

## A clinical study of the fetal outcome of jaundice in pregnancy in a tertiary care centre

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### Abstract

**Introduction:** The maternal outcome and other pregnancy outcomes are strongly influenced by the abnormalities of liver function. This study was undertaken to look at the fetal and perinatal outcome in pregnancy with jaundice irrespective of the cause for jaundice.

**Materials and Method:** The study was done in the department of OBG, Bangalore medical College and research institute over a period of 18 months. All pregnant women with jaundice irrespective of their gestational age were subjected to haematological tests and liver function tests and USG examination and the aetiological diagnosis was established in all the cases. The women were followed during their antenatal, intranatal and postnatal period and the fetal/perinatal outcome were documented and the likely factors influencing the outcome were studied.

**Results:** There were 31 patients with jaundice putting the incidence to be 0.15%. 13% of the patients were in second trimester and 39% were term pregnancy patients. 35% of them had viral hepatitis, 32% had HELLP syndrome and 22% had intrahepatic cholestasis as the aetiology of jaundice. 92% delivered vaginally and 29% delivered as preterm. More than 45% of the deliveries were associated with adverse fetal outcome – intrauterine fetal demise, still birth etc., 45% had MSAF, 61% required NICU admission, 25.8% babies died.

**Conclusion:** Jaundice continues to be a problem both for the pregnant woman and continues to have adverse effects on the perinatal outcome and the aetiology of jaundice could be the most important single determining factor for perinatal outcome.

**Keywords:** Jaundice in pregnancy, perinatal outcome in jaundice, Acute fatty liver, Intrahepatic cholestasis

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### Introduction

Pregnancy is a special clinical state with several normal physiological changes that influence body organs including the liver. Liver is the site of many important metabolic and synthetic functions of the body. In spite of numerous exogenous and endogenous factors, jaundice and pregnancy are infrequent associates. Jaundice is not a disease but it is a manifestation of hepatobiliary dysfunction.

Abnormal liver function tests occur in 3-5% of pregnancies with many potential causes, including coincidental liver diseases (most commonly viral hepatitis and gall stones), underlying chronic liver disease, and disease states unique to pregnancy (hyperemesis gravidarum, preeclampsia and associated HELLP syndrome, intrahepatic cholestasis of pregnancy, acute fatty liver of pregnancy).<sup>(1)</sup>

Despite its low incidence liver disease can cause significant morbidity and mortality to the pregnant mother and the fetus.

Fetal effects causing concern include higher incidence of intrauterine deaths and still births, meconium staining of amniotic fluid and fetal distress; intra uterine and perinatal transmission of viral hepatitis from the mother to the fetus resulting in chronic liver disease.<sup>(2,3)</sup>

Some of the complications in the mother like DIC, coagulation disorders, hepatic encephalopathy, APH and PPH could be responsible for adverse maternal outcomes and perinatal outcomes. But the latter happens in women not just with jaundice but in women with fever, dehydration, hypoglycaemia and severe malnourishment. Genetic input of the fetus may be responsible for certain maternal situation like AFLP. Various studies have reported adverse fetal outcomes like Intrauterine death (1-2%), Meconium staining of amniotic fluid (15-50%), prematurity (2-27%) and sometimes problems associated with iatrogenic prematurity. The UKOSS report puts the perinatal mortality risk at 10% for AFLP, which may be much higher for developing countries. Liver rupture can take the perinatal death percentage upto 60%. Hyperemesis may cause growth restriction, but severe forms with Wernicke's encephalopathy can cause pregnancy loss.<sup>(4)</sup>

### Materials and Method

The study was conducted in the department of Obstetrics and Gynecology, Vani Vilas hospital and Bowring & Lady Curzon hospital attached to Bangalore Medical College and Research Institute, Bangalore, during the study period of October 2014 – April 2016. The following patients were included in the study.

All pregnant patients who present with jaundice or

deranged liver function tests during pregnancy (all trimesters). The following patients were excluded.

1. Jaundice antecedent to pregnancy
2. Jaundice with its onset in the postpartum period
3. Patients not consenting to be a part of the study.

