Liver Dysfunction and Ultrasonographic Findings in Pregnancy Induced Hypertension Compared to Late Normal Pregnancy

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Abstract: Background: Liver pathology may precede pregnancy, develop during pregnancy or result as a direct complication of pregnancy. Differentiation of pathologies can be difficult but is of importance as the appropriate management varies with the diagnosis. **Aim**: of this study was to estimate the pattern and the degree of liver dysfunction in women complaining from pregnancy induced hypertension. **Subjects and Methods:** This study was performed on forty females in their late trimester of pregnancy. Twenty females were complaining from preeclampsia and twenty normal late pregnant females. A control group of twenty non pregnant females was randomly selected. Liver function tests and abdominal ultrasound was done for the studied subjects. **Results:** Statistically significant difference was found between different groups as regards liver echogenicity, liver span and gall bladder abnormalities in abdominal ultrasonography. We noted that liver enzymes were higher in pregnant group more than the normal control group and the enzymes were higher in pregnancy induced hypertension more than the other pregnant group but serum bilirubin and coagulation profile showed no statistically significant difference between the three groups. From this study we **concluded** that liver function tests and abdominal ultrasonographic examination is an important tool to detect hepatic dysfunction in women with pregnancy induced hypertension.
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1. Introduction

Liver diseases are common and currently represent the 12th leading cause of death. Although hepatic diseases are relatively common, most are clinically silent and differential diagnosis often is difficult **(Arias et al., 2003).** Preeclampsia, a vascular disorder of pregnancy, is a leading cause of maternal morbidity as well as perinatal morbidity and mortality. The only intervention that effectively reverses the syndrome is delivery **(Qiu et al., 2006).** Liver pathology may precede pregnancy, develop during pregnancy or result as a direct complication of pregnancy. Differentiation of pathologies can be difficult but is of importance as the appropriate management varies with the diagnosis. Accurate diagnosis is crucial as different pathologies have different implications for the mother and baby, not only in the context of the index pregnancy but for the long-term health of the mother and child **(O'donoghue and Byrne, 2000).** Hepatobiliary disease occurring in a pregnant woman poses a challenge for the consulting physician. Liver dysfunction was seen in 3% of deliveries during a 15 month prospective study and was usually directly related to pregnancy with spontaneous recovery in the puerperium. The incidence of the most serious conditions, acute fatty liver of pregnancy and HELLP syndrome, was much greater than previously reported. Profound effects on maternal and infant health were observed but close medical and obstetric collaboration ensured low mortality **(Ch'ng et al., 2002 and Kingham, 2006)**.

The enlarged liver may become more difficult to palpate because of the expanding uterus within the abdominal cavity. Physical findings such as telangiectasia and palmar erythema, suggestive of liver disease in non pregnant women, may appear in up to 60% of normal pregnancies because of the hyper estrogenic state of pregnancy, as the liver cannot metabolize quickly the large quantity of estrogen and progesterone produced by the placenta **(Guntupalli and Steingrub, 2005).** Hepatic dysfunction in preeclampsia ranges from the presence of mild hepatic enzyme elevations in the serum to the more extreme HELLP syndrome, sub capsular bleeding or even hepatic rupture **(Frishman et al., 2005).** Acute fatty liver of pregnancy (AFLP) is a rare and serious entity associated with significant maternal and neonatal mortality and morbidity. Maternal morbidity includes: hypoglycemia, coagulopathy, encephalopathy and renal failure. With the early recognition of AFLP cases and prompt progressive management, including early termination of pregnancy and large dose infusion of fresh frozen plasma, the prognosis of AFLP is obviously improved **(Mjahed et al., 2006).** Intrahepatic cholestasis of pregnancy (ICP), or icterus gravidarum, is a rare and serious medical condition seen in the third trimester, with fetal mortality rates of 11% to 20% when untreated and prevalence rates

estimated at 1/1,000 to 1/10,000 pregnancies. It is defined as pruritus of onset in pregnancy in association with abnormal liver functions in the absence of any other identifiable liver pathology **(Kenyon and Shennan, 2004).** It is thought that increasing estrogen levels throughout the course of the pregnancy contribute to the development of ICP **(Germain et al., 2002).** This is supported by the fact that women with multiple gestations have an increased risk of having the disorder (multiple gestations cause a proportional increase in the estradiol levels in maternal circulation).

Aim of the Work

To estimate the pattern and the degree of liver dysfunction in pregnancy induced hypertension compared to late normal pregnancy. To study any possible relation between abnormal liver function tests occurring during pregnancy secondary to pregnancy induced hypertension and abnormal sonographic findings in the same women.

2. Subjects and Methods

Subjects:

This study was performed on forty female in their late trimester of pregnancy. Among those, twenty females were showing symptoms and signs of pregnancy induced hypertension. The other twenty, were females in their late trimester of normal pregnancy with no symptoms or signs of pregnancy induced hypertension. A control group of twenty non pregnant females was randomly selected, having no previous history of hypertension, diabetes, chronic liver or kidney diseases or pregnancy induced hypertension.

