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Investigation of liver function tests (LFTs) and renal function tests (RFTs) in pregnant women affected with hypertensive disorders of pregnancy (HDP)

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Abstract

Hypertensive disorders of pregnancy (HDP) are major health burdens in obstetric population and almost 12-22% pregnancies are affected by HDP in the world. In patients with HDP, liver and renal functions abnormality can negatively affect both maternal and fetal health. The present study was performed to compare changes of liver and renal functions in pregnant women suffering with hypertensive disorders. Blood samples of 200 patients who attended the Holy Family Hospital, Rawalpindi were collected randomly and were checked for LFTs and RFTs. Automated chemical analyzer (Beckmann Colter or Selectra) was used; some samples were also quantified by Microlab-300 manually. Out of these 200 patients, 90 (45%), 59 (29.5%),16 (8%), 11 (5.5%) and 24 (12%) women were diagnosed with the Gestational HTN, Pre-eclampsia, Chronic HTN, Pre-eclampsia superimposed on Chronic HTN and Eclampsia respectively. Total bilirubin, ALT and ALP were increased in 60 (30%), 59 (29.5%) and 85 (42.5%) samples respectively while urea, creatinine and uric acid were increased in 46 (23%), 49 (24.5%) and 91 (45.5%) patients, respectively. Almost 75% patients had 31-40 weeks gestational period, 83% patients had no pre- history and 73% had no family history. Almost, 95 % HDP patients were between 17-40 years. Mortality and morbidity rate is higher in developing countries including Pakistan. So, it is recommended to perform the regular examination of LFTs and RFTs in the HDP patients because early diagnosis and treatment can eradicate the risk of mortality of mother and fetus.

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Introduction

Globally, hypertensive disorders of pregnancy (HDP) are one of the leading causes of morbidity and mortality in obstetric population, especially in lower and middle income countries (Say *et al.*, 2014). It is a major health burden related to pregnancy disorders and ranges from pre-eclampsia/eclampsia (PE/E), gestational hypertension, chronic hypertension (CH) and chronic hypertension superimposed pre-eclampsia. Each category has a different pathophysiology and feto-maternal consequences. The overall worldwide incidence is between 12-22% (Hutcheon *et al.*, 2011). In Pakistan its prevalence is quite common about 9% (Jan *et al.*, 2012) and it is one of the leading causes of stillbirth in pregnant women with hypertensive disorders (Shamsi *et al.,* 2010). HDP characterized as a group of disorders which are linked with raised blood pressure during pregnancy. In pregnancy, if blood pressure is more than 140/90 mm Hg along with other complications then expecting female is suspected of having any HDP. Etiology of HDP is still indefinable (Lindheimer *et al.*, 2008). However, a number of risk factors have been recognized, including maternal age, increased inter-pregnancy interval, obesity, family history of hypertension in the mother (Rodriguez *et al.,* 2010), twin gestation, bacterial and viral infections, underlying vascular disorders like diabetes mellitus and antiphospholipid syndrome (Sliwa and Böhm, 2014). Hypertensive disorders during pregnancy are classified into four categories including: gestational hypertension, chronic hypertension, preeclampsia and eclampsia (Brown *et al.,* 2009). Clinical demonstration of HDP is described primarily by hypertension and in some of the cases edema can be present (Kuklina *et al*, 2009). Swelling or edema (especially in the hands and face) was originally considered an important sign for a diagnosis of pre-eclampsia (Young *et al.*, 2010) but in current medical practice only hypertension and proteinuria are necessary for a diagnosis. Typically, the pregnant woman develops hypertension and proteinuria before the onset of a convulsion which is a hallmark of eclampsia. Other cerebral signs may immediately precede the convulsion, such as nausea, vomiting, headaches, and cortical blindness (Rodriguez *et al.,* 2010). If HDP is remained untreated then it may lead to abdominal pain, jaundice, shortness of breath and diminished urine output. Intrauterine fetus growth retardation, placental bleeding and placental abruption may also occur as a result of HDP complications (Lindheimer *et al.*, 2009). For the diagnosis various tests (i.e. blood pressure, liver functions test and renal function tests) are performed as HDP is related to many other disorders (Magee *et al.,* 2014). In HDP, liver and renal functions can be disturbed as it is a multi-disorder disease which results into the abnormal liver function tests (LFTs) and renal function tests (RFTs). About 20%-30% pregnancies with HDP have shown abnormal LFTs. Renal function tests are also seen to be elevated in HDP and especially in preeclampsia (Mammaro *et al.,* 2009). Studies have been done to check the association of HDP with LFTs and RFTs but still further research is required to assess the progress and severity of disease with better understanding (Tayrab and Saladdin, 2016).

