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To study the maternal and fetal outcome in women presenting with jaundice in pregnancy: A prospective observational study

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Abstract

Background: Liver diseases during pregnancy present unique challenges, with diverse clinical manifestations, necessitating specialized care to reduce maternal and fetal morbidity and mortality. This study investigated maternal and fetal outcomes in pregnant women presenting with jaundice, shedding light on this complex interplay between liver function and pregnancy.

Materials and Methods: A prospective observational study was conducted at Dr. Rajendra Prasad Government Medical College, spanning one year during 2020. The study included pregnant women presenting with jaundice, abnormal liver function tests, or relevant symptoms. Data was meticulously collected and analyzed, emphasizing demographic factors, clinical presentations and etiology.

Results: The study included 60 participants, with a mean age of 27.08 years. Most women fell within the 19-25 year age group. Pruritus was the predominant complaint (41.7%), indicative of cholestatic liver diseases. Intrahepatic cholestasis of pregnancy (30%) was the most common etiology of jaundice, followed by pre-eclampsia (20%) and hepatitis (13.3%). Maternal complications included blood transfusions (21.6%) and ICU admissions (8.47%). NICU admissions for neonates (47.2%) were primarily due to neonatal jaundice (57.7%). The study reported 6.8% stillbirths and 1.8% neonatal mortality.

Conclusion: Liver diseases in pregnancy require a multidisciplinary approach involving obstetricians, neonatologists, intensivists, hepatologists, and hematologists. Timely diagnosis, prophylaxis for postpartum hemorrhage, and coagulopathy management are essential. Further research and improved clinical practices are needed to enhance the management of liver diseases during pregnancy, ultimately improving patient outcomes.

Keywords: Liver disease, pregnancy, jaundice, maternal outcomes, fetal outcomes, intrahepatic cholestasis, pre-eclampsia, NICU, stillbirth

Introduction

Jaundice, characterized by the yellowing of body tissues due to elevated bilirubin levels, presents a diagnostic challenge in the general population, with various potential causes falling into categories such as pre-hepatic, intrahepatic, and post-hepatic. The unique enzyme profiles associated with each type are critical in pinpointing the underlying etiology and guiding treatment decisions^[1, 2].

While jaundice can affect individuals of all ages, it is most commonly seen in neonates and the elderly. Clinically, jaundice is diagnosed when bilirubin levels exceed 3 mg/dl, and the approach to management depends on the specific cause^[3, 4].

Pregnancy, a distinct physiological state, entails numerous changes in the female body as it nourishes the developing fetus. These changes can result in various discomforts, with nausea and vomiting, often referred to as morning sickness, affecting a significant portion of pregnant individuals. Morning sickness may persist beyond the 20th week in some cases, while severe forms result in hyperemesis gravidarum, marked by weight loss and ketosis. Additionally, progesterone-induced effects can lead to constipation and reflux^[4, 5].

The liver, with its metabolic, synthetic, and excretory functions, is not exempt from these pregnancy-related shifts. Increased estrogen and progesterone levels can alter liver function. Genetic susceptibility may also play a role, with certain individuals being more prone to cholestasis due to reproductive hormones^[6, 7].

Liver function tests (LFTs) demonstrate noticeable changes during pregnancy.

Alkaline phosphatase (ALP) levels increase due to placental production, while albumin and total protein levels decrease. Liver transaminase levels (AST and ALT), gamma glutamyl transferase (GGT), bilirubin levels, and prothrombin time typically remain stable^[8,9].

Pregnancy-related liver conditions include hyperemesis gravidarum, intrahepatic cholestasis of pregnancy, preeclampsia, eclampsia, HELLP syndrome, and acute fatty liver of pregnancy. Each of these conditions is associated with distinct liver enzyme profiles and requires specific management approaches^[9,10].

This study aims to investigate maternal and fetal outcomes in pregnant women presenting with jaundice. Conducted at Dr. Rajendra Prasad Government Medical College, Tanda, this prospective observational study seeks to explore the role of abnormal liver enzyme profiles in maternal and fetal health during pregnancy. By understanding the intricate relationship between liver function and pregnancy-related jaundice, we aim to improve clinical strategies and healthcare outcomes for expectant mothers and infants.

Aims and Objectives

Aim

The primary aim of this study conducted in the Department of Obstetrics and Gynecology at Dr. Rajendra Prasad Government Medical College, Kangra at Tanda, is to comprehensively investigate the maternal and fetal outcomes of antenatal women presenting with clinical features of jaundice during pregnancy.

