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Original Article

Obstetrics and Gynaecology Section

Liver Disorders in Pregnancy- A Retrospective Study

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ABSTRACT

Introduction: Liver disorders associated with pregnancy are important medical disorders that carries grave prognosis and challenging for both obstetricians and hepatologists. It affects about 3% of pregnancies worldwide and about 3-5% pregnancies in India. It can present with various symptoms like yellowish discolouration of sclera, dark coloured urine, anorexia, nausea, vomiting, abdominal pain etc. The liver disorders unique to pregnancy includes-hyperemesis gravidarum, preeclampsia, eclampsia with liver dysfunction, Haemolysis, Elevated Liver enzymes, Low Platelet count (HELLP) syndrome, Intrahepatic Cholestasis of Pregnancy (IHCP) and acute fatty liver of pregnancy.

Aim: To evaluate demographic variables, causes of liver dysfunction during pregnancy and foeto-maternal outcome of pregnancies complicated by jaundice and liver dysfunction.

Materials and Methods: This was a retrospective hospital based observational study on the pregnant women admitted with jaundice or any liver disorders in Department of Obstetrics and Gynaecology in Rajendra Institute of Medical Sciences, Ranchi, Jharkhand, India, over a period of one year from March 2018 to February 2019. The incidence of liver disorders in pregnancy, its causes, the foetal outcome in terms of preterm birth, stillbirth, Foetal Growth Restriction (FGR) and Intrauterine Foetal Death (IUFD), the maternal outcome in terms of mode of delivery, complications, need for Intensive Care Unit admissions and maternal mortality were evaluated. Descriptive statistics like percentage and mean calculation were used to interpret the data.

Results: Out of 8264 obstetrics admissions, 126 had liver disorder in pregnancy, incidence being 1.52%. Total 87 (69%) cases were primigravida, 115 (91.3%) cases presented during 3rd trimester of pregnancy, 101 (80.1%) were unbooked for our institution. A total of 92 (73%) were referred to us. Preeclampsia, eclampsia, HELLP syndrome was the most common cause of liver dysfunction accounting for 46.8% followed by IHCP in 31 (24.6%) cases. Out of 126, 115 women admitted in labour, of which 75 (65.3%) delivered vaginally, 38 (33%) taken for caesarean section and two died undelivered. Nine cases were admitted in 1st trimester and two cases in second trimester who did not turn up after discharge. Neonatal mortality was seen in 18 (15.6%).

Conclusion: Liver dysfunction in pregnancy carries grave prognosis with high incidence of perinatal and maternal morbidity and mortality. This study emphasises the need for regular Antenatal Care (ANC), need to remain vigilant for preventable causes like haemolytic jaundice, early diagnosis, proper treatment and timely referral of liver disorders with pregnancy to prevent the complications and improve foetal and maternal outcome.

Keywords: Acute fatty liver of pregnancy, Foetal outcome, Intrahepatic cholestasis of pregnancy, Jaundice, Liver dysfunction

INTRODUCTION

During pregnancy, many physiological changes occur in various organs, including liver. Liver receives 25-35% of cardiac output which remains same in pregnancy but the hormonal and immunological changes unique to pregnancy not only alter the course of liver disease but may also affect the foetal and maternal outcome [1]. Changes like rise in oestrogen affect the metabolic, synthetic and excretory functions of liver that may lead to obstetric cholestasis or gallstones. Other changes seen in liver parameters during pregnancy are lowering of serum albumin and bilirubin due to haemodilution [2,3]. Serum Glutamic Oxaloacetic Transaminase (SGOT) and Serum Glutamic Pyruvic Transaminase (SGPT) remains within normal limit but may increase normally during labour probably due to leakage from contracting uterine muscles. Alkaline Phosphatase (ALP) activity increases in third trimester secondary to increase secretion of placental ALP and increased maternal bone marrow turnover [3-5]. More than or equal to twice the rise in level of SGOT and SGPT suggest hepatocellular injury while rise in Gamma Glutamyl Transferase (GGT) and ALP suggest cholestasis, but serum ALP is not a reliable test for assessment of cholestasis in third trimester of pregnancy [1].

