Role of maternal liver sonography and Hepatic artery Dopplerin cases of preeclampsia and HELLP Syndrome

Doaa Mahmoud Effat[1] and Alya A. El Naggar[2]

[1:] Lecturer of Obstetrics and Gynaecology, Faculty of Medicine (Girls), Al Azhar University
[2:] Assistant Professor of Diagnostic Radiology, Faculty of Medicine (Girls), Al Azhar University
effatdoaa942@yahoo.com

Abstract: Background: Preeclampsia is a leading cause of maternal morbidity and mortality worldwide Unfortunately, it may have no noticeable symptoms Ultrasonography in pregnancy, particularly with utilization of Doppler has been increasingly studied and utilized in several conditions,especially in some situation as prediction of preeclampsia, such method of evaluation has demonstrated its positive impact on prenatal follow up. Objective: The purpose of this study was to evaluate the sonographic and hepatic artery blood flow changes in the maternal liver in cases of preeclampsia and how can these changes predict HELLP syndrome. **Study design:** This prospective observational study was conducted at antennatal clinic of obstetrics and gynecology, Alzharaa Hospital Al Azhar University during period from October 2013-December 2014. Method: Sixty pregnant women with gestational age of 28-36 weeks were selected, they were divided equally into 3 groups each one 20 cases. Group I included 20 women with severe preeclampsia, group II with mild preeclampsia and group III included normotensive women as a control. All cases were subjected to initial ultrasound scanning of the maternal liver, including morphological appearance and hepatic artery Doppler resistive indices (pulsatility index (PI) and resistant index (RI)), and laboratory function tests (including liver function tests, and complete blood picture tests) then all were repeated one week after delivery and correlated to initial findings. **Results:** Initial abnormal liver sonography was only detected in75% of group I (severe preeclampsia) and no cases were detected in other groups (II or III). These abnormalities were in the form of right lobe hypertrophy (mean 16.5), left lobe hypertrophy (Mean 11.6 cm), per portal halo sign (mean 5.9 mm), gall bladder thickness (2.2 mm), ascites, abnormal liver texture, and tenderness in right hypochondrium on probe compression. There were higher values of HAPI and HARI in group I as compared to other groups (p=0.000-0.001), about 95%, 100% of group I had high PI and RI respectively. The initial laboratory changes were, only found in group I, They revealed 30% with HELLP syndrome and all of these patients had abnormal liver sonography and hepatic artery resistive indices. After delivery in group I, the morphological sonographic changes of liver were significantly improved ($p<0.05$). Although Doppler of HA resistive indices improved postpartum in group I but that had no statistically significant ($p>0.05$). Postpartum laboratory findings showed decreased one case of HELLP syndrome who diagnosed initially while there were 2 additional cases developed HELLP syndrome postpartum. **Conclusion**: The sonographic abnormalities of the maternal liver and decrease hepatic blood flow in cases of severe of preeclampsia might precede its biological abnormalities, especially for HEELP syndrome. Thus routine ultrasound liver scanning and hepatic artery Doppler should be contributed in obstetric care for all patients with severe preeclampsia. These may help the owners of opinion for conservative treatment with severe preeclampsia, to select their cases (after normal liver sonography and laboratory function tests had been detected).

[Doaa Mahmoud Effat and Alya A. El Naggar. **Role of maternal liver sonography and Hepatic artery Dopplerin cases of preeclampsia and HELLP Syndrome.** *J Am Sci* 2016;12(3):7-16]. ISSN 1545-1003 (print); ISSN 2375-7264 (online). http://www.jofamericanscience.org. 2. doi:10.7537/marsjas12031602.

Keywords: HELLP syndrome, Doppler ultrasonography, hepatic artery resistance index (HARI), hepatic artery pulsatility index (HAPI)

1. Introduction

Hypertensive disorders of pregnancy affect about 10% of all pregnant women around the world. This group of diseases and conditions includes gestational hypertension, preeclampsia and eclampsia (1). In Asia and Africa, nearly one tenth of all maternal deaths are associated with hypertensive disorders of pregnancy (2). Preeclampsia a disorder peculiar to human pregnancy is of unknown origin it is occurring after 20 weeks of pregnancy. It accounts for 70% of hypertension seen in 6-8% of pregnancies and remains a leading cause of perinatal morbidity and mortality worldwide (3). Diagnosis of preeclampsia is based on new onset of hypertension more than 130/90 mmHg or more, taken on two occasions more than 4 hours a part or a single diastolic blood pressuremore than 110 mmHg and proteinuria more than 300 mg/24 hours or mid-stream 2 + or more proteinuria by dipstick test on two occasions 4 hours apart (4). But according to new ACOG guidelines, the diagnosis of preeclampsia has no longer requires the detection of protein in the urine. Evidence show organ problems with the kidneys and livers can occur without signs of proteinuria and that amount of protein in the urine does not predict how