The three groups were matched for age. The mean age (± SD) of the females with pregnancy induced hypertension was 25.5 ± 5 years. It was 24 ± 4.6 years for the females in their late trimester of normal pregnancy, while it was 26.1 ± 4.1 years for the control normal non pregnant females. There was no significant difference between them.

Methods:

I) All groups were subjected to the following:

A. Detailed history taking (including obstetric history) and complete clinical examination.

B. Laboratory investigations: from each subject the blood was withdrawn, after a written consent was taken and explanation of the nature of the study was explained. Blood was withdrawn (7 cc) through a venipuncture using a dry sterile plastic syringe. Of these, (2 cc) were added into a clean tube containing dipotassium ethylene diamine tetra acetate (EDTA) for the analysis of complete blood picture. While, 5 cc were allowed to clot and then centrifuged for separation of the serum for the other investigations.

1) Liver function tests:
Aspartate transaminase (AST), Alanine transaminase (ALT), Alkaline phosphatase, Albumin, LDH, Total bilirubin and Prothrombin time. They were all analyzed on automated Boehringer Mannheim Hitachi 912 analyzer using standard methods.

2) Dipstick Protein:
The initial presence of proteinuria is usually determined by the use of a protein reagent dipstick in a random urine sample. The used strips were Glucostrips (Pasteur Lab.).

3) Kidney function tests:
Blood urea: The scalvo diagnostic method
Serum creatinine: Modified Jaffe s kinetic method.

C. Abdominal Ultrasonography: This study was done by an apparatus Philips HDI 5000. It involved scanning of the liver size and echogenicity, detecting any focal lesions in the liver or the spleen, screening gall bladder diseases including: GB stones, biliary sludge, etc.

In all subjects during ultrasound examination we observed for "periportal halo" sign, gallbladder wall thickness, painful compression of the liver and gallbladder and ascites. It also involved measuring of the caliber of the portal vein and the span of the liver and the spleen.

II) Data Analysis:

Data were statistically described in terms of range, mean, standard deviation (±SD), median, frequencies (number of cases) and relative frequencies (percentages) when appropriate.

Comparison of quantitative variables between more than two groups in the present study was done using Kruskal Wallis analysis of variance (ANOVA) test with Mann Whitney *U* test posthoc multiple 2-group comparison. For comparing categorical data, Chi square (X^2) test was performed. Yates correction was used instead when expected frequency is less than 5.

A probability value (*p* value) less than 0.05 was considered statistically significant. All statistical calculations were done using computer programs Microsoft Excel version 7 (Microsoft Corporation, NY, USA) and SPSS version 15 (Statistical Package for the Soacial Science; SPSS Inc., Chicago, IL USA) statistical program.

3. Results and Discussion

The pregnant woman experiences physiological changes to support fetal growth and development. Particularly the physiological changes of the liver are the results of the increment of estrogens and progesterone during the pregnancy and also the hemodynamics changes (hemodilution) **(Angel García Alonso, 2006).** This study showed no statistically significant difference between different groups as regards age and obstetric history **(table 1),** but there was statistically significant difference between different groups as regards blood pressure **(table 1).**

Table (1): Obstetric history, blood pressure and albumin in urine among examined groups

Group / Data	PIH (N= 20)	Late normal pregnancy (N= 20)	Control (N= 20)	*p* – value
Age	25.5 ± 5	24 ± 4.1	26.1 ± 4.12	> 0.05
Gravidity	2.2 ± 1.21	2.5 ± 1.35	2.4 ± 1.15	> 0.05
Parity	2.2 ± 1.2	2 ± 0.7	1.9 ± 0.1	> 0.05
SBP	165 ± 12.22	112 ± 8.2	121 ± 4.77	< 0.05
DBP	105 ± 12.4	75 ± 8.06	80 ± 4.1	< 0.05

We concluded that there was no statistically significant difference between different groups as regards complete blood count **(table 2).**

Table (2): Complete blood count values among examined groups

Group / Data	PIH (N= 20)	Late normal pregnancy (N= 20)	Control (N= 20)	*p* - value
Hb	9.73 ± 1.13	10.17 ± 0.59	11.1 ± 0.70	> 0.05
MCV	77.51 ± 3.71	78.61 ± 4.1	79.5 ± 2.5	> 0.05
MCHC	33.11 ± 0.88	32.38 ± 1.41	32 ± 1.59	> 0.05
Platelets	265500 ± 51341.66	272000 ± 60911.53	272200 ± 75238.81	> 0.05
WBCs	13400 ± 3334	11125 ± 2364.8	10840 ± 2515.5	> 0.05