Liver diseases complicate upto 3% of pregnancies. It can be classified in three categories:

1. Specifically related to pregnancy
   - IHCP, Acute fatty liver of pregnancy, Hyperemesis gravidarum, HELLP (Haemolysis, Elevated Liver enzyme, Low Platelet count) syndrome and Preeclampsia
2. Co-incidental to pregnancy
   - Acute viral hepatitis- A,B,C,D,E, Gallstones.
3. Chronic liver disease that predate pregnancy.
   - Chronic hepatitis, Cirrhosis, Esophageal varices, Wilson disease [6].

Liver disorders during pregnancy carry a grave prognosis which adversely affects the foeto-maternal outcome especially in developing countries like India. It accounts for 14% of maternal mortality and 60% of perinatal mortality [7]. It is also, a diagnostic challenge for both obstetricians and hepatologists.

Advances in understanding the pathophysiological mechanism, diagnostic tool and management of liver disorder unique to pregnancy have resulted in a significant improvement in the outcome of both mother and the foetus [8]. Clinical presentation of various liver diseases is very non specific. There is very limited data on liver disorders in pregnancy in tribal dominant state of Jharkhand. So, there is need for study, to bring out data not only about the magnitude of problem in this region but also to analyse the demographic variables, its causes and to assess the foetal and maternal outcome in pregnancies complicating with liver disorders. The objective of this study was to evaluate demographic variables

along with the causes of liver dysfunction during pregnancy and also the feto-maternal outcome of pregnancies complicated by jaundice and liver dysfunction.

MATERIALS AND METHODS

This was a retrospective observational study, carried out in a tertiary care centre, in Department of Obstetrics and Gynaecology of Rajendra Institute of Medical Sciences (RIMS), in Ranchi, Jharkhand, India, on the basis of patients data, who were admitted during one year period, from March 2018 to February 2019. Approval for the study taken from Institutional Ethical Committee (IEC No. 389). Total 8264 obstetrics admissions were there during this period, out of which 126 cases were diagnosed as pregnancy with liver disorder. Data of these patients were collected and analysed in March and April 2019.

Inclusion criteria: All pregnant women admitted and diagnosed with jaundice and/or liver dysfunctions admitted in RIMS, Ranchi, through Outpatient Department (OPD) or emergency ward were included.

Exclusion criteria: Pregnant women who left against medical advice. Postpartum women admitted with jaundice or liver disorders were excluded in this study.

Study Procedure

Data was obtained from labour room records and medical record department. The incidence of liver disorders in pregnancy, its causes, demographic variables like age, parity, gestational age, booking status, referral, the presenting sign and symptoms, parameters of Liver Function Test (LFT) in terms of serum SGOT, SGPT, ALP, serum bilirubin, serum protein, the foetal outcome in terms of preterm birth, stillbirth, FGR and IUFD, neonatal death, the maternal outcome in terms of mode of delivery, complications, need for ICU admissions and maternal mortality were evaluated. The cases of HELLP syndrome were classified as per Mississippi classification on the basis of platelet count [1].

STATISTICAL ANALYSIS

Proper template for data entry was generated on MS Excel to enter the data. Descriptive statistics like percentage and mean calculation were used to interpret the data by using Microsoft 2007.

