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RESEARCH ARTICLE

A study of materno-fetal outcomes in cases of jaundice during pregnancy

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ABSTRACT

Objectives: This study aimed to determine clinico-etiological, biochemical factors and materno-fetal outcome in women with jaundice during pregnancy and to study its correlation with jaundice in pregnancy. **Methodology:** A total of 25 pregnant patients with abnormal liver functioning were included in this observational study. Demographics and the detailed clinical history were recorded. The detailed laboratory investigation was carried out to study the complications concerning biochemical parameter. **Results**: HELLP syndrome was the most common aetiology (40%). Decreased levels of hemoglobin observed in 76%, increased total leukocyte count observed in 28% and low platelet count observed in 32% respectively. Among mothers, most common adverse outcome was requirement of emergency lower segment caesarean section (LSCS) (44%). Raised serum total bilirubin level, direct bilirubin level and thrombocytopenia were significantly associated with adverse fetal outcomes (P=0.046, P=0.024, P=0.027 respectively). Maternal outcomes were significantly associated with raised direct bilirubin, raised serum glutamic pyruvic transaminase (SGPT), raised alkaline phosphatase and thrombocytopenia (P=0.034, P=0.010, P=0.023, P=0.001 respectively). **Conclusion**: Hepatic dysfunction during pregnancy is associated with adverse events for both the mother and the fetus.

Keywords: Alanine transaminase, alkaline phosphatase, bilirubin, liver diseases, low birth weight, thrombocytopenia.

Liver diseases during pregnancy presents a distinctive clinical challenge for gynaecologist and herpatologist as they are poorly studied and may lead to materno-fetal complications.[1] The prevalence of liver dysfunction during pregnancies ranges between 3-10%. [2] Jaundice, also referred as hyperbilirubinemia, is presented by accumulation of bile pigments in the skin that results in yellowing mucous membranes and the skin.[3,4] Jaundice in pregnancy may lead to adverse materno-fetal outcomes including perinatal and maternal mortality which accounts for around 60% and 14% respectively.[5] However, it is caused by a number of causes, some related and some coincidental including abnormal liver functioning distinctive to pregnancy, pre-hepatic causes, hepatic causes and post-hepatic causes of jaundice.

Abnormal liver functioning distinctive to pregnancy are HELLP syndrome, pre-eclampsia, acute fatty liver, hyperemesis gravidarum and intrahepatic cholestasis of pregnancy. Pre-hepatic causes including hepatic pathologies (viral hepatitis), haemolytic anaemia, drug-induced hepatitis, Wilson's disease and Budd–Chiari syndrome. Post-hepatic causes include CBD obstructions, pancreatitis, choledochal cyst and gall stones.

Although jaundice in pregnancy is relatively rare, it may lead to serious materno-fetal complications. This study aimed to determine clinico-etiological, biochemical factors and materno-fetal outcome in women with jaundice during pregnancy and to study its correlation with jaundice in pregnancy.

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Materials and methods

Post receiving institutional ethical committee clearance, the observational study was conducted in department of obstetrics and gynaecology of a tertiary care hospital, in western Maharashtra from July 2018 to December 2019. The sample size was calculated in R studio software using standard formula [pwr. Chisq. test (effect size=0.60, df=1, power=0.80, sig. level = 0.05)] at 95% significance level, power being 80% and the minimum sample size was found to be 21. A total of 25 patients with abnormal liver functions were included. All pregnant patients with abnormal liver function tests were included in this study. Patients with normal liver functioning were excluded. Written informed consent was obtained from all the patients prior to the study. Demographic data and a detailed clinical history were collected including age, obstetrical profile, gravida, aetiology. The detailed laboratory investigation was carried out to study the complications concerning biochemical parameter. Maternal and fetal outcomes were also recorded.

The data collected were organized in MS-Excel (2016). Association between the biochemical factors and the maternal and fetal outcomes were analysed by chi square test in Statistical Package for the Social Sciences (SPSS) software. P value < 0.05 was considered as statistically significant.