Objectives

Primary Outcome

- To study the maternal and fetal outcomes of antenatal women presenting with clinical features of jaundice during pregnancy.

Secondary Outcome

- To analyze the clinical profile and determine the etiology of jaundice in pregnant women presenting with this condition.

Materials and Methods

Study Design

This prospective observational study was conducted in the Department of Obstetrics and Gynecology at Dr. Rajendra Prasad Government Medical College, Kangra at Tanda, Himachal Pradesh. The study involved pregnant women who exhibited clinical features of jaundice, elevated bilirubin levels in liver function tests, or those who were referred due to deranged liver function tests.

Study Duration

Data collection, organization, presentation, analysis, and interpretation were carried out over a one-year period, from January to December 2020.

Study Population

The study included all booked, unbooked, and referred pregnant women who presented with recent-onset jaundice or symptoms such as pruritus, fever, increased vomiting, or high blood pressure records during pregnancy.

Inclusion Criteria

- Antenatal patients with clinical manifestations of jaundice during pregnancy.
- Patients with yellowish discoloration of the sclera/skin, pruritus, vomiting, fever, headache, epigastric pain, elevated

bilirubin levels in liver function tests, or those referred with deranged liver function tests during any trimester of pregnancy.

- Cut-off for total serum bilirubin was set at >1.2 mg/dl.

Exclusion Criteria

- Jaundice antecedent to pregnancy.
- Jaundice with onset in the postpartum period.
- Patients who did not consent to participate in the study.
- Patients with other concurrent medical illnesses.

Methodology

Detailed medical histories, including demographic data, obstetric history, and menstrual history, were collected from the patients. Information about current and past pregnancies, symptomatology, and relevant medical history was obtained. General physical examinations, including vital signs and systemic evaluations, were performed. Laboratory investigations were conducted to ascertain the cause of jaundice, and hepatic consultations were sought when necessary. Gestational age was established through menstrual history and clinical examination, confirmed by ultrasound. Patients were followed up during the antepartum, intrapartum, and postpartum periods, with a focus on pregnancy progress and fetal outcomes. Newborns were thoroughly examined, and their outcomes were documented. Patients were followed up after discharge, and any postpartum complications were noted.

Data Collection

Data was collected and recorded in Microsoft Excel.

Statistical Analysis

Demographic variables were analyzed and presented as frequencies and percentages. Epi-Info software was employed for data analysis.

Ethical Issues

The study did not involve drug trials or human/animal experiments. Patients were treated in their best interest, and ethical considerations were diligently observed.

Results & Observations

This was an observational study conducted for one year from January 2020 to December 2020 in the Department of Obstetrics and Gynecology, Dr. Rajendra Prasad Government Medical College, Kangra at Tanda, Himachal Pradesh. The following observations have been made in our present study.

The mean age in the study was 27.08±4.20 years. Twenty-five (41.7%) participants belonged to 19 to 25-year age group, twenty-four (36.7%) in 26 to 30-year age group, twelve (20%) in 31 to 35-year age group and only one (1.7%) belonged to >35 years of age. The mean BMI of the participants was found to be 21.95±1.33. All the participants had their BMI ranging between 18.5 and 24.9. Fifty-seven participants (95%) had a positive booking status, and only three (5%) participants had a negative booking status. Of all the participants enrolled in the study, twenty nine (48.3%) were primigravida and twenty (43%) participants had a gravidity of 2, six (10.1%) had a gravidity of 3 and five (8.4%) participants had a gravidity of 4. Thirty-two (53.3%) participants belonged to the lower socio-economic status, and rest twenty-eight (46.7%) belonged to middle socio-economic status as per Modified Kuppaswamy Scale. The mean gestational age at the time of presentation with hyperbilirubinemia at Dr. R.P.G.M.C. was 32.68 ± 6.64 weeks.

Thirty-four (57%) participants had a period of gestation between 28-36 weeks at presentation, followed by fourteen (23%) participants with a gestational age above 36 weeks at

presentation and twelve (20%) participants had gestational age below 28 weeks at presentation.