disease will progress. so it was found that presence of proteinuria is not a condition for diagnosis of preeclampsia, authors defined preeclampsia when diastolic blood pressure 90 mmHg or more and any organ affection as cardiovascular system, liver, kidney etc. (5). Preeclampsia is characterized by inadequate maternal vascular response to abnormal placentation, endothelial dysfunction (due to abnormal oxidative stress with antioxidant deficit), generalized vasospasm, platelets activation, and abnormal hemostasis. These anomalies result in pathophysiologic vascular lesion in various organ system including the liver (6). A severe variant of preeclampsia and eclampsia is hemolysis, elevated liver enzymes and low platelet counts less than 100,000/µL (HELLP) syndrome (7). Hemolysis, defined as the presence of microangiopathic hemolytic anemia, the classic findings of microangiopatic hemolysis include abnormal peripheral smear (schistocytes, burr cells, ethinocytes), elevated serum bilirubin, low serum hepatoglobin levels, elevated lactate dehydrogenase (LDH) levels and significant drop in hemoglobin level (8). Pre-eclampsia and HELLP syndrome are the most common causes of abnormal liver function tests in the third trimester. Liver function tests are abnormal in 20-30% of patients with preeclampsia (9). Some studies have shown varying results for ability of liver function tests to predict adverse maternal outcomes (10). While some studies have found strong association between liver function test and adverse outcomes (2). Liver is a major target organ in patients with preeclampsia with often devastating consequences the pathogenesis of hepatic damage in case of severe preeclampsia and HELLP syndrome is not understood. The classic hepatic lesion associated with HELLP syndrome is periportal or focal parenchymal necrosis, in which hyaline deposits of fibrin like material can be seen in the hepatic sinusoids. The fibrin obstruction of hepatic sinusoids causes hepatocellular injury, which is manifested by elevated liver enzymes and pain localized to the right upper quadrant or mid epigastric regions 911), Hepatic perfusion was found to increase in the third trimester of normal pregnancy, mostly due to increased portal blood flow. It is well known, the adaptive regulation of maternal blood volume disturbed in preeclampsia (12). Abnormal venous hemodynamics, and venous congestion are responsible for secondary dysfunction in liver and other organs. In pregnant women the uterine circulation was evaluated first and has become standard US examination for prediction of preeclampsia, other vascular bed may be of interest during pregnancy are those affected in preeclampsia (13). Early detection of hepatic disturbance in preeclampsia may include Doppler evaluation of liver circulation. Increase hepatic artery resistance blood flow was seen in preeclampsia in presence or absence of HELLP syndrome, however a decrease in dual hepatic blood supply was reported only with HELLP syndrome and precede its biological onset (14). Also some authors reported that women with severe preelcampsia who had HELLP syndrome showed liver abnormalities on ultrasound before biological laboratory abnormalities were detected (15, 16). Sonographic abnormalities of liver include liver hypertenoply, hyperechoic thickening of periportal area, striated thickening of gall bladder wall, hyperechoic thickening of Glisson capsule, subcapsular hematoma subcapsular calcification and probe compression of the liver enhanced abdominal pain (17). The aim of this study was to evaluate the sonographic and hepatic artery blood flow changes in the maternal liver in cases of preeclampsia and how can these changes predict HELLP syndrome.

2. Materials and methods

2.1. Research design and patients:

This prospective observational study was performed on sixty pregnant women who attended the antenatal clinic of obstetrics and gynecology Alzharaa Hospital, Al Azhar University between October 2013 and December 2014. They were divided into three group I, II, III each 20 cases. Group I consisted of 20 pregnant women with severe preeclampsia (arterial blood pressure equals to or more than 160/110 mmHg. Group II consisted of 20 pregnant women with mild preeclampsia (arterial blood pressure equals to or more 130/90 but less than 160/110 mmHg. Group III, consisted of 20 normal pregnant women as a control group.

2.2. Eligibility criteria

Inclusion criteria were: primigravidae, singleton pregnancy from the 28 to the 36 weeks. Patients with liver or gall bladder diseases, medical disorders were excluded from this study except pregnancy induced hypertension, also patients with history of antihypertensive drugs intake were excluded.

2.3. Research ethics

Oral consent was taken from all participants before enrolling this study.

2.4.History and Examinations

All participants were underwent to the followings: - full history taking, including history of present illness(headache, epigastric pain, blurring of vision, nausea, pain in right hypochondrium), - examinations which included general examination (pallor, jaundice, BP, BMI, heart, breast, edema), abdominal examinations included (obstetrics examination, and tenderness in right hypochondrium),- U/S to detect(gestational age and biophysical profile) and mid-stream urine was taken to detect protein in urine by dipstick test.

Then all women were underwent to: abdominal sonographic examinations on the liver included morphological examinations and Doppler hepatic artery blood flow, and laboratory investigation on day of admission and both were repeated within the first week after delivery.