Results and observations

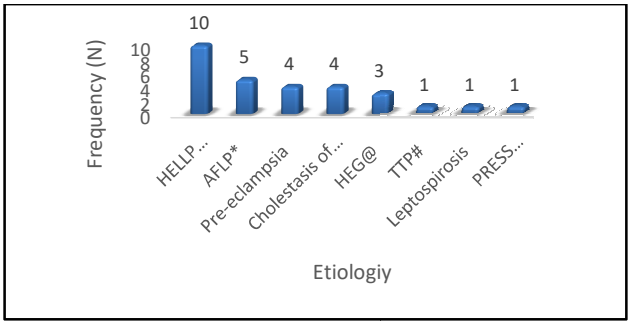
Mean age of the patients was 25.2 ± 3.78 years. Of the 25 patients, 11 patients (44%) belonged to the age group 21- 25 years. Distribution of the patients concerning their age is given in table 1.

Table 1: Age group

Age groups	No. of patients (n=25)	Percentage (%)
<20 years	3	12
21 to 25 years	11	44
26 to 30 years	9	36
>31 Years	2	8

Figure 1 represents that HELLP syndrome was the most common etiology (40%). Whereas, thrombotic thrombo-cytopenic purpura (TTP) (4%), leptospirosis (4%) and PRESS syndrome (4%) were least common.

High number of patients had low level of Hb (76%), total leukocyte count between 7000-11000 cells/ µL (60%), platelets >150000 cells/µL (40%), total bilirubin <2 mg/dL (60%), direct bilirubin >0.2 mg/ dL (80%), serum glutamic oxaloacetic transaminase (SGOT) >70 U/Lit (76%), serum glutamic pyruvic transaminase (SGPT) >70 U/Lit (76%), alkaline phosphatase >180 IU/Lit (68%), lactase dehydrogenase >600 U/Lit (84%), albumin >2.5 gm/ dL (60%), total protein >8.5 gm/dL (52%), urea >6.8 mg/ dL (60%) and creatinine >1.42 mg/ dL (60%), as shown in table 2.



(* Acute fatty liver of pregnancy; @ Hyper-emesis gravidarum; # Thrombotic thrombocytopenic purpura)

Figure 1: Etiological factors

Table 2: Lab parameters

Laboratory values	Category	No. of patients (n=25)	Percentage (%)
Hb (gm%)	< 7	19	76
	>7	06	24
Total leukocyte Count (cells/µL)	<7000	03	12
	7000-11000	15	60
	>11000	07	28
Platelets (cells/µL)	<50000	08	32
	51000-150000	07	28
	>150000	10	40
Total bilirubin (mg/dL)	<2	15	60
	>2	10	40
Direct bilirubin (mg/dL)	<0.2	05	20
	>0.2	20	80
SGOT (U/Lit)	<70	06	24
	>70	19	76
SGPT (U/Lit)	<70	06	24
	>70	19	76
Alkaline phosphatase (IU/Lit)	<180	08	32
	>180	17	68
Lactase dehydrogenase (U/Lit)	<600	04	16
	>600	21	84
Albumin (gm/dL)	<2.5	10	40
	>2.5	15	60
Total protein (gm/dL)	<8.5	12	48
	>8.5	13	52
Urea (mg/dL)	<6.8	10	40
	>6.8	15	60
Creatinine (mg/dL)	<1.4	10	40
	>1.4	15	60

Hb - Haemoglobin, SGOT - Serum glutamic oxaloacetic transaminase, SGPT - Serum glutamic pyruvic transaminase

Among 25 cases showed, adverse maternal and fetal outcomes were observed in 17 and 19 cases, respectively. Low birth weight was observed as commonest adverse fetal outcomes in 56% of cases. Among mothers, most common adverse outcome was requirement of emergency lower segment caesarean section (LSCS) (44%) (table 3).