Table 1: Distribution of Socio-demographic variables among study participants

Variables	No. (n)	Percent (%)
Age group (in years)		
19-25	25	41.7
26-30	22	36.7
31-35	12	20
>35	1	1.7
Booking status		
Booked	57	95
Unbooked	3	5
Gravida		
1	29	48.3
2	20	43
3	6	10.1
4	5	8.4
Socio-economic status		
Lower	32	53.3
Middle	28	46.7
Total (N)	60	100
Gestational age at the time of presentation		
< 28 weeks	12	20
28 to 36 weeks	34	57
>36 weeks	14	23
Total (N)	60	100

The most common complaint with which the women presented to the OPD, was pruritus presenting in twenty-five (41.7%) of the participants. This was followed by yellowish discoloration of skin (37%), headache (32%), swelling of hands and feet (20%). Vomiting was observed in eleven (18%) participants while abnormal body movements and decreased fetal movements were observed in four (6.7%) patients each. Fever and clay colored stools were observed in two (3%) of the participants each. Thirty-six participants presented with two or more complaints due to which there was a discrepancy in the total number. Of all

the participants enrolled in the study, eighteen (30%) participants had intrahepatic cholestasis of pregnancy (ICP), followed by twelve (20%) participants with pre-eclampsia and eight (13.3%) participants with hepatitis while eclampsia and AFLP was seen in five (8.3%) participants each and two (3.3%) participants had HELLP syndrome. Four (6.7%) participants had hyperemesis gravidarum. Three (5%) had CLD with portal HTN, and one (1.7%) participant each had Budd Chiari syndrome, obstructive jaundice and hemolytic anemia.

Table 2: Distribution of study participants according to Chief complaints and etiology

Variables	No. (n)	Percent (%)
Complaints		
Pruritus	25	41.7%
Yellowish discoloration	22	37
Headache	19	32
Swelling of hands and feet	12	20
Vomiting	11	18
Abnormal body movement	4	6.7
Decreased/ Absent Fetal Movement	4	6.7
Fever	2	3.3
Clay Colored Stools	2	3.3
Etiology		
Intrahepatic Cholestasis of Pregnancy	18	30
Pre-eclampsia	12	20
Hepatitis	8	13.3
Eclampsia	5	8.3
Acute Fatty Liver of Pregnancy	5	8.3
Hyperemesis Gravidarum	4	6.7
CLD with Portal Hypertension	3	5
HELLP syndrome	2	3.3
Budd Chiari Syndrome	1	1.7
Obstructive jaundice- Cholelithiasis	1	1.7
Hemolytic anemia	1	1.7
Total (N)	60	100

Nineteen (32 %) participants were found to be hypertensive while forty-one (68%) patients were normotensive. Serum bilirubin was divided into three categories. Forty-seven (78%) participants had serum bilirubin in between 2-4 g/dl. Seven (12%) participants had the serum bilirubin between 4 and 6 g/dl

and six (10%) participants had it above 6 g/dl. The levels of serum transaminases were also analyzed and twenty-eight (47%) participants had a level between 100 to 400 IU/L, nineteen (32%) participants had it above 400 IU/L, and thirteen (22%) participants had below 100 IU/L.

Table 3: Distribution of study participants according to various clinical and biochemical parameters

Variables	No (n)	Percent (%)
Blood Pressure (n=60)		
Hypertensive	19	32
Normotensive	41	68
Serum Bilirubin(n=60)		
2-4 g/dl	47	78
4-6 g/dl	7	12
>6 g/dl	6	10
Serum Transaminases(n=60)		
<100 IU/L	13	22
100-400 IU/L	28	47
>400 IU/L	19	32
Total (N)	60	100

Of the 60 participants, one (1.7%) had an abortion during the current study. Thirty-seven (61.7%) participants had term deliveries and only twenty-two (36.7%) participants had pre-term deliveries. The mean gestational age of delivery was 36.59 ± 1.86 weeks. Twenty-two (37.3%) participants delivered below 37 weeks and thirty-seven (62.7%) participants delivered beyond 37 weeks of gestation. Of the total, thirty-one (52.5%) participants had spontaneous onset of labor, whereas in twenty-eight (47.5%) participants labor was induced. Forty-six (77.96%) participants had normal vaginal delivery, twelve (20.3%) participants required LSCS, and one (1.7%) had

instrumental assisted delivery. Thirteen (21.6%) participants required blood transfusion, five (8.47%) were admitted in ICU, four (6.8%) each had atonic PPH and hepatorenal failure, esophageal varices and thrombocytopenia in two (3.4%) each and DIC in one (1.69%) participant. Nine participants had more than one complication. Seven patients were referred to PGIMER, Chandigarh who could not be managed at our centre. Five women in the study required ICU admission. Two (40%) participants out of the five were admitted in the ICU due to hepatorenal failure, one (20%) each due to atonic PPH, DIC and encephalopathy.