All the study subjects were analyzed in full detail regarding demographic data, parity, gestational age at presentations, symptomatology at presentation, detailed history of current and past pregnancies and any other relevant past history specifically history of recurrent anaemia, blood transfusions in the past, family history of haemolytic anaemia etc., History of fever, pruritus, features suggestive of hepatic failure, duration of jaundice, vomiting, urinary colour, colour of stools, appreciation of fetal movements were all documented.

Subjects were followed further by a thorough general physical examination where in presence of jaundice, dehydration, clinical severity, signs of liver failure, features of hypertensive disorders of pregnancy were noted. Systemic and obstetric examinations were performed and duration of gestation, features of IUGR, hepatomegaly, splenomegaly ascitis were looked for. Patients presenting in labour underwent pelvic examination, and decision regarding mode of delivery was taken. CTG, if necessary ultrasound examination was done and fetal well being/distress documented.

The following set of investigations were performed on the study subjects:

1. Hematological: Complete blood counts, liver function tests, coagulation profile (prothrombin time, activated partial thromboplastin time), serology for hepatitis A, B, C, E; serum lactate dehydrogenase, peripheral smear
2. Urine examination: Urine for protein and albumin, bile salts and bile pigments
3. Ultrasonography of the abdomen and pelvis
4. In late pregnancies, CTG, BPP by ultrasound were done.

The study subjects were then carefully followed up in the antepartum, intrapartum and postpartum period. The pregnancy and labour events and outcome were noted including gestational age at delivery, whether labour was spontaneous or induced, and the mode of delivery – vaginal or Caesarean delivery. Treatment provided to the study subjects – drugs, blood and blood component transfusions were noted. The fetal outcome was noted in terms of gestational age at delivery (term/preterm), live birth/intrauterine fetal demise/still birth, meconium staining of amniotic fluid signifying fetal distress, need for resuscitation immediately following birth, neonatal intensive care unit (NICU) admissions and early neonatal deaths. The study subjects were followed up till duration of stay in the hospital and maternal outcome was recorded and any complications like fulminant liver failure, disseminated intravascular coagulation, eclampsia, acute renal failure, postpartum hemorrhage, need for intensive care unit (ICU) monitoring and maternal deaths were noted.

## Results

A total of 31 pregnant women presented with jaundice or deranged liver function tests during the study period October 2014 – April 2016. The total number of deliveries during this study period was 20167. The incidence of jaundice in the present study was 0.15%.

Majority of the study subjects belonged to the age group of 20-30 years. The minimum age was 18 years and the maximum age was 29 years. (Mean  $\pm$  SD: 23.52 $\pm$ 2.76)

Majority of the study subjects (61%) were primigravidas with singleton pregnancies. 61% subjects belonged to lower socioeconomic group and there were no study subjects in the upper class.

The mean gestational age of presentation and diagnosis of the study subjects was 34.32 weeks, in the third trimester of pregnancy. But there were 13% of patients in 2<sup>nd</sup> trimester and 13% in early 3<sup>rd</sup> trimester. (Table 1)

The most common cause of jaundice in this study was found to be viral hepatitis which was confirmed by serological tests for the same after making a presumptive diagnosis based on symptomatology. The most common type of viral hepatitis among the study subjects in this study was acute hepatitis E – 7 patients, acute hepatitis A in 2 patients, coinfection of hepatitis E and A in 1 patient and acute hepatitis B in 1 patient. This was closely followed by HELLP syndrome (32.3%) and intrahepatic cholestasis of pregnancy (22.6%). The other causes are shown in Table 2.

Among the 31 study subjects majority of the study subjects (93.5%) delivered vaginally with LSCS being performed in 2 cases for obstetric indications – previous LSCS and fetal distress. 9 of them delivered prior to term which was spontaneous and vaginal whereas 71% of them had term delivery. The patients who presented with jaundice in the 2<sup>nd</sup> and early 3<sup>rd</sup> trimester were followed up till delivery and out of the 8 women 2 had pre term delivery and the rest had term delivery.

All the babies weighed less than 3.5 kg with maximum being in the range between 2.5 kg to 3.5 kg (53.8%). There were a total of 26 live births. APGAR score assessing the baby's respiratory effort, heart rate, muscle tone, reflexes and skin colour was noted at 5 minutes of birth. Babies who had APGAR scores of less than 7 at 5 minutes required resuscitation in the form of either bag and mask ventilation or intubation and further intensive care unit observation.

