56% of the cases were primigravida, The major presenting symptoms in our study were hypertension(100%),proteinuria (100%),right upper quadrant pain(55%)this is also found in the study done by Schwerk C,et al

who studied 28 cases of proved HELLP syndrome ,82% of cases were primigravida ,proteinuria present is71% of cases , right upper quadrant pain 75% .(17)
HELLP syndrome is associated with particularly poor maternal and perinatal outcomes. The reported perinatal foetal mortality rate ranges from 7.4% to 20.4%,and the reported maternal mortality is 1% , from 1 to 25 percent of affected women develop serious complications such as placental abruption ,adult respiratory distress syndrome ,hepatorenal failure ,pulmonary oedema sub capsular hematoma ,and hepatic rupture (16).maternal morbidity is common.(8)all the affected women involved in the study had serious complication such as subcapsular liver hematoma ,placental abruption pulmonary oedema ,and acute renal failure. This can be reduced by regular antenatal care and early diagnosis and management as the patient can be misdiagnosed in the early stages leading to increase the risk of morbidity.
Richa ,-F;Yazigi,-A et al,(2005)found that patients with HELLP syndrome are at greater risk of pulmonary oedema ,respiratory distress syndrome ,abruption placentae,intracerebral haemorrhage , disseminated intravascular coagulation ,rupture liver hematomas &acute renal failure(2)
Infant morbidity and mortality rates rangefrom10 to 60 present ,depending on the severity of maternal disease (18) .infants affected by HELLP syndrome are more likely to experience intrauterine growth retardation and respiratory distress syndrome ((19) in our study we have two preterm stillbirth, and one case early neonatal death. and the infant mortality in the studying group is33%
Schwerk C; et al in their retrospective analysis in1986 -1991 ,28 cases of proved HELLP syndrome , 82%of the women were primiparas ,92% of cases delivered by caesarean section and from the healthy baby through which were 75% premature infants (16).and this is also found in our study as 5 out of 9 patient were
primigravida (55%) and the incidence of caesarean section were 66% .78%of the neonate were preterm .

CONCLUSION :

HELLP a syndrome characterized by haemolysis, elevated liver enzyme and low platelet count, is an obstetric complication that is frequently misdiagnosed at initial presentation .the pathogenesis of HELLPsyndrome remain unclear.Platelet count appears to be the most reliable indicator of the presence of HELLP syndrom.Early diagnosis is critical because this syndrome caring high risk of maternal morbidity and infant mortality . So women that proved to have HELLP syndrome should be treated in a tertiary care centre that has a neonatal intensive care unit and a perinatologist available for consultation.

TABLE (1) FREQUANCY OF THE SIGNS AND SYMPTOMS IN THE STUDYING GROUP

SIGN S AND SYMPTOMS	*PERCENTAG*
PROTEINURIA	*100%*
HYPERTENSION	*100%*
RIGHT UPPER QUADRANT/EPIGASTRIC PAIN	*55%*
NAUSEA , VOMITING	*67%*
HEADACHE	*55%*
VISUAL CHANGES	*22%*
*CLINICAL JAUNDCE (TSB >3mg/dl)**	*22%*

* (TSB =TOTAL SERUM BILIRUBIN)

TABLE 2) CLINICAL DISCRIPTION OF THE STUDYING SAMPLE

CASES	AGE(YEARS)	PARITY	GESTATIONAL AGE	BLOOD PRESSURE	PROTEINURIA	**PLATELET COUNT/cubic mm**	TSB mg/dl
1	16	G1P0	34 WEEKS	160/120	++	**75000**	4.5
2	30	G1P0	33WEEKS	160/100	++	**80000**	2
3	21	G1P0	28WEEKS	160/100	+++	**90000**	1.2
4	18	G1P0	29WEEKS	150/100	+	**95000**	1.2
5	38	G1P0	38WEEKS	140/90	++	**65000**	1.5
6	45	G5P4	30WEEKS	170/120	+++	**80000**	1.7
7	36	G6P5	37WEEKS	240/130	++	**<50000**	2.5
8	20	G2P1	31WEEKS	150/90	+++	**100000**	4
9	25	G3P2	32WEEKS	150/100	+++	**90000**	1.3

MATERNAL COMPLICATION	NUMBER OF CASES	PERCENTAGE
SUBCAPSULAR LIVER HEAMATOMA	1	11%
PLACENTAL ABRUPTION	2	22%
ACUTE RENAL FAILURE	1	11%
DIC**	2	22%
PULMONARYODEMA	1	11%
TEMPORARYBLINDNESS	1	11%