2.5. Sonography

Color Doppler abdominal ultrasound (Toshiba Xanio 200, Japan) examinations were performed by single examiner using transducer with frequency of 3.5MHz. All subjects had fasted for 6-8 h before scanning, scans were performed with patients in the supine and left decubitus position using both Gray-scale and color Doppler imaging to identify vascular landmarks. Doppler tracings were acquired during suspended respiration. The evaluations were performed in right hypochondrial regions. The following features were evaluated at conventional US and Color Doppler:

1) Hepatic morphology: includes, the size, echo texture and peri portal thickening (peri portal halo sign) in the liver. The gall bladder wall was measured and any mud or stones were documented. Tenderness during examination of liver or gallbladder were observed. Ascites and pleural effusion were also observed. The uterus and other abdominal organ as (pancreas, spleen and kidneys) also were studied(17). Liver hypertrophy was diagnosed when right lobe of the liver, measured in sagittal plane on the midclavicular line was larger than16 cm and when the left lobe of liver measured in sagittal plane on the xiphoid line, was larger than 10 cm. The gall bladder was considered thickened if it measured on an axial plane greater than 3mm the per portal halo sign was considered, if the periportal area thickened greater than 5mm.

2) Then color Doppler was applied on common hepatic artery (CHA) which was seen where the celiac trunk bifurcation into the splenic and common hepatic artery, is visualized in longitudinal axis. The artery can be identified adjacent to the main portal vein with color flow US which is used for localization of the artery, flow within the artery is characterized with spectral Doppler US. Hepatic arterial flow typically has a pulsatile low resistance waveform with abroad systolic peak, antegrade diastolic flow, and spectral broadening. The Doppler gate was placed over the lumen of the artery and velocity measurements were conducted at Doppler angle (<60) and waveforms were recorded. Hepatic artery Pulsatility index (HAPI) and Hepatic artery resistance index (HARI) were calculated automatically by machine, at least three similar sequential Doppler waveform were measured.

2.6. laboratory investigation

Venous blood sample was taken from all participants for laboratory investigation to evaluate i- maternal liver function which include liver enzymes (aspartate aminotransferase (AST), alanine aminotransferase (ALT), lactic acid dehydrogenase (LAD)), total bilirubin, total protein), ii- complete blood picture

2.7.Follow up

Follow up of participants was done (blood pressure, proteinuria, edema, any drugs taken for controlling disease in group I or II were recorded (antihypertensive, corticosteroid and or MgSo4), mode of delivery, obstetrics outcome, complications as eclamptic fits and maternal ICU admission, prematurity and, neonatal deaths also recorded if were present. Liver sonography, Doppler of hepatic artery resistive indices and liver functions tests were repeated within the first week after delivery for all cases to reevaluate the changes.

3. Results

There were no significant differences as regards to mean of maternal age, gestational age, BMI among the studied groups ($p>0.05$). But there significant differences were detected as regards to BP, protein in urine, drugs intervention (antihypertensive drugs, MgSo4 and corticosteroid) among three group. All cases (100%) of women in both groups (group I and group II) versus (0%) in group III were taken antihypertensive drugs. All patients in group I (100%) were taken MgSo4, versus (0%) in group II and III. Three cases (15%) were taken corticosteroid in group I versus 14 cases (70%) in group II..There was a significant difference as regard to mode of delivery among studied groups, about 16 cases (80%) in group I, 7 cases (35%) in group II, 2 cases(10) in group III were underwent to C.S for termination of pregnancy ($p=0.000$). There was high significant difference among three groups as regards to preterm babies (<34 weeks). Twelve (60%) of babies in group I were preterm versus (0%) in group II and III ($p<0.001$). There was no significance difference among three groups as regarding eclamptic fits, 2 patients (10%) in group I had eclamptic fits versus (0%) in other groups $p>0.05$ (Table 1). There was high significant difference among studied groups as regards to number of mothers who admitted to ICU, 15 cases (75%) in group I versus (0%) in other groups $P<0.001$.Also there was high significant difference as regard to neonatal deaths among the studied groups, about 7 babies died(35%) for group I versus (0%) for other groups were recorded ($p<0.001$) (Table 1). Initial songraphic findings of maternal liver showed; the mean length of the right lobe of the liver in group I (severe preeclampsia) was 16.5 cm, while that of the left lobe was 11.6 cm. The mean gall bladder wall thickness was 2.2 mm, and that of the periportal halo sign was 5.9 mm. The mean length of the right lobe in group II was 12.8 cm, the left

lobe of the liver was 6.3 cm, the mean of the gall bladder wall thickness was 1.9 mm, there no periportal halo sign was detected in this group while the mean length of the right lobe of liver in group III (Normal or Control group) was 12.1 cm, the left lobe of the liver was 6.3 cm, the gall bladder thickness was 0.9mm, Also there no periportal halo sign was detected in this group (Table 2). There were statistical significant differences among studied groups as regarding sonographic findings (Table 2). Abnormal sonographic changes were only detected in 15 cases (75%) in group (I). In group I, 11 cases (55%) showed hepato-megally, 3 cases (15%) with ascites, 6 cases (30%) showed thickened gall bladder wall, periportal halo sign was detected in 10 cases (50%) of that group, 11cases (55%) showed abnormal liver texture and 12 cases (60%) of those patients showed tenderness in right hypochondrial area on probe compression (Table 3, Figure 1).