Table 3: Maternal and foetal outcomes

Neonatal Outcomes	No. of patients	Percentage
Low birth weight	14	56 %
IUGR	11	44 %
Preterm	10	40 %
Neonatal death	03	12 %
Maternal outcomes	**No. of patients**	**Percentage**
LSCS	11	44 %
ICU admission	10	40 %
Blood transfusion	09	36 %
Maternal mortality	01	04%

IUGR - Intrauterine growth retardation, LSCS - Lower segment caesarean section, ICU - Intensive care unit.

Raised serum total bilirubin level, direct bilirubin level and thrombocytopenia were significantly associated with adverse fetal outcomes. Maternal outcomes were significantly associated with raised direct bilirubin, raised SGPT, raised alkaline phosphatase and thrombocytopenia (table 4).

Table 4: Association between abnormal lab parameters and adverse fetal and maternal outcomes

Laboratory parameters	Adverse fetal outcome (n=17)	P value	Adverse maternal outcome (n=19)	P value
Total bilirubin>2mg/dL	10(58.82%)	0.046*	10(52.63%)	0.33
Direct bilirubin >0.3mg/dL	17 (100%)	0.024*	19 (100%)	0.034*
SGOT>70 U/Lit	11 (64.71%)	0.18	13 (68.42%)	0.010*
SGPT>70U/Lit	10 (58.82%)	0.37	10 (52.63%)	0.62
Alkaline phosphatase >180IU/Lit	06 (35.29%)	0.57	08 (42.11%)	0.023*
LDH>600U/Lit	08 (47.06%)	0.65	07 (36.84%)	0.63
Albumin<2.5gm/dL	04 (23.53%)	0.62	04 (21.05%)	0.95
Total protein <8.5gm/dL	17 (100%)	1.0	19 (100%)	1.0
Urea >6.8 mg/dL	16 (94.12%)	0.51	18 (94.74%)	0.38
Creatinine >1.4 mg/dL	2 (11.76%)	0.90	02 (10.53%)	0.52
Hemoglobin<7gm%	5 (29.41%)	0.05*	05 (26.32%)	0.05*
Total leukocyte count>11000cells/µL	8 (47.06%)	0.84	09 (47.37%)	0.63
Platelet count <50000 cells/µL	3 (17.65%)	0.027*	02 (10.53%)	0.001*

*Statistically significant, LDH - Lactate dehydrogenase, SGOT - Serum glutamic oxaloacetic transaminase, SGPT - Serum glutamic pyruvic transaminase

Discussion

HELLP syndrome is defined as increased blood pressure with proteinuria or end-organ dysfunction in absence of proteinuria seen post 20 weeks of gestation.[7] However, in the present study, HELLP syndrome was the most common syndrome seen (44%) followed by acute fatty liver of pregnancy (AFLP) (32%), preeclampsia (28%), cholestasis of pregnancy (28%) and hyperemesis gravidarum (HEG)(12%). Similarly, in study by Reddy et al, HELLP syndrome was most common and was observed in 33.3% patients, followed by acute fatty liver of pregnancy in 22.2% and intrahepatic cholestasis of pregnancy in 11.1% patients.[8] Contradictorily, in a study conducted by Suresha et al and Allen et al, HELLP syndrome was the second common aetiology after eclampsia and preeclampsia, respectively. [2, 9] Satia et al, reported viral hepatitis (62%) as the commonest aetiology followed by cholestasis of pregnancy (24%).[10] The pathogenesis of HELLP is still not clear but is believed to involve abnormalities in placental vasculature and defects in maternal vascular endothelial cells, which results in poor perfusion.[7]

In developing countries, anaemia is a public health problem especially during pregnancy.[11] World Health Organization (WHO) has defined anaemia in pregnancy as the haemoglobin concentration of less than 11 g/dl.[12] Laboratory investigation in the present study revealed that 76% of the patients had haemoglobin <7 gm/dl and 28% had raised total leukocytic count. Platelets were found to be <50000 cells/µL in 32%. These laboratory findings are comparable with the study conducted by Suresha et al where, anaemia (37%), thrombocytopenia (31%) and coagulopathy (26%) were observed. [2]