**DIC (DISSEMINATED INTRAVASCULAR COAGULATION)

TABLE (3) MATERNAL COMPLICATION IN THE STUDYING SAMPLE

CASES	GESTATIONAL AGE	MODE OF DELIVARY	FETAL WAIGHT(GRAM)	SEX	ADMISSION TO NEONATALCARE UNITE
1	34WEEKS	C/S*	1700	MALE	+
2	33WEEKS	NVD**	1750	MALE	+
3	28WEEKS	C/S	1250	MALE	+
4	29WEEKS	NVD	900	MALE	STILLBIRTH
5	38WEEKS	C/S	3000	FEMAL	_
6	30WEEKS	C/S	2000	FEMAL	+(EARLY NEONATALDEATH
7	37WEEKS	C/S	3250	FEMAL	_
8	31WEEKS	C/S	2100	MALE	+
9	32WEEKS	NVD	1600	FEMAL	STILLBIRTH

*C/S (CESAREAN SECTION) **NVD (NORMAL VAGINAL DELIVARY)

TABLE (4) FETAL OUTCOME IN THE STUDYING SAMPLE

REFERANCE:

1-Weinstein L.Syndrome of haemolysis, elevated liver enzymes and low platelet count: a severe consequence of hypertension in pregnancy.AmJ. Obstet Gynecol 1982; 142:159-67.

2-Richa,-F ;Yazigi,-A et al .General anaesthesia with remifentanil for caesarean section in a patient with HELLPsyndrome:Acta- Anaesthesiol -Scanel.2005 Mar; 49 (3):418-20.

3-Shames ,-B -D; Fernandez,-L-A et al.Liver transplantation for HELLP syndrome: Liver transpl. 2005 Feb; 11 (2):224-8.

4 -Magann EF,Chauhan SP,Naef RW,Blake PG,MorrisonJC ,Martin JN Jr.Standard parameters of preeclampsia: can the clinician depend upon them to reliably identify the patient with the HELLP syndrome ?Aust N Z J Obstet Gynaecol 1993;33: 122 -6 .

5- Magann EF, Perry K G Jr, Meydrech EF,Harris RL,Chauhan SP,Martin JN Jr .Postpartum corticosteroids: accelerated recovery from the syndrome of haemolysis, elevated liver enzymes and low platelets (HELLP) AmJ Obstet Gynecol 1994; 171; 1154-8.

6- Ihle, BU, Long, P, Oats, J.Early onset preeclampsia: Recognition of underlying renal disease .Br Med J 1987; 294:79.

7-Barry N. J. Walters 1999, Hepatic and gastrointestinal disease, High risk pregnancy.

8-Robert K. Creasy. Robert Resnik .Disease of the liver, biliary system and pancreas, maternal foetal medicine 1999. 9- S. C. Robson ,Hypertension and renal disease in pregnancy . Dewhurst's textbook of obstetrics and gynaecology for postgraduates, sixth edition . 1999 :167 -76.

10- Sibai BM. The HELLP syndrome (haemolysis, elevated liver enzymes, and low platelets): much ado about nothing? AmJ Obstet Gynecol 1990 ;162:311-6

11-Sibai, BM.The HELLPsyndrome (haemolysis, elevated liver enzyme, and low platelets): Much ado about nothing? AmJ Obstet Gynecol 1990; 162:311.

12-Martin JN Jr, Rose, CH, Briery, CH.Understanding and managing HELLPsyndrome: the integral role of aggressive glucocorticoids for mother and child .AmJ Obstet Gynecol 2006:195:914.

13-Ibdah, JA,Bennet,MJ,Rinaldo,P,et al.A foetal fatty-acid oxidation disorder as a cause of liver disease in pregnant women .N Engl J Med 1999;340 :1723.

14- Yang ,Z,Yamada,J,Zhao,Y,et al.Prospective screening for paediatric mitochondrial trifunctioal protein defect in pregnancies complicated by liver disease .JAMA2002 ;288:2163.

15-Nelson, J, Lewis, B, Walters, B.The HELLPsyndrome associated with foetal medium-chain acyl-CoA dehydrogenase deficiency.J Inherit Metab Dis. 2000; 23:518.

16 -Sibai ,BM,Ramadan, MK,Usta,I,et al.Maternal morbidity and mortality in 442 pregnancies with haemolysis ,elevated liver enzymes, and low platelets(HELLP syndrome).AmJ Obstet Gynecol 1993;169 :1000-6.

17-Schwerk C; Schmidt-Rhode P; et al.Clinical and chemical laboratory course of HELLPsyndrome -a retrospective analysis.Z Geburtshilfe Neonatol.1996;200(3):109-14(ISSN:0948-2393).

18-Dotsch J,Hohmann M, Kuhl PG.Neonatal morbidity and mortality associated with maternal haemolysis ,elevated liver enzymes and low platelets syndrome,Eur J Pediatr 1997;65:37-47.

19-Sibai B.Diagnosis ,controversies ,management of syndrome of haemolysis ,elevated liver enzyme ,low platelet count ,Obstet Gynecol 2004;103:981.