Table 1. Maternal and perinatal characteristics of women and outcome in studied groups.

Variables		Group I	Group II	Group III	p-value
Maternal age /years	Mean ± SD	27.0 ± 9.9	27.0 ± 11.31	25.5 ± 10.6	0.876
Gestational age/weeks	Mean ± SD	32.0 ± 4.24	31.2 ± 4.62	34.5 ± 4.33	0.508
BMI	Mean ± SD	23.5 ± 6.7	24.5 ± 5.5	24.0 ± 6.49	0.880
Systolic BP (mm Hg)	Mean ± SD	172.5 ± 17.68	145.0 ± 7.07	105 ± 20.21	<0.001
Diastolic BP (mm Hg)	Mean ± SD	122.5 ± 17.6	97.5 ± 10.6	70.0 ± 14.1	<0.001
Protein uria at admission (dipstick test)		+++ / ++++	+ / ++	Nil	
Drugs Intervention	Antihypertensive drugs	20 (100.0%)	20 (100.0%)	0 (0.0%)	<0.001
	MgSo4	20 (100.0%)	0 (0.0%)	0 (0.0%)	< 0.001
	Corticosteroid	3 (15.0%)	14 (70.0%)	0 (0.0%)	< 0.001
Mode of delivery	NVD	4 (20%)	13 (65.0%)	18 (90.0%)	0.000
	CS	16 (80%)	7 (35.0%)	2 (10.0%)	
History of preterm < 34weeks		12 (60.0%)	0 (0.0%)	0 (0.0%)	<0.001
Patients with eclamptic fits		2 (10%)	0 (0.0%)	0 (0.0%)	0.126
Number of mothers who admitted to ICU		15 (75.0%)	0 (0.0%)	0 (0.0%)	<0.001
History of neonatal deaths		7 (35.0%)	0 (0.0%)	0 (0.0%)	<0.001

Table 2. Initial sonographic assessment of the maternal liver and hepatic artery Doppler in studied groups

Variables			Group I	Group II	Group III	T1 P1	T2 P2	T3 P3
Right lobe (cm)		Mean ± SD	16.5 ± 3.5	12.8 ± 3.2	12.1 ± 2.5	3.489	4.575	0.771
		Range	12 – 21	11 - 17	11 - 15	0.001	<0.001	0.445
Left lobe (cm)		Mean ± SD	11.6 ± 1.6	7.0 ± 1.1	6.3 ± 1.8	10.595	9.842	1.484
		Range	9 – 15	6 - 8	5 - 7.5	<0.001	<0.001	0.146
Gall bladder thickness (mm)		Mean ± SD	2.2 ± 0.6	1.8 ± 0.6	0.9 ± 0.5	2.290	7.444	5.726
		Range	1.5 - 3.5	1.5 - 2.2	0.6 - 1.5	0.027	<0.001	<0.001
Periportal halo sign (mm)		Mean ± SD	5.9 ± 3.8	-	-	NA	NA	NA
		Range	0 – 10	-	-			
Hepatic artery resistive indices	P1	Mean ± SD	1.85 ± 0.83	1.13 ± 0.35	1.08 ± 0.17	3.575	4.064	0.575
		Range	1.45 – 2.48	0.98 – 1.45	0.96 – 1.21	0.001	0.000	0.568
	R1	Mean ± SD	1.1 ± 0.35	0.66 ± 2.8	0.65 ± 0.28	103.713	4.490	104.717
		Range	0.83 – 1.65	0.61 – 0.71.8	0.59 – 0.69	0.000	0.001	0.000

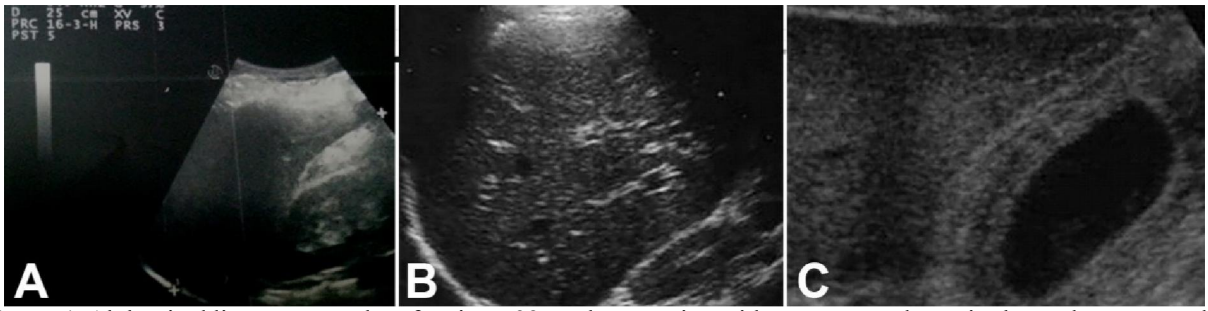

Figure 1. Abdominal liver sonography of patients 32 weeks gestation with severe preeclampsia shows, hepatomegally (a), periportal halo sign (b)and thickened gall bladder wall(c).

