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Original Article

Obstetrics and Gynaecology Section

Foetomaternal Outcomes of Jaundice in Pregnancy at a Tertiary Care Centre: A Prospective Cohort Study

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ABSTRACT

Introduction: Jaundice complicates 3 to 5% of pregnancies and is one of the important causes of maternal and neonatal morbidity and mortality worldwide. It is responsible for approximately 10% of maternal deaths.

Aim: To study the prevalence of jaundice in pregnancy, evaluate the important causes of jaundice encountered in pregnancy, and study the effects of jaundice during pregnancy on both maternal and foetal outcomes.

Materials and Methods: This prospective cohort study was conducted at the Department of Obstetrics and Gynaecology, RG Kar Medical College and Hospital, Kolkata, West Bengal, India, from March 1, 2021, to August 31, 2022. A total of 90 cases of pregnancy with jaundice were included in the present study. Detailed history, clinical examination, laboratory investigations, diagnosis, management, and outcomes in terms of maternal and perinatal morbidity and mortality were recorded. Data were analysed using the Chi-square test, with a statistical significance level set at $p<0.05$.

Results: The total number of deliveries was 20,087, out of which 90 (0.45%) patients had jaundice. The prevalence of jaundice in pregnancy was 4.5 per 1000. The aetiologies of jaundice were viral hepatitis in 23 cases (25.55%), followed by intrahepatic cholestasis in 22 cases (24.44%), preeclampsia in 13 cases (13.33%), and Haemolysis, Elevated Liver Enzymes and Low Platelets (HELLP) syndrome in 6 cases (6.66%). There were 12 (13.33%) maternal deaths and 17 (18.88%) neonatal deaths. Two (2.22%) babies were stillborn, and 1 (1.11%) case experienced Intrauterine Foetal Death (IUFD). The maternal death rate due to HELLP syndrome was 66.66% (4 deaths out of 6 cases).

Conclusion: Viral hepatitis is the most common cause of jaundice in pregnancy. Although viral hepatitis due to the faeco-oral route is more common in India, the present study showed that Hepatitis B is more common during pregnancy.

Keywords: Foeco-oral root, Foetal outcomes, Maternal outcome, Perinatal outcome

INTRODUCTION

The word "jaundice" is derived from the French word "jaune," meaning yellow [1]. International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) defines jaundice as a clinical manifestation of hyperbilirubinaemia, which involves the deposition of bile pigments in the skin, resulting in a yellowish staining of the skin and mucous membranes [2]. According to the literature, jaundice is clinically manifested when the serum bilirubin level exceeds 2 mg/dL [3]. The incidence of jaundice in pregnancy is 3 to 5%, and it is one of the significant causes of maternal and neonatal morbidity and mortality worldwide [2]. Studies show that jaundice in pregnancy accounts for 10% of maternal deaths [4]. It is already a well-established fact that viral hepatitis is quite common among people with low socio-economic status, densely inhabited areas of urban slums lacking basic hygiene and sanitation, with a seasonal increase in incidence during the summer and monsoon seasons [5]. The most common maternal complications in pregnant mothers with jaundice include hepatic encephalopathy, ascites, hypoglycaemia, renal failure, haematemesis, preeclampsia, and Postpartum Haemorrhage (PPH). The foetal outcomes in pregnancies complicated by jaundice may include preterm birth (live or intrauterine foetal demise) and term birth (live or intrauterine foetal demise). The prognosis of the foetus in pregnancy with jaundice depends on factors such as the underlying cause of jaundice, gestational age at the presentation of jaundice, and the timing of delivery [5]. Fulminant hepatitis E has the highest mortality rate at 22%, followed by acute fatty liver of pregnancy at 18% [6,7].

Jaundice in pregnancy is associated with various pathologies, including viral hepatitis, leptospirosis, malaria, increased haemolysis, and pregnancy-related conditions such as preeclampsia, HELLP syndrome, acute fatty liver, cholestasis of pregnancy, and hyperemesis gravidarum [8]. The maximum incidence of jaundice occurs in the third trimester, and the complications are also higher during that period [9-11]. The liver is affected during pregnancy due to altered expression of the cytochrome P450 system, mediated by oestrogen, progesterone, and other pregnancy hormones [12].

Literature shows that jaundice and pregnancy are a deadly combination, leading to very high perinatal as well as maternal morbidity and mortality, requiring early diagnosis and careful management [13]. The rationale for the present research work was to understand the prevalence of jaundice in pregnancy in this part of India and to study the socio-demographic characteristics of pregnant women with jaundice, to determine the common causes of jaundice in pregnancy and its effect on foetomaternal outcomes, so that timely appropriate measures could be taken to significantly reduce foetomaternal morbidity and mortality. The present study will enhance the understanding of this fatal disease in pregnancy in developing countries like India.