The aim of current study was to evaluate and compare liver and renal function tests in pregnant women with HDP with normal pregnancy.

Materials and methods

Study design, settings, duration and sampling

It was a descriptive study which was conducted at the settings of gynaecology department of Holy Family Hospital, Rawalpindi. The present study was carried out from September 2017 to December 2017 and a total of 200 samples were included in this study.

Sample selection

Inclusion criteria: Patients of gynaecology department of Holy Family Hospital were included in this study. Pregnant women diagnosed with hypertensive disorders of pregnancy were included in the study.

Exclusion criteria: All patients other than the gynaecology department of Holy Family Hospital were excluded from this study. Non-pregnant women

were excluded from this study.

Data collection methods and tools

Data was collected by using a structural interviewing questionnaire, which was designed to collect and maintain all valuable information from the cases after filling the informed consent.

Materials required for sampling

Gloves, mask, tourniquet, antiseptic solution, 5ml disposable syringe, gel and clot activator tube, cotton.

Sample collection

First of all, asked the patients full name and matched these against requisition form. Checked the requisition form for requested tests, evaluated the patient information and any other special draw requirements. Then tubes and supplies were assembled which were needed for sample collection. Positioned the patient in a chair, or sitting or lying on a bed. Before sample collection hand was washed and gloves on. A suitable site for venipuncture was selected by placing the tourniquet 3 to 4 inches above the puncture site. Careful measures were adopted and did not put the tourniquet on too tightly or left it on the patient longer than 1 minute. Disinfected the sampling site on the patient with 70% alcohol and allowed it to dry. Inserted the needle into the vein and withdrew blood until required quantity of blood was obtained. Withdraw piston carefully as too forcefully it could collapse the vein. Once the needle has entered into vein the tourniquet was released. Placed cotton immediately on the puncture site. Applied and held adequate pressure to avoid formation of hematoma. Then 3-5 ml of blood was transferred in gel or clot activator tube for the estimation of LFTs and RFTs. Labeled the sample accordingly and delivered it to the lab.

Sample transportation

Sample was transported immediately to the lab without any further delay. In case of delay, serum was stored at -20 ˚C.

Sample processing

Serum was used for the estimation of LFTs and RFTs. The sample preparation was done by the method of centrifugation at 3000 rpm for 10 minutes. All samples were processed on Beckmann Coulter or Selectra depending upon their availability of LFTs and RFTs estimation respectively.

Results

Distribution of patients according to type of HDP

A total of 200 blood samples were included in this study. These 200 samples were collected from the pregnant women with Hypertensive Disorders of Pregnancy. Of these 200 samples, 90 (45%) were of women with Gestational HTN, 59 (29.5%) were of women with Pre-eclampsia, 16 (8%) women had Chronic HTN, 11 (5.5%) women had Pre-eclampsia superimposed on Chronic HTN and 24 (12%) women had Eclampsia. Distribution of patients according to type of HDP can be seen in Table 1.

Table 1. Distribution of patients according to type of HDP.

Type of HDP	Number	Percent
Gestational HTN	90	45%
Pre-eclampsia	59	29.5%
Chronic HTN	16	8%
Pre-eclampsia superimposed on CH	11	5.5%
Eclampsia	24	12%
Total	200	100%

Distribution of patients according to age

Age group of patients in this study ranged between 17 to 45 yrs. A maximum number of patients (82) fell in the 24-30 years range, followed by 67 patients in the 31-37 years range. There were 19 patients who fell in 38-45 years range and 32 patients fell in 17-23 years range. Details of age distribution can be seen in Table 2.

Table 2. Age distribution of the patients.

Years	17-23 Years	24-30 Years	31-37 Years	38-45 Years	Total
No. of patients	32(16%)	82(41%)	67(33.5%)	19(9.5%)	200(100%)

Table 3. Distribution of patients according to Gestational Week.

Gestational Weeks	11-20 Weeks	21-30 Weeks	31-40 Weeks	Total
No. of patients	16(8%)	35(17.5%)	149(74.5%)	200(100%)

Distribution of patients according to Gestational Week

In this study, patient's gestational week ranged between 11-40 weeks of gestation because of different types of HDP. In chronic HTN gestational week should be less than 20 weeks so some of the values fell in that range. A maximum number of patients fell in the 30-40 weeks range because of the patients had pre-eclampsia, eclampsia and gestational HTN. 35 patients fell in the 21-30 weeks range. Only 16 patients fell in the 11-20 weeks range because less than 20 weeks are in chronic HTN only. Details can be seen in Table 3.