There was significant difference among studied groups as regard to Doppler of hepatic artery pulsatility index (HAPI), the mean of PI of hepatic artery was (1.85) in group I, (1.13) in group II and (1.08) in group III with p=0.000-0001 (Table 2). Abnormal HAPI was only found in group I (severe preeclampsia), the percentage of patients who had abnormal HAPI was 95% (Table 2,3, Figure 2). There was significance difference among studied groups as regard to hepatic artery resistance index (HARI), the mean of HARI was (1.1) in group I, (0.66.) in group II and (0.65) in group III (Table 2). Abnormal HARI was found in group I, the percentage of patients who had abnormal RI was 100% (Table 2,3, Figure 2). Initial abnormal laboratory function tests were only detected in12 cases (60%) in group I. Six cases (30%) with HELLP syndrome were diagnosed during initial laboratory testing. All cases with HELLP syndrome had abnormal sonographic findings of the liver during initial scanning including abnormal hepatic artery blood flow (Table 4).

Table 3. The percentage of cases with abnormal sonography and hepatic artery resistive indices in severe preeclampsia group (group I)

Parameters		n	%
Liver hypertrophy		11	55.0
Ascites		3	15.0
Gall bladder thickness		6	30.0
Peri portal halo sign		10	50.0
Tender probe compression		12	60.0
Abnormal liver texture		11	55.0
Hepatic artery resistive indices	P1	19	95
	R1	20	100

Table 4. Initial laboratory values, sonographic changes, and hepatic artery Doppler with HELLP syndrome in group(I)

Parameters		Range	*Mean ± SD*
Liver function	AST(ul)	75-170	*120.78 ± 18.57*
	ALT(ul)	80-225	*137.18 ± 38.7*
	Platelets count (µL)	48,000-100,000	*67.8 ± 19.5*
	Protein(g/dl)	3.7-5.5	*4.41 ± 1.6*
	Bilirubin (mg/dl)	1.7-3.0	*2.3 ± 0.9*
Sonographic changes	Right lobe (cm)	14-21	*17.5 ± 3.2*
	Left lobe (cm)	10.6-15	*13.1 ± 2.08*
	Gall bladder thickness(mm)	1.2-3.5	*2.61 ± 1.27*
	Periportal halo sign (mm)	0 -10	*5.6 ± 3.21*
Hepatic artery resistive indices	PI	1.61-2.48	*2.0 ± 0.3*
	RI	0.91-*1.65*	*1.24 ± 0.26*

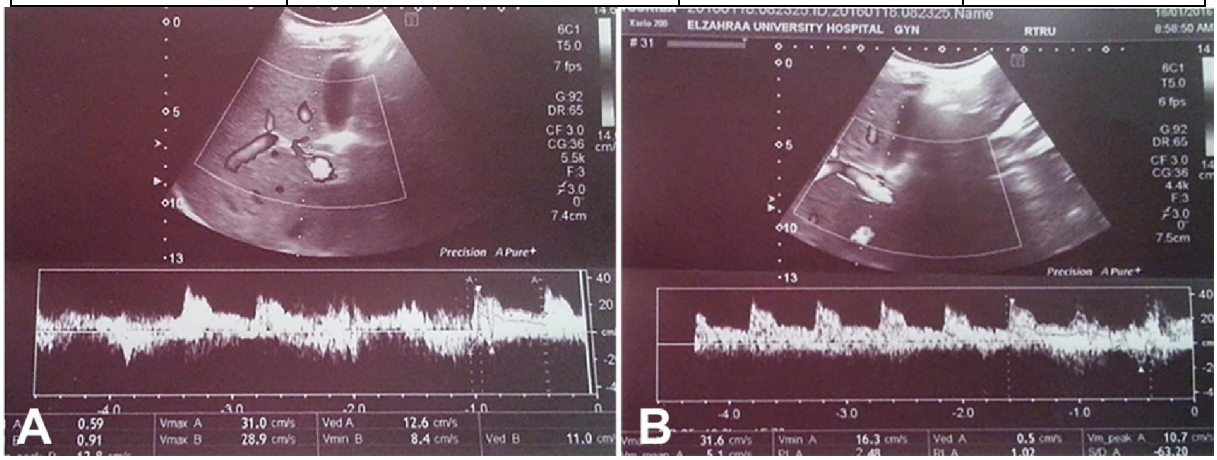

Figure 2. a) Color Doppler ultrasonography of hepatic artery in pregnant women 30 weeks of gestation with normal blood pressure shows normal RI: 0.59 and normal PI:0.91. b) Color Doppler ultrasonography of hepatic artery in pregnant women 33 weeks of gestation with HELLP syndrome shows elevated RI: 1.0., and elevated PI: 2.84.