This study showed that there was statistically significant difference between different groups as regards albumin in urine **(table 3).** But no statistically significant difference between different groups as regards urea and creatinine levels was observed **(table 3).**

Table (3): liver and kidney function among examined groups

Group / Data	PIH (N= 20)	Late normal pregnancy (N= 20)	Control (N= 20)	*p* - value
AST	97.3 ± 73.31	42.3 ± 11	40 ± 19.23	< 0.05
ALT	65.3 ± 55	32.5 ±6	33.4 ± 15.44	< 0.05
ALP	165.2 ± 66.06	86.1 ± 45.54	75.8 ± 12.82	< 0.05
Total protein	6.2 ± 0.41	7.92 ± 0.25	7.5 ± 0.50	< 0.05
Albumin	2.41 ± 0.34	3.1 ± 0.47	4 ± 0.55	< 0.05
Total bilirubin	0.44 ± 0.36	0.58 ± 0.32	0.61 ± 0.28	> 0.05
PT	13.41 ± 0.68	13.24 ± 0.86	13.14 ± 0.65	> 0.05
PC	81.20 ± 13.06	80.6 ± 11.10	87.3 ± 9.23	> 0.05
INR	1.170 ± 0.11`	1.19 ± 0.07	1.110 ± 0.08	> 0.05
Urea	27.6 ± 8.20	32.1 ± 5.28	35 ± 3.03	> 0.05
Creatinine	0.81 ± 0.19	0.83 ± 0.11	0.94 ± 0.31	> 0.05
Albuminuria	2.6 ± 0.94	0 ± 0.00	0 ± 0.00	< 0.05

This was partially in concordance with Shammas and Maayah, 2000, who showed that serum urea and creatinine levels were not significantly affected in pre-eclampsia and in pregnancy induced hypertension. They also concluded that the risk of development of chronic hypertension 10 years after pregnancy complicated by pre-eclampsia and pregnancy induced hypertension is increased and this is closely related to residual renal disorder.

As regards liver function tests, statistically significant differences was found between different groups in the levels of liver enzymes (AST, ALT, ALP). It was higher in the pregnant group with hypertension more than the pregnant group without hypertension. The total bilirubin and coagulation profile showed no statistically significant difference between the different groups (table 3).

Serum values for liver function tests are usually low in normal pregnancy. Possible mechanisms are via a dilution effect as a result of the expanded plasma volume of pregnancy, an increase in hepatic blood flow or reduced function of the enzymes (and therefore reduced release) (Kenyon and Shennan, 2004). So an increase in serum ALT, AST and GGT activities and serum bilirubin during pregnancy may be pathologic

and should prompt further evaluation (Angel García Alonso, 2006).

Serum albumin level was significantly lower in the group of patients with pregnancy induced hypertension and this may be due to loss of albumin in urine or impaired liver functions.

A study conducted by Demir et al., 2006, concluded that the most important biochemical marker for maternal mortality is bilirubin levels. Maternal mortality was statistically higher in cases with jaundice. In our study there was no elevation in serum bilirubin .

In our study we found that there was statistically significant difference between different groups as regards liver span, however there was no statistically significant difference between different groups as regards PV caliber (table 4). Also there was statistically significant difference between different groups as regards liver echogenicity (table 4).

Table (4): Abdominal ultrasonography among examined groups

Data \ Group		PIH (N= 20)	Late normal pregnancy (N= 20)	Control (N= 20)	*p* - value
Liver span		16.51 ± 1.3	14 ± 1.9	13.15 ± 1.9	< 0.05
PV caliber		0.92 ± 0.17	0.91 ± 0.17	0.79 ± 0.18	> 0.05
Liver	Normal	2 10%	14 70%	20 100	
	Diffuse pathology	14 70%	2 10%	0 0	
	Periportal halo sign	4 20%	4 20%	0 0	< 0.05
Gall Bladder	Normal	8 40%	20 100%	20 100	
	Thick wall	12 60%	0 0	0 0	
	Stones	1 5%	0 0	0 0	< 0.05

In this study we found that there was a statistically significant difference between different groups as regards gall bladder abnormalities in abdominal ultrasonography (thick gall bladder wall in 12 women with pregnancy induced hypertension and gall bladder stone in 1 women with pregnancy induced hypertension) **(table 4).**

That result was concomitant with a prospective study of 3254 women who underwent serial ultrasound examination during pregnancy. It was found that stones or sludge were present in 5 and 8 percent of women by the second and third trimesters, respectively, and 10 percent of women by four to six weeks postpartum. Regression of sludge and stones was common in the post-partum period.

From this study we concluded that liver function tests and abdominal ultrasonography are important tools to detect hepatic dysfunction in women with pregnancy induced hypertension.

Large scale prospective study is recommended for studying any possible correlation between abnormal liver function tests in patients with pregnancy induced hypertension and abnormal sonographic findings.

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