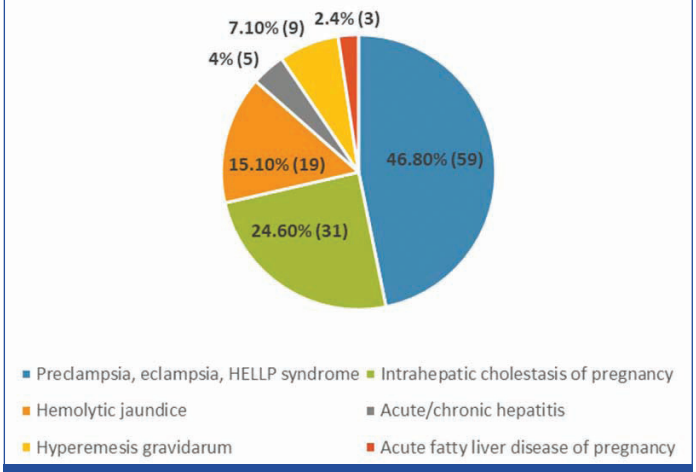
RESULTS

During the study period, there were 8264 obstetric admissions, out of which 126 were diagnosed as pregnancy with liver disorders on the basis of clinical features and laboratory investigations, thus the magnitude of problem comes out to be 1.52%. As shown in [Table/Fig-1] of demographic variables, 65 (51.6%) cases out of 126 were between 20-30 years of age group, the mean age was 24.4 years and standard deviation was 5.3. Most cases, 102 (81%) were Hindu, 87 (69%) women were primigravida and 101 (80.1%) had not received minimum 3 antenatal check-ups and were unbooked at the institute. About 100 (79.4%) patients were term while 17 (13.5%) were preterm (15 delivered among preterm). Total 9 (7.1%) came in first trimester with hyperemesis gravidarum, were managed but did not deliver here.

As depicted in [Table/Fig-2], the most common aetiology for liver disorders in this study was preeclampsia, eclampsia and HELLP syndrome accounting for 59 (46.8%) cases. Out of 59 cases of preeclampsia, eclampsia and HELLP syndrome, 21 cases were in HELLP syndrome and on the basis of platelet count 15 were in class 2 of Mississippi classification [1]. Second most common cause of liver disorders in pregnancy was IHCP, 31 (24.6%). Haemolytic jaundice due to malaria and haemoglobinopathy was present in 19 (15.1%) cases. Hepatitis was seen in only 5 (4%) cases, and all were Hepatitis B positive with one patient having very high level of HBeAg. The least common cause was acute fatty liver of pregnancy, 3 (2.4%).

Variables		Number of cases (N=126)	Percentage (%)
Age (years)	<20	40	31.8%
	20-30	65	51.6%
	>30	21	16.6%
Mean age±SD (years)		24.4±5.35	
Religion	Hindu	102	81%
	Muslim	22	17.4%
	Christian	02	1.6%
Residence	Urban	31	24.6%
	Rural	95	75.4%
Socio-economic status	Low	86	68.2%
	Middle	38	30.2%
	Upper	02	1.6%
Parity	Primi	87	69%
	Multi	39	31%
Booking status	Booked	25	19.9%
	Unbooked	101	80.1%
Gestational age at time of admission	Term	100	79.4%
	Preterm	17*	13.5%
	First trimester	09	7.1%
Referral cases	-	92	73%

[Table/Fig-1]: Demographic variables.
*2 cases in second trimester included in preterm



[Table/Fig-2]: Aetiology (causes of liver disorders).

The signs and symptoms of the patients are described in [Table/Fig-3], jaundice being the most common symptom in 78 (61.9%) cases. A 31 (24.6%) presented with pruritis, diagnosed as IHCP. Pallor is the most common sign observed. One patient came unconscious in state of hepatic encephalopathy.

Symptoms	No. of cases (N=126)	Percentage (%)
Jaundice	78	61.9%
Nausea, vomiting, anorexia	23	18.3%
Pruritis	31	24.6%
Fever	56	44.4%
Pain in right hypochondrium	23	18.2%
Signs		
Pallor (moderate, severe)	64	50.8%
Oedema	46	36.5%
Ascites	07	5.55%
Hepatomegaly	04	3.2%
Unconscious	01	0.8%

[Table/Fig-3]: Sign and symptoms.

Alkaline phosphatase found >400 units in 71 (56.4%) patients, in all cases of IHCP [Table/Fig-4,5].

Parameters	Levels	No. of cases (N=126)	Percentage (%)
Serum bilirubin (mg/dL)	<10 mg/dL	102	81%
	>10 mg/dL	24	19%
SGOT (U/L)	<200 U/L	58	46%
	>200 U/L	68	54%
SGPT (U/L)	<200 U/L	72	57.2%
	>200 U/L	54	42.8%
ALP (U/L)	<400 U/L	55	43.6%
	>400 U/L	71	56.4%
Serum total protein (mg/dL)	6-8 mg/dL	13	10.3%
	4-5.9 mg/dL	110	87.3%
	<4 mg/dL	3	2.4%

[Table/Fig-4]: LFT parameters.