MATERIALS AND METHODS

A prospective cohort study was conducted at the Department of Gynaecology and Obstetrics, RG Kar Medical College and Hospital, Kolkata, West Bengal, India, from March 1, 2021, to August 31, 2022. Ethical clearance was obtained through the proper channel from the review and Ethics Committee of the Institution (ICE approval No-RKC/335 dated February 12, 2021).

Sample size calculation: The sample size was calculated using formula:

$$n=\frac{Z^2P(1-P)}{d^2}$$

where n=Sample size,

Z=Z statistic for a level of confidence,

P=Expected prevalence or proportion (If the expected prevalence is 20%, then P=0.2), and d=Precision (If the precision is 5%, then d=0.05).

P=0.03 [13], Z=1.96, q=(1-0.03)=0.07, d=0.05

$$n=\frac{1.96\times1.96\times0.03\times(1-0.03)}{(0.05)\times(0.05)}=44.71$$

A further 10% was included to account for missing data/technical failures.

So, the sample size was 44.71+10% of 44.71=49.18. The minimum sample size was 50, but to minimise the error, the sample size was increased to 90 in the present study.

Inclusion criteria: All women with jaundice complicating pregnancy after 20 weeks of gestational age, irrespective of age group and parity, admitted to the Department of the study institute.

Exclusion criteria: The cases of jaundice with the following causes were excluded from the study: chronic liver disease, gallstones, jaundice before the start of pregnancy, cardiac disease, diabetes mellitus, renal disease, bronchial asthma, liver malignancy, and those who were lost to follow-up.

Study Procedure

A detailed history, clinical examination, laboratory investigations, diagnosis, management, maternal and perinatal outcomes were recorded in respect of the following independent and dependent parameters. Independent variables include age, residence, socio-economic status, gravida, parity, gestational status, labour status, mode of termination of pregnancy, and birth weight.

Outcomes were observed and analysed with respect to primary outcome, which included maternal morbidity and mortality and perinatal morbidity and mortality in cases of jaundice in pregnancy and secondary outcome, which included maternal outcome: mode of termination of pregnancy, maternal complication, foetal outcome: low birth weight baby, Intrauterine Growth Restriction (IUGR), perinatal asphyxia, meconium aspiration syndrome and preterm birth.

STATISTICAL ANALYSIS

Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS version 20.0; Inc., Chicago, IL, USA). Quantitative variables were compared using mean values, and qualitative variables were compared using proportions. Data were analysed using the Chi-square test. The statistical significance level was set at $p<0.05$.

RESULTS

A total of 20,087 pregnant women were admitted to the present hospital during the study period, out of which 90 patients had jaundice. The prevalence of jaundice in pregnancy was 4.5 per 1000 pregnant women. The majority of cases were found in the age group of 20-29 years, accounting for 88 cases (62.23%). The mean age of the study population was 25.8 years±9.12 [Table/Fig-1]. The majority of patients (52 out of 90, 57.77%) were primigravida, followed by 23 patients (25.6%) who were second gravida [Table/Fig-2]. A significant number of babies (75 out of 88) were delivered with low birth weight (birth weight <2.5 kg), with a statistically significant association (p-value=0.00201).

The incidence of emergency Lower Segment Caesarean Section (LSCS) and vaginal deliveries was almost equal among the study sample (46.66%) [Table/Fig-3].

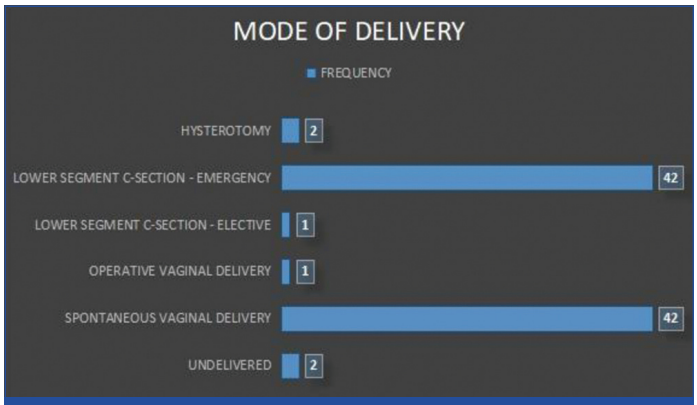
The aetiologies of jaundice were viral hepatitis (25.55%), followed by intrahepatic cholestasis (24.44%), preeclampsia (13.33%), and HELLP syndrome (6.66%) [Table/Fig-4]. Among viral hepatitis cases, the most common was Hepatitis B infection in 11 patients (47.82%), followed by Hepatitis A infection in 6 patients (26.08%).