Among the 6 patients who diagnosed as HELLP syndrome, there were 90 % of cases with hepato-megally, 40 % with ascites, 30% showed thickened gall bladder, periportal halo sign was detected in 70% of those patients, 80% of patients had abnormal liver texture and 98% had tenderness on probe compression and all cases 100% had abnormal resistive indices of hepatic artery (PI,RI). All participants of this study were subjected to maternal liver sonography and laboratory function tests re-evaluation one week after delivery. There was high significant difference between group I, II and between group I, III as regarding postpartum liver morphological sonography ($p<0.001$) (Table 5). Group I showed improvement in all morphological sonographic liver abnormalities after delivery as compared to initial one, that had statistically significant $p<0.05$ (Table6). Percentage of patients who had abnormal sonographic findings after delivery decreased than initial one as follows: hepato-megally by 40%, as cites by (5%), gall bladder thickness by (5%), periportal halo sign by (30%), tenderness on probe compression by (25%) and patients with abnormal liver texture decreased by 30% than initial sonographic one. No cases with sub capsular hematoma were detected at initial or postpartum scanning. Doppler of HA resistive indices increased post partum in group II, III but that had no significant difference ($p>0.05$) (Table 5). In group I there was improvement in postpartum resistive indices in HA as compared to initial Doppler scanning, but that had no statistically significant ($p>0.05$) (Table 5,6), the percentage of women who had abnormal HAPI and HARI postpartum were decreased 15%, and 20% respectively than before delivery. There was improvement in laboratory function tests in group I after delivery as compared to initial one, but also there was no statistical significant difference ($p>0.05$) except of the platelets count ($p=0.001$) (Table 7). The patients with HELLP syndrome were increased in group I to 7 patients (35%) but that increased was no statistical significance ($p>0.05$) (Table 7).

Table 5. Post-partum sonographic findings of liver and hepatic artery Doppler in the studied groups

Variables		Group I	Group II	Group III	T1 P1	T2 P2	T3 P3
Right lobe (cm)	Mean ± SD	13.0 ± 2.5	10.5 ± 1.5	9.6 ± 4.2	3.835 0.001	3.111 0.004	0.902 0.372
	Range	10 – 20	13– 16	12 – 15			
Left lobe (cm)	Mean ± SD	10.6 ± 1.1	7.0 ± 1.1	6.6 ± 1.3	10.349 <0.001	10.505 <0.001	1.050 0.300
	Range	8 – 13	6 – 8	5 – 7.5			
Gall bladder thickness (mm)	Mean ± SD	1.8 ± 0.6	1.2 ± 0.3	1.1 ± 0.5	4.000 <0.001	4.008 <0.001	0.767 0.448
	Range	1.5 – 3	1 – 1.5	0.5 – 1.5			
Periportal halo sign (mm)	Mean ± SD	3.1 ± 2.7	-	-	NA	NA	NA
	Range	0 – 8	-	-			
Hepatic artery resistive indices							
PI	Mean ± SD	1.68 ± 0.24	1.29 ± 0.18	1.19 ± 0.21	5.814 <0.001	6.871 <0.001	1.617 0.114
	Range	1.41 - 2	1.19 – 1.40	1.09 – 1.30			
RI	Mean ± SD	1.0 ± 0.31	0.69 ± 0.11	0.67 ± 0.18	4.215 <0.001	4.117 0.002	0.424 0.674
	Range	0.79 – 1.35	0.64 – 0.71	0.62 – 0.69			

Table 6. Relation between initial & postpartum maternal liver sonography and hepatic artery Doppler in group I

Variables			Pre	Post	Test	p-value
Right lobe (cm)		Mean ± SD	16.5 ± 3.5	13.0 ± 2.5	3.639	0.001
Left lobe (cm)		Mean ± SD	11.6 ± 1.6	10.6 ± 1.1	2.303	0.026
Gall bladder thickness(mm)		Mean ± SD	2.2 ± 0.6	1.8 ± 0.6	2.108	0.041
Periportal halo sign (mm)		Mean ± SD	5.9 ± 3.8	3.1 ± 2.7	2.686	0.011
Hepatic artery resistive indices	PI	Mean ± SD	1.85 ± 0.83	1.68 ± 0.24	0.880	0.384
	RI	Mean ± SD	1.1 ± 0.35	1.0 ± 0.31	0.957	0.345

Table 7. Relation between the initial and postpartum liver function tests in group I

Group I		Pre	Post	Test	p-value
AST (u/l)	Mean ± SD	90 ± 30.7	72.2 ± 26.5	1.963	0.057
ALT (u/l)	Mean ± SD	107 ± 33.5	95.5 ± 20.7	1.306	0.199
LDH (u/l)	Mean ± SD	335 ± 111	275 ± 98.6	1.807	0.079
Bilirubin (mg/dl)	Mean ± SD	2.1 ± 0.9	2.1 ± 1.0	0.000	1.000
Total protein(g/dl)	Mean ± SD	5.2 ± 1.5	5.6 ± 1.2	0.931	0.357
Platelets count/ µL	Mean ± SD	112 ± 25.3	148.3 ± 25.6	4.510	0.001
HELLP syndrome	Negative	14 (70.0%)	13 (65.0%)	0.114	0.736
	Positive	6 (30.0%)	7 (35.0%)		