Alteration in blood count is a common phenomenon in pregnancy.[13, 14] However, in this study, it can also be attributed to the presence of HELLP syndrome, which is associated with vascular endothelial abnormalities. [15]

Liver dysfunction was quite evident in high number of patients due to increased level of bilirubin. SGOT, SGPT and level of bilirubin were high in 76%, 76% and 40% of cases respectively. However, in a similar study, Ronceglia et al reported moderately increased bilirubin level of 1-10 mg% and hypoglycaemia.[16] Shinde et al, also reported elevated bilirubin level in the pregnant patients with jaundice compared to non-pregnant patients. [17] In their study, serum bilirubin levels between 11 - 15 mg/dl and between 16 and 25 mg/dl were recorded in 38.4% and 19.2% of pregnant patients, respectively. However, among non- pregnant patients, 36.5% had serum bilirubin between 6 and 10 mg/dl.[17]

Most common adverse neonatal outcome was low birth weight (56%) followed by intrauterine growth retardation (IUGR) (44%). Forty percent of the neonates were preterm,

and rate of neonatal death was found to be 12%. In the present study percentage of fetal deaths due to jaundice amongst total perinatal deaths was 12%. Parveen et al also reported low birth weight as the commonest adverse fetal outcomes. [18] This can be attributed to the low levels of haemoglobin among mothers, as it limits the oxygen supply to the fetus which results in restriction of intrauterine growth and low birth weight.[19] Bora et al reported the significant association between fetal birth weight and anaemia (mild and severe).[20] Interestingly, very high perinatal mortality rate of 45.45% was reported by Singh et al. [21]

Among mothers, most common adverse outcome was requirement of emergency LSCS (44%), need of ICU admission (40%) and blood transfusion (36%). In the present study one maternal death (4%) was observed. Fascinatingly, D'Souza et al, reported disseminated intravascular coagulation (DIC) as the commonest adverse maternal outcomes.[22] High number of maternal deaths were reported by Kamalajayaram et al and Singh et al as 33.3% and 10% respectively. [23, 21]

HELLP syndrome is associated with weight gain and oedema in 60%, maternal mortality of 20%, and neonatal mortality rate of 31%.[23] In acute fatty liver during pregnancy, maternal mortality is 18% while preterm labour is increased, and the perinatal mortality is 23%.[23]

Raised serum total bilirubin level (P=0.046), direct bilirubin level (P=0.024), thrombocytopenia (P=0.027), low haemoglobin level (P=0.05) was significantly associated with adverse fetal outcomes. Although median levels of maternal haemoglobin were normal overall, a significantly lower level was seen in females who had adverse events. Various studies have described the relationship between maternal anaemia and adverse fetal outcome. [20, 24] Raised direct bilirubin (P=0.034), raised SGOT (P=0.010), raised alkaline phosphatase (P=0.023), low haemoglobin level (P=0.05) and thrombocytopenia (P=0.001) were found to be significantly associated with adverse maternal outcome among the patients. Maternal deaths were directly proportional to the level of the serum bilirubin. Trivedi et al also reported similar findings.[25] Trivedi et al also stated that the initial bilirubin level at admission, > 10 is associated with poor maternal outcome and high maternal mortality.[25] Therefore, these laboratory parameters could be considered as a predictor of adverse maternal and fetal outcomes.

The studies on this topic are rather limited in recent years; therefore, this study contributes widely to understanding the effect of jaundice during pregnancy.

However, comparative study between pregnant women with and without jaundice would contribute to derive conclusive results.

Conclusion

In pregnancies, patients with hepatic abnormalities form a special subset. The symptoms are usually non-specific. Overall, hepatic abnormalities during pregnancies consequently have the adverse effect on both maternal and neonatal outcomes. Maternal anaemia, thrombocytopenia, coagulopathy, and hyperbilirubinemia are also evident. Early diagnosis of these patients is crucial and may reduce the adverse outcomes of both mother and the new-born.

Conflict of interest: None. **Disclaimer:** Nil.

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