As seen in the Table 3, little less than 50% of the deliveries in the study subjects were associated with adverse fetal outcome – intrauterine fetal demise, still birth or the need for resuscitation following birth. There were 14 babies with meconium stained amniotic fluid of whom 8 had APGAR at 5 mins of <7 and 6 had APGAR of >7. All the babies with APGAR of <7 at 5 minutes were admitted to NICU, 2 of them requiring ventilation and both didn't survive the cause of death

was HIE stage 3. There were a total of 8 perinatal deaths inclusive of still born births both fresh and macerated among the 31 deliveries. Three live born babies succumbed in the first week of birth to HIE stage 3.

Out of the 19 babies admitted to NICU (61% admission rate), 2 babies with meconium stained amniotic fluid aspiration and asphyxiated and one more baby of a mother with HELLP syndrome succumbed but all the preterm babies were salvaged.

As a whole the strikingly increased adverse fetal outcomes are shown in Table 4.

Hepatitis E and HELLP syndrome patients had maternal deaths 2 in each group. 75% was the perinatal mortality out of these four and one of the baby of a hepatitis E mother died in the neonatal period. All the babies of HELLP syndrome mothers who died had IUD. Details shown in Table 5.

**Table 1: Gestational age at diagnosis distribution of patients studied**

Gestational age of diagnosis (weeks)	No. of patients	%
16-28	4	12.9
28-32	4	12.9
32-36	11	35.5
37-40	11	35.5
>40	1	3.2
Total	31	100.0

**Table 2: Cause of Jaundice**

Cause of Jaundice	No of patients	%
Viral Hepatitis	11	35.5%
HELLP syndrome	10	32.3%
Intrahepatic cholestasis of pregnancy	7	22.6%
Acute fatty liver of pregnancy	1	3.2%
Acute cholecystitis	1	3.2%
Hyperemesis gravidarum	1	3.2%
Total	31	100%

**Table 3: Fetal outcome – condition of the baby at birth**

Conditions of baby	No. of patients	%	Survival
APGAR > 7 at 5 minutes	16	51.6	All
APGAR <7 at 5 minutes	10	31.0	7
Intrauterine death	3	9.7	-
Still born	2	6.5	-
Total	31	100.0	23

**Table 4: Summary of adverse fetal outcome**

Event	Number	Percentage
Intrauterine death	3	9.7%
Still birth	2	6.4%
Perinatal death	3	9.7%
MSAF	14	45%
NICU admission	19	61.3%
Pre term delivery	9	29%

**Table 5: Fetomaternal outcome**

Cause of Jaundice	Neonatal Outcome				Maternal Mortality
	IUD	Still birth	Live birth	Neonatal death	
Hepatitis E	Nil	Nil	5	1	2
Hepatitis A	Nil	Nil	6	Nil	Nil
Hellp Syndrome	2	1	7	2	2
Acute Fatty Liver of Pregnancy	Nil	1	Nil	Nil	Nil
IHCP	1	Nil	6	Nil	Nil
Hyperemesis	Nil	Nil	1	Nil	Nil
Cholecystitis	Nil	Nil	1	Nil	Nil
Total	3	2	26	3	4

## Discussion

The present study aimed at analysing the variables of fetal outcome with the presence of jaundice or deranged liver function tests in pregnancy. The various parameters in the study subjects were analysed and compared with standard literature readings available.

During the study period there were a total of 20,167 deliveries and 31 patients were admitted with jaundice. The incidence of jaundice in this study was found to be 0.15%. Studies conducted by Nagaria et al, Oladokun et al, Patel et al and Neema Acharya et al have reported an incidence of 0.5%, 0.3%, 0.4% and 0.4% respectively.<sup>(5,6,7,8)</sup>

61.3% of the study subjects belonged to lower socioeconomic class as per modified Kuppuswamy's scale. There were no patients from the upper class, possibly because the study was conducted at a government tertiary referral centre. However, predominance of study subjects in the lower socioeconomic class underscores the importance of nutrition and sanitation as a predisposing factor for jaundice especially in India. The finding of a good number of patients with hepatitis infection strengthens this explanation.