Parameters	Categories	Frequency	Percentage
Age group (years)	≤20	18	20.0%
	21-30	56	62.23%
	31-40	14	15.6%
	>40	2	2.2%
Residency	Rural	36	40%
	Urban	54	60%
Educational status	Illiterate	12	13.33%
	Middle school	34	37.77%
	Higher education	44	48.88%
Socio-economic status	Lower class	43	47.77%
	Upper lower class	4	4.44%
	Lower middle class	27	30%
	Upper middle class	16	17.77%
	Upper class	0	0%

[Table/Fig-1]: Socio-demographic characteristics (N=90).

Parameters	Categories	Frequency	Percentage
Gravida	Primigravida	52	57.77%
	Multigravida	38	42.22%
Parity	P0+0	52	57.77%
	P0+1	2	2.22%
	P0+2	1	1.11%
	P1+0	21	23.33%
	P1+1	10	11.11%
	P2+0	2	2.22%
	P3+1	1	1.11%
	P5+0	1	1.11%
Gestational age (weeks)	Preterm	34	37.77%
	Term	55	61.11%
	Post term	1	1.11%
Labour status	Operative intervention	12	14%
	Spontaneous onset	72	84%
	Induced labour	6	2%

[Table/Fig-2]: Obstetrics characteristics (N=90).



[Table/Fig-3]: Mode of delivery in study population (n=90).

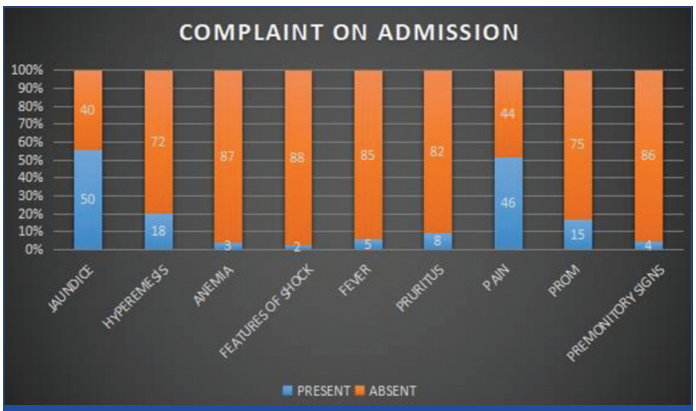
Diagnosis	No of cases (n=90)	Percentages
HELLP Syndrome	06	6.66%
Viral Hepatitis	23	25.55%
Intrahepatic cholestasis	22	24.44%
Preeclampsia	13	14.44%
Acute fatty liver of pregnancy	09	10%
Leptospirosis	04	4.44%
Malaria	03	3.33%

Haemolytic jaundice	04	4.44%
Others	03	3.33%
Unknown	03	3.33%

[Table/Fig-4]: Distribution of study population according to aetiology of Jaundice (n=90).

In the present, 55.55% of the study population presented with jaundice as the main complaint, followed by abdominal pain (51.11%) [Table/Fig-5].

The most common complication encountered in the present study was postpartum haemorrhage in 35 patients (38.88%), followed by Acute Kidney Injury (AKI) in 12 patients (13.33%) and Disseminated Intravascular Coagulation (DIC) in 8 patients (8.88%). In the study population, 23.33% of patients needed admission to the High-dependency Unit (HDU), 44.44% required blood transfusion, and 13.33% needed haemodialysis [Table/Fig-6].



[Table/Fig-5]: Bar diagram showing complaint on admission (n=90).

[Table/Fig-6]: Bar diagram showing management of pregnancy with jaundice.

In the present study, there was a maternal mortality rate of 13.33% and a neonatal mortality rate of 18.88% [Table/Fig-7]. The most common cause of maternal death was HELLP syndrome and acute fatty liver of pregnancy (four cases each). The maximum number of perinatal deaths was observed in intrahepatic cholestasis (four cases), followed by viral hepatitis and acute fatty liver of pregnancy (three cases each) [Table/Fig-8]. A high level of total serum bilirubin was directly related to high foetomaternal death, and this finding was statistically significant (p-value <0.00001) [Table/Fig-9].

Foetomaternal outcome			Frequency	Percentage
Maternal outcome (n=90)	Discharged		78	86.66%
	Maternal death		12	13.33%
Foetal outcome (n=90)	Discharged		68	75.55%
	Undelivered		2	2.22%
	Death	IUFD	1	1.11%
		Stillborn	2	2.22%
		Neonatal death	17	18.88%

[Table/Fig-7]: Fetomaternal outcome in pregnancy with jaundice (n=90).