4. Discussion

Preeclampsia is disorder of wide spread vascular endothelial dysfunction and vasospasm that occurs after 20 weeks of gestation and can present as late as 4-6 weeks post-partum (18), it constitutes of major sources of morbidity and mortality worldwide. Overall 10-15% of maternal deaths are directly associated with preeclampsia and eclampsia (5, 19). Liver dysfunction with preeclampsia has long been recognized, liver involvement in severe form commonly manifested by epigastric or right hypochondrium pain. Elevated serum transaminaseoccure in approximately one fourth of patients with severe preeclampsia and up to 90% of those with eclampsia (15). Liver circulation is unique due to dual perfusion and the phenomenon of interaction between blood stream. The application of Doppler US for evaluation of maternal circulatory changes could be useful in the intensive follow up of high risk pregnancies with preeclampsia (13). In the current study there no significant differences as regard to age, gestational age, BMI were detected among three groups. But there were significance differences among three groups as regard to BP, proteinuria, drugs intervention (antihypertensive drugs, corticosteroid, Mgso4), and mode of delivery. All cases (100%) were taken antihypertensive drugs in group I inform of (hydralizin, lebatolol) aiming to control BP then immediate termination of pregnancy regardless maturity of babies. Also all cases (100%) in group II were taken antihypertensive drugs in form of alpha methyldopa (aldomet) and Ca^{++} channel blocker (nifedipine) aiming to control their BP until maturity of babies occur. All patients (100%) in group I versus (0%)in other groups were taken mgso4 to guard against convulsions, however one patient developed post-partum eclampsia after initial dose of mgso4.In the current study, 3cases (15%)in group I versus 14cases (70%) in group II were taken corticosteroid, the main cause of administration of corticosteroid in group I to improve the liver function tests especially platelets. But the cause of administration of corticosteroid in group II was to enhance the fetal lung maturity especially if the gestational age less than 34 weeks. In the current study 16 cases (80%), 7 cases (35%) and 2 cases (10%) were underwent to C.S in group I, II, III respectively. The cause of increased the number of patients who underwent to C.S in group I due to most of them were not in labor and Bishops score ↓5they were required long time for vaginal delivery after controlling their BP. In the current study there were significant differences among the studied groups as regard to history of preterm babies <34 weeks, number of mothers who admitted to ICU, and neonatal deaths. Seven cases (35%) had neonatal deaths in group I mainly due to prematurity. But there was no significant difference as regard to number of patients had eclamptic fits among the studied groups $p>0.05$.In the present study, there was statistical significant difference among the studied groups as regarding the initial liver sonography ($p<0.05$-0.001). The initial sonographic liver abnormalities were only found in cases of severe preeclampsia (group I). Sonographic changes included liver hypertrophy, gall bladder thickening, periportal halo sign, abnormal liver texture, tenderness on probe compression and ascites. Histopathological abnormalities in the maternal liver with severe preeclampsia or HELLP syndrome due to microthrombi and vasospasm which leads to focal necrosis, hemorrhage, and deposition of hyaline fibrin like material and periportal granulocyte filtration (16, 20). Liver hepatomegally may be due to deposition of hyaline material and granulocyte infiltration. Striated thickening of gall bladder wall may be caused by severe hypoalbuminaemia (21), periportal halo sign (hyperechoic thickening of the portal vein) it is may be due to periportal hepatocellular necrosis and periportal granulocyte infiltration (17), abnormal liver texture due to microinfarcts and congestion. The cause of ascites unknown but may be due to wide spread endothelial damage and severe hypoalbuminaemia (22). Tenderness or pain on compression due to hepatocellular injury, swelling of liver and distention of Glisson capsule (17).The current study revealed postpartum improvement in abnormal morphological liver sonography (in group I) and there were regression of liver abnormalities within the first week after delivery and that had statistically significant($p<0.05$), this result agree with the previous studies which stated that the liver complications which occur with severe preeclampsia or eclampsia were rapidly normalize after delivery (15, 17). In the present study there no cases of subcapsular hematoma were detected in severe preeclmpsia (group I) either before or after delivery. This result agrees with *Koleif et al. (15)* who found that no cases were detected in their cases with severe preeclampsia. On other hand some authors inconsistent with our result and they recorded this complication with their cases of severe preeclampsia (23-26).Hepatic blood flow measurement may be extremely important in prediction and evaluation of women with preeclampsia and HELLP syndrome, which has been done in few studies with limited number of participants (12). All of those studies evaluated total blood flow in hepatic artery and portal vein which sometimes may be difficult especially in third trimester. *Markovic et al. (13)* suggested that hepatic artery Doppler may be more useful in quick orientation of potentially altered liver circulation in preeclamptic patients and HELLP syndrome. Hepatic artery indices decrease during third trimester in uncomplicated pregnancies as result of systemic vasodilatation and retained to their original level within 6-10 weeks. PI was reported between 0.6