Table 4. Evaluation of Total Bilirubin in HDP.

Type of HDP	T.BIL (Raised)	T.BIL (Normal)	Total
Gestational HTN	20 (22.23%)	70 (77.77%)	90 (100%)
Pre-eclampsia	23 (38.99%)	36 (61.01%)	59 (100%)
PE imposed on CH	3 (27.28%)	8 (72.72%)	11 (100%)
Chronic HTN	3 (18.75%)	13 (81.25%)	16 (100%)
Eclampsia	11 (45.83%)	13 (54.17%)	24 (100%)

Table 5. Evaluation of ALT in HDP.

Type of HDP	ALT (Raised)	ALT (Normal)	Total
Gestational HTN	12 (13.33%)	78 (86.67%)	90 (100%)
Pre-eclampsia	20 (33.90%)	39 (66.10%)	59 (100%)
PE imposed on CH	2 (18.19%)	9 (81.81%)	11 (100%)
Chronic HTN	6 (37.5%)	10 (62.5%)	16 (100%)
Eclampsia	19 (79.16%)	5 (20.83%)	24 (100%)

Hypertensive history of patients

Hypertension is most important in this study and patients who had severe pre-eclampsia and eclampsia had increased blood pressure which caused complications while patients with gestational hypertension had a bit lower blood pressure range. 200 patients were included in this study and the HTN range was different in different patients.

About 34 patients were included in 130/100 mmHg that count for 17% of total. About 36 patients were included in 160-180/100-120 mmHg range and it comprised 18% of the total and that much high blood pressure was mainly present in eclampsia and a little bit in pre-eclampsia patients. And the remaining 130 patients were included in 140-150/90-110 mmHg range and almost 65% patients were present in this range which was most abundant of all other ranges. In this study, about 16% of the patients had a previous hypertensive history and out of which 23% of the patients had pre-eclampsia. Details of history of hypertensive patients are given in Fig. 1.

Table 6. Evaluation of ALP in HDP.

Type of HDP	ALP (Raised)	ALP (Normal)	Total
Gestational HTN	27 (30%)	63 (70%)	90 (100%)
Pre-eclampsia	29 (49.15%)	30 (50.85%)	59 (100%)
PE imposed on CH	6 (54.55%)	5 (45.45%)	11 (100%)
Chronic HTN	7 (43.75%)	9 (56.25%)	16 (100%)
Eclampsia	16 (66.66%)	8 (33.34%)	24 (100%)

Table 7. Evaluation of Urea in HDP.

Type of HDP	Urea (Raised)	Urea (Normal)	Total
Gestational HTN	6 (6.67%)	84 (93.33%)	90 (100%)
Pre-eclampsia	12 (20.33%)	47 (79.67%)	59 (100%)
PE imposed on CH	4 (36.37%)	7 (63.63%)	11 (100%)
Chronic HTN	4 (25%)	12 (75%)	16 (100%)
Eclampsia	20 (83.33%)	4 (16.67%)	24 (100%)

In this study, about 27% of the patients had family history of hypertension. Mother, father or any other close relative were affected by hypertension. Details of family history are given in Fig. 2.

Evaluation of liver functions tests (LFTs)

LFTs in patients with hypertensive disorders of pregnancy were raised especially in pre-eclampsia and eclampsia and were quite normal in gestational hypertension and others.

Total bilirubin, ALT and ALP were increased in 60 (30%), 59 (29.5%) and 85 (42.5%) samples respectively. Results have shown in Tables 4, 5 and 6.

Table 8. Evaluation of Creatinine in HDP.

Type of HDP	Creat. (Raised)	Creat. (Normal)	Total
Gestational HTN	17 (25.56%)	67 (74.44%)	90 (100%)
Pre-eclampsia	19 (32.2%)	40 (67.80%)	59 (100%)
PE imposed on CH	2 (18.19%)	9 (81.81%)	11 (100%)
Chronic HTN	2 (12.5%)	14 (87.5%)	16 (100%)
Eclampsia	9 (37.5%)	15 (62.5%)	24 (100%)

Evaluation of Renal functions tests (RFTs)

The renal function test in patients with hypertensive disorders of pregnancy were slightly raised especially in pre-eclampsia and eclampsia and were quite normal in gestational hypertension and others. Uric Acid was raised most. Results have shown in Tables 7, 8 and 9.

Table 9. Evaluation of Uric Acid in HDP.