The gestational ages at presentation of most jaundice related diseases specific to pregnancy is the third trimester. This is reflected in the present study also with 87.1% of the study subjects presenting in their third trimester. Mean gestational age at diagnosis was  $34.32 \pm 5.11$  weeks.

In the present study, infective hepatitis was the commonest cause of jaundice and among the infectious hepatitis, hepatitis E was the most common – 72.7%, followed by hepatitis A. HELLP syndrome was the second most common cause of jaundice – 32.3% followed by intrahepatic cholestasis of pregnancy – 22.6%. Altered liver function due to hyperemesis gravidarum was seen in 1 patient who presented with intractable vomiting in early 2<sup>nd</sup> trimester. In a study conducted by Ching ling Yi et al, 50% of the patients had jaundice due to an infective etiology.<sup>(9)</sup> Hepatitis E was the most common cause of viral hepatitis in their study with a high mortality rate of 50%. In the present study also the maternal mortality was encountered in 2 patients with hepatitis E. In a study by Wani et al examining the prevalence of acute viral hepatitis in women presenting with jaundice, viral hepatitis was the cause of jaundice in 70% of cases, with hepatitis E accounting for 45% of the cases.<sup>(10)</sup>

The preferred route of delivery in a woman with jaundice would be vaginal and the study subjects also delivered vaginally except in 2 cases who had cesarean delivery for obstetric indications. Meconium staining of the amniotic fluid is a common finding in women with jaundice and the same was encountered in 12 of the women of whom 8 babies had APGAR of <7 at 5 minutes. This also was an important clinical determinant of adverse perinatal outcome as 25% was the mortality amongst these 8 babies.

HELLP syndrome was one more important etiological factor causing jaundice which showed a higher perinatal mortality with 2 cases of intrauterine fetal demise with macerated babies, 1 baby who had intrapartum still birth and two babies who succumbed to HIE stage 3 secondary to meconium aspiration and birth asphyxia. The basic pathology in these women with severe pre-eclampsia causing uteroplacental insufficiency could be the cause for this many perinatal adverse outcome. Presentation late in labour with impending delivery was an association in these women.

Jaundice in pregnancy due to the mentioned causes was associated with significant fetal and maternal morbidity and mortality. Significant number of deliveries were preterm, either spontaneous or iatrogenic due to obstetric indications. The perinatal mortality including intrauterine and neonatal deaths was 25.8%. Many of the infants required admission and monitoring in the neonatal intensive care unit. The adverse perinatal outcome due to jaundice has been substantiated in other similar studies. In a study by Ch'ng et al, 46% of the delivered were preterm and 27% of the infants required admission to special care baby units.<sup>(11)</sup> Patel et al reported a preterm delivery rate of 68.8% and a still birth rate of 8.8%.<sup>(7)</sup> The perinatal outcome in this study was comparable to the findings in a study conducted by Oladokun et al.<sup>(6)</sup>

Though the perinatal mortality has been found to be high in the present study, probably the NICU facility could be the confounding factor. The preterm delivery rate too is higher in the study by Oladokun et al, but perinatal mortality is less.<sup>(6)</sup>

The maternal and perinatal morbidity and mortality was significantly more in study subjects with higher serum bilirubin levels. In this study the mean serum bilirubin level was  $7.53 \pm 4.43$  mg/dl. 64.6% of the patients had serum bilirubin in the range of 4-10 mg%. There was only maternal death with bilirubin in this range.

**Table 6: Comparison of adverse perinatal outcome**

Perinatal outcome	Oladokun et al <sup>(5)</sup>	Present study
Preterm delivery	39.6%	29%
Perinatal mortality rate	10.9%	25.8%
Intrauterine deaths	8.3%	9.7%

## Conclusion

Jaundice in pregnancy is rare, but remains clinically important because of serious adverse effects on both the mother and the fetus. These disorders are complex and should be managed by experienced physicians in specialised centres. Maternal and fetal survival can be improved with better understanding of the pathogenesis of these disorders and higher standards of clinical care. Proper timing of delivery, antepartum fetal surveillance, good NICU care could be the modifiable determinants of a good fetal outcome in women with jaundice.

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