Cause of jaundice	Frequency	Maternal outcome (n=90)		Perinatal outcome (n=88)	
		Healthy	Death	Healthy	Death
HELLP syndrome	6	2	4	4	2
Viral hepatitis	23	23	0	20	3
Intrahepatic cholestasis	22	22	0	17	4
Preeclampsia	13	13	0	12	1
Acute fatty liver of pregnancy	9	5	4	6	3
Leptospirosis	4	2	2	2	2
Malaria	3	3	0	2	1
Haemolytic jaundice	4	4	0	2	1
Others	3	1	2	1	2
Unknown	3	3	0	2	1
Total	90	78 (86.66%)	12 (13.33%)	68 (77.27%)	20 (22.72%)

[Table/Fig-8]: Distribution of study sample according cause of jaundice vs maternal/perinatal outcome (n=90).

Serum bilirubin (mg %)	Frequency (n=90)	Maternal outcome		p-value
		Healthy (78)	Death (12)	
2-5	34	32	2 (5.88%)	<0.00001
6-10	44	44	0	
11-15	6	1	5 (83.33%)	
16-20	5	1	4 (80%)	
>20	1	0	1 (100%)	
Serum bilirubin (mg %)	**Frequency (n=88)**	**Perinatal outcome (n=88)**		**p-value**
		Healthy (68)	Death (20)	
2-5	34	29	5 (14.70%)	0.04519
6-10	42	33	9 (21.42%)	
11-15	6	4	2 (66.66%)	
16-20	5	2	3 (60%)	
>20	1	0	1 (100%)	

[Table/Fig-9]: Relationship between serum bilirubin level and maternal/perinatal outcome (N=90).

An increased level of liver enzymes (ALT) was directly related to adverse foetomaternal outcomes, and this association was statistically significant for ALT [Table/Fig-10].

Liver enzymes level		Frequency	Maternal outcome (n=90)		Foetal outcome (n=88)	
			Healthy (78)	Death (12)	Healthy (68)	Death (20)
AST (IU/L)	<200	46	41	5	37	7
	200-400	32	28	4	25	7
	>400	12	9	3	6	6
Chi-square			2.1464889		4.2096920	
p-value			0.34189743		0.1218644	
ALT (IU/L)	<200	47	42	5	40	7
	200-400	31	29	2	25	6
	>400	12	7	5	3	7
Chi-square			9.90242		10.661523	
p-value			0.007074		0.0048403	

[Table/Fig-10]: Distribution of study population according to liver enzymes level vs foetomaternal outcome.

DISCUSSION

The study population had a normal distribution for age, with 62.25% falling between 21 to 30 years, which is consistent with the findings of Desai A et al., where 68% of cases belonged to the 21-29 age group [5]. Padh JP et al., also reported that 58% of patients belonged

to the age group of 20-30 years in their study [13]. Sharma S et al., reported that jaundice affected a younger age group, with the peak age being 21-25 years (66.6%) [14].

In this present study, 60% of patients were from urban areas, mainly from urban slums of Kolkata, and 40% were from rural areas. This is in contrast to the study by Tiwari R et al., who showed that jaundice was more prevalent among rural cases (76%) compared to urban cases (24%) [15]. This disparity seems to be due to differences in the catchment area.

In the present study, 47.77% of patients receiving treatment belonged to the lower socio-economic class. Desai A et al., also reported that in their study, 50% of pregnant patients with jaundice came from the lower socio-economic class [5]. According to Sharma S et al., 60% of the study population was of lower socio-economic status [14]. According to the present study, 30% of patients belonged to the lower middle class. Changede P et al., showed that 42% of the study population belonged to the upper lower class, followed by the lower middle class (35%) and the lower class (23%) [16]. The majority of patients (57.77%) in the present study were primigravida and primipara, followed by second gravida, which is comparable to the findings of Sharma S et al., and Tiwari R et al., who reported that 66.66% and 56%, respectively, were primipara [14,15].

In the present study, 61.11% of patients delivered at term gestation, and 28.88% delivered preterm. Studies done by Sharma S et al., and Mitta P and Rao SV reported 73.3% and 62.2% of term deliveries, respectively, which are similar to the present study. However, Desai A et al., reported 52% preterm delivery [5,14,17].

The most common symptom in the present study was jaundice (55.55%), followed by abdominal pain (51.11%). In contrast to our results, Desai A et al., in their study, showed that 82% of patients presented with jaundice (serum bilirubin >2), followed by upper abdominal pain in 74% of cases and yellow-colored urine in 62% [5].