Type of HDP	U.A (Raised)	U.A (Normal)	Total
Gestational HTN	29 (32.22%)	61 (67.78%)	90 (100%)
Pre-eclampsia	25 (42.37%)	34 (57.63%)	59 (100%)
PE imposed on CH	8 (72.73%)	3 (27.27%)	11 (100%)
Chronic HTN	5 (31.25%)	11 (68.75%)	16 (100%)
Eclampsia	24 (100%)	0 (0%)	24 (100%)

Discussion

There are many studies conducted on specific causes of abnormal LFTs and RFTs in pre-eclampsia or gestational hypertension but little work is documented on testing and evaluation of LFTs and RFTs in hypertensive disorders of pregnancy. Thus, the purpose of the present study was to evaluate LFTs and RFTs in HDP and to examine the normal and raised the values of ALT, ALP, total bilirubin, urea, creatinine and uric acid in many types of hypertensive disorder of pregnancy.

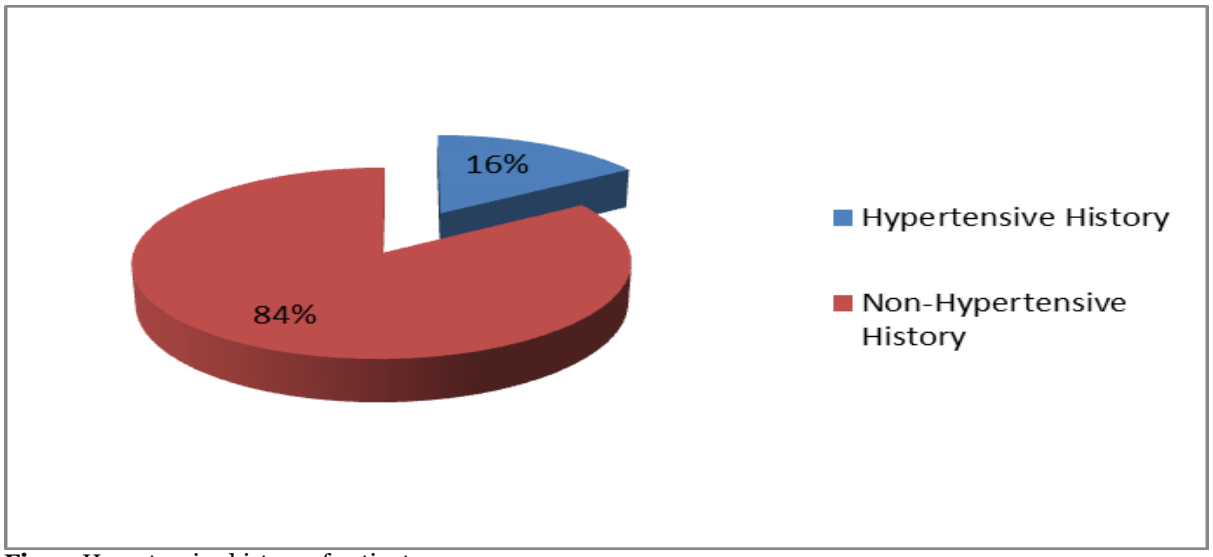

Fig. 1. Hypertensive history of patients.

An investigation has shown that there is a correlation between the hypertensive disorder of pregnancy and age (Sibai and Stella, 2009). In current study the most women was within 24-30 years, including 17-45 years of age range and there was gestational hypertension in 45% females, pre-eclampsia in 29.5%, CH in 8%, PE superimposed on CH in 5.5% and 12% are with eclampsia. There are 27% females with a family history of HTN, 16% women with a previous history of hypertension and gestational week was between 11-40 weeks of gestation. As compared to other renal function tests, uric acid was found to be elevated in many women with HDP (Bainbridge and Roberts, 2008). In LFTs, the ALP, ALT and total bilirubin was raised in women with HDP (Lee and Brady, 2009).