Parameters	Preec-lampsia eclampsia HELLP (n=59)	IHCP (n=31)	Haemolytic jaundice (n=19)	Acute/ Chronic hepatitis (n=5)	AFLP (n=3)	Hyper-emesis gravidarum (n=9)
Serum bilirubin >10 mg/dL	7 (11.9%)	-	15 (78.9%)	1 (20%)	1 (33.3%)	-
SGOT >200 U/L	32 (54.2%)	14 (45.2%)	15 (78.9%)	3 (60%)	3 (100%)	1 (11.1%)
SGPT >200 U/L	31 (52.5%)	7 (22.5%)	9 (47.4%)	3 (60%)	3 (100%)	1 (11.1%)
ALP >400 U/L	28 (47.4%)	31 (100%)	7 (36.8%)	2 (40%)	3 (100%)	-

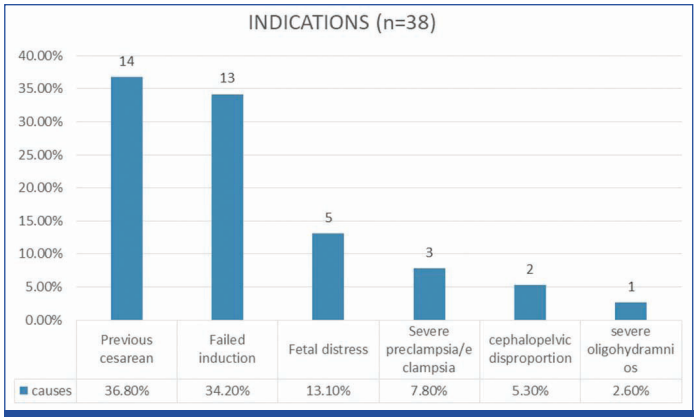
[Table/Fig-5]: Liver parameters in respective causes.

As shown in [Table/Fig-6], Out of 126 cases, 113 delivered in the institution (nine cases in first trimester while 2 in second trimester <26 weeks were managed for hyperemesis gravidarum and IHCP respectively, did not deliver in our institution). A 36 (28.6%) patients needed ICU admission and 11 (8.7%) went on ventilatory support. Blood and blood product transfusion was required in 95 (75.4%) cases as the patients with jaundice are more susceptible for Postpartum haemorrhage (PPH). A 9 (7.8%) mothers died out of 115, two cases due to each Disseminated Intravascular Coagulation (DIC), shock after PPH and Multi-organ Dysfunction Syndrome (MODS), and one case due to each hepatic encephalopathy, pulmonary oedema and pulmonary embolism in sickle cell anaemia.

Mode of delivery	No. of cases (n=115)	Percentage (%)
Vaginal	75	65.3%
LSCS	38	33%
Undelivered	2	1.7%
Morbidities	**No. of cases**	**Percentage (%)**
PPH	17 (n=113)*	15%
ICU admission	36 (n=126)	28.6%
Ventilatory support	11 (n=126)	8.7%
Transferred to medicine department after delivery	11 (n=126)	8.7%
Needed blood and blood products	95 (n=126)	75.4%
Maternal mortality	9 (n=115)	7.8%

[Table/Fig-6]: Maternal outcome.

Most cases 75 (65.3%) had vaginal delivery, 38 (33%) underwent Lower Segment Caesarean Section (LSCS), most common indication being previous caesarean section followed by failed induction, as depicted in [Table/Fig-7]. Two cases (1.7%) patients died undelivered.



[Table/Fig-7]: Indication of caesarean section.

The [Table/Fig-8] shows the foetal outcome, 85 (74%) babies born alive. Twenty one (18.2%) babies died in utero, among which 2 remain undelivered. Nine (7.8%) were stillborn and same was the incidence of Intra-Uterine Growth Retardation (IUGR) babies. Forty one (35.6%) babies required NICU admission. Eighteen (15.6%) neonatal death recorded.

Outcome	No. of cases	Percentage (%)
Live birth	85	74%
IUFD	21	18.2%
Stillbirth	9	7.8%
FGR	9	7.8%
NICU admission	41	35.6%
Neonatal death	18	15.6%

[Table/Fig-8]: Foetal outcome.
Number of cases may be overlapping between different outcomes presented.
IUFD: Intrauterine foetal death; FGR: Foetal growth restriction; NICU: Newborn intensive care unit

DISCUSSION

Liver disorder in pregnancy may range from mild clinical presentation like constitutional symptoms to severe changes in liver function test and can be fatal for mother and fetus both. Its incidence has decreased from past due to better understanding of physiological changes in pregnancy, early recognition and timely management of the patients [9-11].