In the present study, the most common cause of jaundice was viral hepatitis (25.55%), followed by intrahepatic cholestasis (24.44%), preeclampsia (14.44%), and HELLP syndrome (6.66%). A study by Ambreen A et al., also showed that the most common causes of jaundice in pregnancy were viral hepatitis (51.02%), intrahepatic cholestasis of pregnancy (33.89%), HELLP syndrome (12.13%), and acute fatty liver of pregnancy (1.25%) [18]. In the study by Desai A et al., viral hepatitis was also the most common cause of jaundice in pregnancy (52%), followed by HELLP syndrome (36%) and intrahepatic cholestasis of pregnancy (10%). In the present study, among viral hepatitis cases, the most common was Hepatitis B infection in 11 (47.82%) patients, followed by Hepatitis A infection in 5 (22.19%) patients. However, the study by Desai A et al., reported that Hepatitis E was the most common cause of jaundice in pregnancy (42%) [5].

In the present study, the incidence of maternal death was significantly higher in those with bilirubin levels >10 mg/dL compared to those with bilirubin levels <10 mg/dL. A study by Jayanti N et al., reported that 7.84% of patients had serum bilirubin levels >16 mg/dL with a mortality rate of 10.0% [19]. In the study by Patel BJ et al., 21.4% had bilirubin levels >10 mg/dL at the time of admission [20]. Mitta P and Rao SV reported that 14.3% had bilirubin levels >10 mg/dL at the time of admission with a mortality rate of 4.76% [17]. Krishnamoorthy J and Murugesan A reported that 7.84% had bilirubin levels >10 mg/dL at the time of admission with a maternal mortality rate of 7.8% [9].

The rate of vaginal delivery in the present study differs from other studies such as Sharma S et al., (100%), Mitta P and Rao SV (69.2%), and Patel BJ et al., (82.3%), where most of the patients delivered vaginally [14,17,20]. This difference is probably due to the fact that most of the patients in the present study were referral patients from peripheral centres. In the present study population, the most common complications were postpartum haemorrhage (38.88%), renal failure (13.33%), and disseminated intravascular coagulation (8.88%), and these findings corroborate with the study by Sharma S et al., (60%, 13.3%, and 20%, respectively) [14].

In the present study, 23.33% of patients needed HDU admission, 44.44% received blood transfusion, and 13.33% required haemodialysis. In contrast to this observation, a study by Mitta P and Rao SV reported that blood and its components were given in only 9 cases (21.42%) [17].

In the present study, the incidence of maternal death due to jaundice was 13.33%. These findings are comparable to other studies by Roychowdhary G et al., and Rao KB and Rudra G where the incidence of maternal death was 13.3% and 15.8%, respectively [21,22]. We observed that 75.55% of newborn babies were discharged in stable condition, while the incidence of neonatal death, stillbirth, and intrauterine foetal death was 18.8%, 2.22%, and 1.11%, respectively. A study by Desai A et al., reported a stillbirth rate of 7.6% and an early neonatal death rate of 38.4%, which is higher than our results [5]. In the present study, the majority (75 out of a total of 88 babies) had low birth weight, which is comparable (84%) to the observation by Desai A et al., [5].

The present study shows that higher maternal mortality is related to high serum bilirubin levels, and 100% of deaths were noted when the serum bilirubin level was more than 20 mg/dL. This is a statistically significant finding and is supported by the study of Trivedi SS et al., [23].

In the present study, the authors observed that high perinatal mortality is correlated with higher bilirubin levels, and the results are statistically significant. The present study also showed that viral marker status does not affect the complications in jaundice patients.

Limitation(s)

The notable shortcomings of the present study are that it is a single-centre study involving a small number of patients. Therefore, a multicentre trial involving a larger sample size would be more accurate and conclusive. Moreover, as the present study was carried out in a tertiary care hospital, hospital bias cannot be ruled out.

CONCLUSION(S)

Viral hepatitis was the most common cause of jaundice in pregnancy. Although viral hepatitis due to the faeco-oral route is more common in India, the present study shows that Hepatitis B is more common during pregnancy. In present study, a high serum bilirubin level is directly related to poor maternal and foetal outcomes, leading to high maternal and perinatal mortality. Measures such as increasing public health knowledge regarding the different types of hepatitis and its aetiology, improving sanitation, providing adequate preventive measures, promoting routine and regular antenatal check-ups, and including viral marker tests as universal antenatal screening can help reduce the burden of jaundice in pregnancy.

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