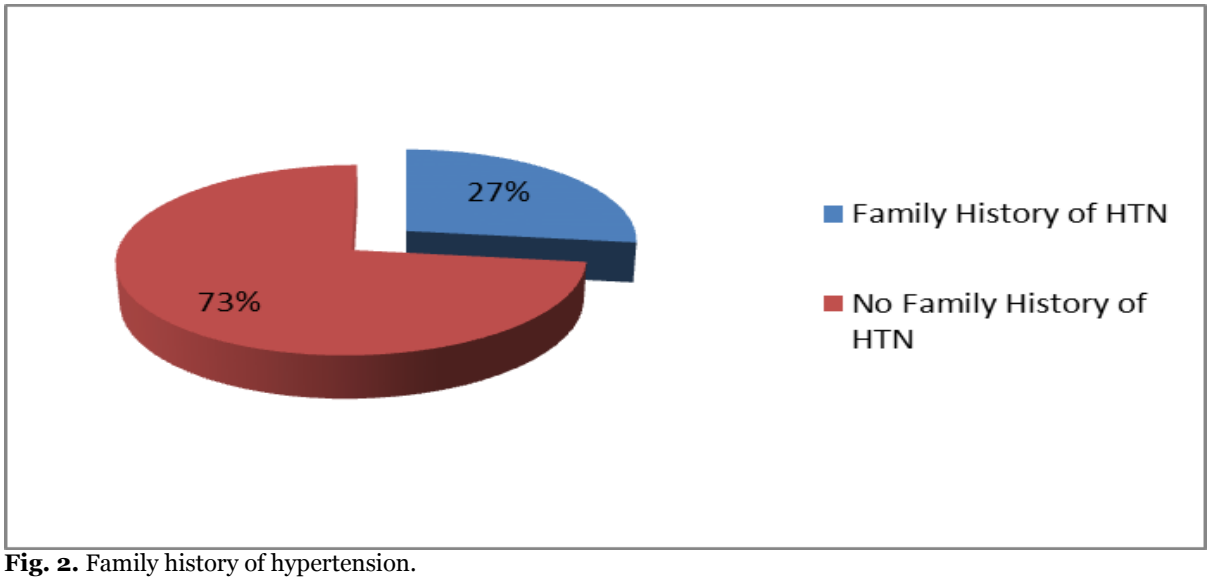

Fig. 2. Family history of hypertension.

The incidence of pregnancy induced hypertension and prescription pattern of antihypertensive drugs in pregnancy showed that highest incidence of hypertension was occurred in the age group of 18-22 years (41.3%) with the overall occurrence of hypertensive disorder in pregnancy was 7.8% and prevalence of pre-eclampsia, eclampsia, gestational hypertension and chronic hypertension were 5.6 %, 0.60%, 1.5% and 0.15 % respectively. The results were in accordance with our study as 41% patients in the 24-30 years range group and the frequency of gestational HTN, pre-eclampsia, chronic HTN and eclampsia were 45%, 29.5%, 8% and 12% respectively (Sajith *et al.*, 2014).

A study on alteration of LFTs and RFTs in pre-eclampsia showed that ALT, AST, serum bilirubin and alkaline phosphatase levels were elevated with more proteinuria among patients with pre-eclampsia and eclampsia. In their study ALT, AST, bilirubin and alkaline phosphatase were elevated in 23(48.93%), 15 (31.91%), 6(12.7%) and 12 (25.53%) patients respectively. These results were in accordance with current study as results showed the elevated levels of ALT, total bilirubin and ALP in 59 (29.5%), 60 (30%) and 85 (42.5%) samples respectively (Bhowmik *et al.*, 2013).

Another study on serum uric acid levels in pre-eclampsia has exhibited that the observed mean serum uric acid levels in preeclampsia was 7.52±0.77 mg/dl as compared to 3.70±0.94 mg/dl in controls and the results were similar to our study as the levels of uric acid were elevated in HDP patients (Sirajwala *et al.*, 2013). An investigation was conducted on biochemical assessment of renal and liver function among preeclamptics in Lagos Metropolis which supported our research findings. They concluded that preeclampsia has deleterious effects on renal and liver function due to the high level of urea, uric acid, creatinine, serum ALT, AST, alanine aminotransferases and other biomarkers of renal function test (Ekun *et al.*, 2018). Our study results were similar to another prospective study done on liver function tests in hypertensive disorders of pregnancy and the results of this research concluded that severe pre-eclampsia was seen in younger age group <25 years and 50 pregnant women with 28-40 weeks of gestation with diastolic BP≥110 mm Hg recorded 6 hours apart. The severe pre-eclampsia incidence was 78% in overall cases and 88% in patients with raised LFTs. The raised LFTs levels were reported in 28% of the cases with renal complications were evaluated in 16% of the total cases (Sirajwala *et al.*, 2013).

Conclusion

Both the diastolic and systolic blood pressure increases in women with hypertensive disorder of pregnancy. Almost 75% patients had 31-40 weeks gestational period, 83% patients had no pre- history and 73% had no family history. Almost, 95 % HDP patients were between 17-40 years. This may be due to the fact that people prefer to take babies before 40 years. Mortality and morbidity rate is higher in developing countries including Pakistan. Hence, it is recommended to perform the regular examination of LFTs and RFTs in the HDP patients to curtail the risk of mortality of mother and fetus.

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Conflict of interest

There is no conflict of interest among authors.

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