and 0.7, while values above 0.8 are considered to be high, PI value may be vary, but usually are under 1.5 (13). On other hand, *Nakai et al. (27)* reported that Doppler indices remained unchanged during pregnancy. In the current study, found that there was significant difference among studied groups as regard to HAPI and HARI. The mean PI of hepatic artery was (1.85), (1.13), and (1.08) in group I, II and III respectively with p=0.000-0.001. Abnormal PI index of HA was only found in group I (severe preeclampsia) including patients with or without HELLP syndrome, their numbers were 19 (95%). The mean of RI was (1.1), (0.66) and (0.65) in group I, II, and III respectively with p =0.000- 0.001. Abnormal R I was only found in group I including all cases with or without HELLP syndrome, their numbers were 20(100%).The current study agree with *Oosterhof et al. (28)* who found that both HAPI, HARI values were significantly increased in severe preeclampsia either with HELLP or without HELLP syndrome as compared to normal group. These findings indicate the hepatic artery resistance to blood flow is increased in preeclampsia in the presence or absence of HELLP syndrome. The result also demonstrated that vasoconstriction of hepatic arteries is not more pronounced in the HELLP syndrome that in other manifestation of preeclampsia. Therefore factors other than vasoconstriction are likely to be responsible for the development of the HELLP syndrome. Postpartum Doppler re-evaluation of hepatic artery showed increased in both resistive indices in group II, III (mild preeclampsia and normal groups) but that had no statistically significant (p>0.05). Group I showed decreased in both resistive indices postpartum as compared to initial one and that had no statistically significant (p>0.05). In present study, abnormal liver function tests were only found in group I, about 6 (30%) of them had HELLP syndrome. All patients with HELLP syndrome were also showed abnormal liver sonography and hepatic artery blood flow at initial scanning. The criteria of diagnosis of HELLP syndrome through the laboratory testing are; platelets count less than 100, 000 μL, AST more than 70 u/L, LDA more than 160 u/L - 600 u/L (this discrepancy depending on particular laboratory LDH kits used, in this study we used LDH kits with normal reference ranging from 81-224U/L) and total bilirubin more than 1.2 mg/dL (29, 30).

The decreased in circulating platelets in HELLP syndrome is secondary to an increased rate of consumption at the site of damaged vascular endothelium this often early finding in the development of preeclampsia (8, 31). The elevation in total LDH is probably caused by ischemia (32). In the present study, postpartum laboratory reevaluation tests revealed improvement in liver function tests after delivery in group I as compared to initial one but this difference had no statistically significant (p>0.05), except for platelets count (p=0.001). This result agree with *Kholief et al. (15)* who found that there was improvement in laboratory measurement after delivery in cases with severe preeclampsia, but there was no statistical significant difference except for platelets count. Also *Barton a nd Sibai (9)*, agree with the current study, they found that there was no correlation between imaging and severity of liver function tests abnormalities except for the thrombocytopenia. In this study The number of patients with severe preeclampsia who had HELLP syndrome before delivery were decreased one case (5%) after delivery, other cases with initial HELLP showed improvement in liver function tests after delivery, but they still were under definition of HELLP syndrome (elevated liver enzymes more than 2 standard deviation over laboratory's mean or AST ↑ 70 U/L and low platelets, etc..). On other hand two new cases (10%) were developed postpartum HELLP syndrome. In the present study, patients who had HELLP syndrome at initial laboratory function tests they had abnormal liver sonography and blood flow. Also the additional two cases who developed post-partum HELLP syndrome, those patients had initial abnormal liver sonography and Doppler hepatic blood flow before they were had laboratory manifestation or biological liver abnormalities. *Kholief et al. (15)* were in keeping with the current study, they found that increased the number of patients who developed HELLP syndrome post partum by 16% is compared to before delivery and those patients were initially had abnormal liver sonography.

5. Conclusions

This study concluded that sonographic liver abnormalities and blood flow changes in hepatic artery precede the biological abnormalities in cases of severe preeclampsia especially for HELLP syndrome. So serial liver sonographic examinations should be contributed to the obstetrics care of preeclamptic patients and HELLP syndrome especially if conservative treatment was decided.

Acknowledgements:

The authors would like to express my great thanks to Dr. Zakia Abu Eldahab Mohamed, assistant professor in clinical pathology Elzhara university Hospital for help them in this study.

Corresponding Author:

Doaa Mahmoud Effat, Lecturer of Obstetrics and Gynaecology, Faculty of Medicine (Girls), Al Azhar University, Tel.: +20.1016663451, E-mail: effatdoaa942@yahoo.com

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2/15/2016