The magnitude of problem in present study was 1.52%. The incidences recorded in other studies held in different regions of India ranges from 0.22-2.37% [Table/Fig-9] [8,9,12-15].

Author name	Incidence of liver disorder
Tiwari A et al., study [8]	2.37%
Vinayachandran SN et al., [9]	0.22%
Acharya N et al., [12]	0.4%
Jyothi GS et al., [13]	2.32%
Choudhary N et al., [14]	0.28%
Mishra N et al., [15]	0.9%
Present study	1.52%

[Table/Fig-9]: Incidence of liver disorders in pregnancy in published studies [8,9,12-15].

About 51.6% cases in the present study belonged to 20-30 years of age which is comparable with other studies too [7,8]. About 75.4% came from rural population which tallies with the incidence recorded in other studies [7,8]. Around 68.2% belonged to low socio-economic status, which is consistent with the status noted by Jain M and Thaker H and Tiwari A et al., in their studies [7,8]. Also 73% patients were referred from peripheral regions of the state due to lack of adequate management facilities in peripheral areas and also because these patients need delivery and treatment in tertiary care level facilities.

Maximum 69% cases were primigravida and 79.5% were admitted at term gestation which is similar to findings of Tiwari A et al., study [8]. About 91.3% patients presented in 3rd trimester which is almost similar to the incidence recorded in other studies [7,8,15]. Nearly 80.1% patients did not receive a minimum of three antenatal visits. This might be due to illiteracy, lack of knowledge and ignorance regarding importance of ANC for early diagnosis and treatment of complications. Lack of ANC has also been mentioned in other studies [8,15].

The most common aetiology found here is liver involvement in cases of preeclampsia, eclampsia and HELLP syndrome in 46.8% followed by IHCP (24.6%) and least common being acute fatty liver disease of pregnancy in 2.4%. Preeclampsia, eclampsia and HELLP syndrome was also the most common cause observed in studies by Tiwari A et al., Choudhary N et al., in Udaipur and Mishra N et al., in Raipur [8,14,15]. The incidence of HELLP syndrome was reported maximum in Vinayachandran SN et al., study [9]. Acute viral hepatitis and IHCP were observed as the most common causes in some studies [7,12]. This finding is in contrast to the present study where only 5 (4%) patients were admitted with acute hepatitis, all being hepatitis B positive. No cases of hepatitis A, C, D, E found in the present study. Jain M et al., and Mishra N et al., found AFLP in 1.8% and 1.2% of cases respectively which is almost comparable to the present study [7,15]. Around 15.1% patients in present study had haemolytic jaundice due to malaria, sickle cell anaemia and thalassaemia. The high incidence can be explained by the fact that this region had a endemic of malaria and also has high prevalence for haemoglobinopathies. The incidence of jaundice due to haemolysis were 30%, 8.62% and 3.75% in other studies done at different parts of India [12,14,15]. These are preventable causes of jaundice in pregnancy, which can be prevented with regular ANC and early diagnosis and treatment, genetic counselling in cases of haemoglobinopathies, chemoprophylaxis and use of insecticide treated nets, proper sanitation in malaria endemic region. Lack of knowledge and awareness about symptoms of malaria and haemoglobinopathies in low literacy state like Jharkhand has resulted in deficient data. But, in recent times, improved awareness, decentralisation of health facilities, early diagnosis and referral, prompt investigations and improvement in data collection is bringing out the prevalence of various diseases in this region. The high percentage of haemolytic jaundice can be effectively reduced, so the overall incidence of disease and can be improved the foetal and maternal outcome in these cases.

The most common symptom was jaundice (61.9%) followed by pruritis in 24.6% cases. Signs like pallor was found in 50.8%, fever in 44.4%. This observation is compare to the features observed by Choudhary N et al., [14].

Coming to the liver parameters, on comparing with Vinayachandran SN et al., study, here serum bilirubin >10 mg/dL was found in more patient but almost equal to the Jain M et al., study [7,9]. SGOT and SGPT were >200U/L in 54% and 42.8% cases, respectively which is almost one and a half times more than shown in Vinayachandran SN et al., study [9]. ALP >400U found in 56.4% cases. The more the value of ALP, more is the severity of cholestasis, not so precise in 3rd trimester and raised SGOT or SGPT more than twice of normal, point towards more hepatocellular injury. Hypoproteinemia was seen in 89.7% cases which is almost comparable to the same study [9].

On analysing the obstetrical outcome, out of 115, 113 delivered and two died undelivered. Nine patients came in 1st trimester with hyperemesis gravidarum and two in 2nd trimester and not deliver in our institution, so 11 cases excluded from total 126 cases. Out of 115, 65.3% delivered vaginally, which is consistent with the result (65.51%) of study by Choudhary N et al, nearly equal to the values 60% and 55.67% observed by Acharya N et al and Jyothi GS et al in their studies [12-14]. Around 33% pregnant women with liver disorders underwent LSCS which is more than the incidences noted by Acharya N et al., and Choudhary N et al., [12,14]. Jyothi GS et al., showed cesarean section in 44.32% cases which is more than noted in present study [13]. The common indications were previous caesarean pregnancy, followed by failed induction in cases of hypertensive disorder of pregnancy. A 2 (1.7%) patients died undelivered, one due to pulmonary embolism in sickle cell anaemia patient and other due to hepatic encephalopathy. 3.45% cases died undelivered in Choudhary N et al., study [14].

Around 13.5% patients had PPH, which is almost half as seen in Tiwari A et al., study [8]. A 28.6% needed ICU admission which is double of incidence shown by Jyothi GS et al., [13]. Nearly 75.4% needed blood and blood products transfusion which is very high than other study [8]. One patient developed hepatic encephalopathy and three developed DIC, which is very less than the other studies [7,8,13].

There was nine maternal deaths, case fatality rate was 9 (7.8%) out of 115 cases which is similar to that reported by Krishnamoorthy J study (7.8%) and near to Mishra N et al., study [10,15]. Maternal mortality due to liver disorders in pregnancy ranges from 2-18% in different studies done in different parts of India [7-15].

In this study, 74% live birth recorded, was similar to the rate (77.7%) recorded by Jain M et al., study [7]. Live birth was comparatively less (58.75%) in Mishra N et al., and (62%) in Choudhary N et al., but more (87.12%) in Jyothi GS et al., study [13-15]. Still birth (7.8%) is less than mentioned in Jain M et al., and more than in Jyothi GS et al., study [7,13]. Still birth rate depends on the aetiology, maternal condition, vigilance and decision capability of an obstetrician and management by a paediatrician. Here, the incidence of IUFD is 18.2%, which is very less than noted by Mishra N et al., [15]. 35.6% babies were admitted in NICU, near to the values given by Tiwari A et al., (24.47%), Mishra N et al., (27.5%), Jain M et al., (30.9%) and Jyothi GS et al., (38.63%) [7,8,13,15]. Neonatal death in present study is 15.6% which matches with other studies [7,8] but very less in Jyothi GS et al., study [13]. Most of the neonatal deaths were due to birth asphyxia.

Limitation(s)

The duration of this retrospective study is only one year with relatively small data. The foetal and maternal outcome data in terms of mode of delivery, maternal and foetal morbidity and mortality is missing for 11 cases who did not deliver in the institution. We do acknowledge the need for larger studies for robust and more significant data.

CONCLUSION(S)

Liver disorder complicating pregnancy carries a grave prognosis for both the mother and the fetus. This is a clinically important group of disease due to the increased morbidity and mortality of mother and fetus both, hence needs an early diagnosis and coordinated multidisciplinary approach for management involving an obstetrician, hepatologist and paediatrician. The spectrum of disease varies widely, can present with mild symptoms and subtle changes in LFT to severe changes. This study emphasises the need for regular ANC, need to remain vigilant for preventable causes like haemolytic jaundice, early diagnosis, proper treatment and timely referral of liver disorders with pregnancy to prevent the complications and improve foetal and maternal outcome.

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