Table 4: Distribution of study participants according to various maternal outcome

Variables	No (n)	Percent (%)
Outcome of pregnancy (n=60)		
Term deliveries	37	61.7
Preterm deliveries	22	36.7
Abortion	1	1.6
Period of gestation (weeks) (n=59)		
<37 weeks	22	37.3
≥ 37 weeks	37	62.7
Onset of labor(n=59)		
Spontaneous	31	52.5
Induced	28	47.5
Mode of delivery(n=59)		
Vaginal	46	77.96
Assisted instrumental	1	1.7
Caesarean	12	20.3
Maternal complications(n=59)		
Blood/ blood component transfusion	13	21.6
ICU admissions	5	8.47
Atonic PPH	4	6.8
Hepatorenal failure	4	6.8
Esophageal varices	2	3.4
Thrombocytopenia	2	3.4
DIC	1	1.69
Reasons for ICU admissions(n=5)		
Hepato-renal failure	2	40
Atonic PPH	1	20
DIC	1	20
Encephalopathy	1	20

Out of the 59 deliveries, fifty-five (93.2%) had live births while four (6.8%) had stillbirths. Stillbirths were seen 2 patients of ICP, 1 patient of AFLP and 1 patient of eclampsia. Ten (18.2%) neonates born had Apgar of < 7 at 1 minute of birth while two (3.6%) neonates had Apgar < 7 at 5 minutes. Forty-five (81.8%) neonates had Apgar score of ≥ 7 at 1 minute and fifty-three (96.36%) neonates had Apgar score of ≥ 7 at 5 minutes. It was observed that four (7.3%) neonates required some kind of resuscitation. Out of them, three (5.5%) required bag and mask ventilation and one (1.8%) required intubation. Prematurity was observed in twenty-two (40%) newborns, hypoglycemia was seen in five (9%) and sepsis in one (1.8%). It was observed that twenty-six (47.2%) newborns were admitted in the NICU and there was one (1.8%) early neonatal death on 2nd postnatal day due to hypoxic ischemic encephalopathy. Of the total newborns admitted in NICU, fifteen (57.7%) were due to neonatal jaundice, nine (34.6%) due to low birth weight and two (7.7%) due to birth asphyxia.

Table 5: Distribution of study participants according to various neonatal outcome

Variables	No (n)	Percent (%)
Neonatal outcomes (n=59)		
Live births	55	93.2
Still births	4	6.8
Apgar (n=55)		
	At 1 minute n (%)	At 5 minutes n (%)
<7	10 (18.2)	2 (3.6)
≥ 7	45 (81.8)	53 (96.36)
Neonatal Resuscitation (n=55)		
Not required	51	92.7
Bag and mask	3	5.5
Endotracheal tube	1	1.8
Neonatal complications (n=55)		
Prematurity	22	40
Sepsis	1	1.8
Hypoglycemia	5	9
Low birth weight	23	41.8
Neonatal jaundice	15	57.7
Birth asphyxia	4	7.3
Early neonatal outcomes (n=27)		
NICU admissions	26	47.2
Early neonatal death	1	1.8
Reasons for NICU admissions (n=26)		
Jaundice	15	57.7
Low birth weight	9	34.6
Birth asphyxia	2	7.7

Discussion

This study delves into the intricate dynamics of liver diseases during pregnancy, which can present as mild conditions with elevated liver enzymes or as severe entities culminating in liver failure, jeopardizing both maternal and fetal well-being. This discussion provides a comprehensive analysis of the study's findings in the context of the existing body of research on liver diseases during pregnancy.

The study's participants spanned a range of ages, from 19 to 38 years, with a mean age of 27.08 years (SD: 26). This age distribution is consistent with a study by Demir CS *et al.* [11], which reported a mean age of 28.42 years. Notably, the majority of patients fell within the 19 to 25-year age group. However, it's important to acknowledge the evolving trend of delayed marriages in contemporary society, which might influence the age distribution of pregnant women.

In terms of gravidity, the study revealed that 51.7% of the patients were multigravidas, a finding consistent with similar

research conducted by Negi LM *et al.* [12] and K.V.S.M. Sandhya Devi and Y.V.L. Bhavani [13]. This observation underscores the importance of considering the gravidity of patients when managing liver diseases during pregnancy.

Regarding the socioeconomic status of the participants, the study indicated that nearly 53.3% of women belonged to the low-income group, while 46.7% belonged to the medium-income group. These findings align with research conducted by Dsouza AS *et al.* [14], which reported that 62.7% of women were from the low-income group. Understanding the socioeconomic distribution of patients is crucial, as it reflects healthcare accessibility and potential disparities in care.

The study highlighted that a substantial portion (80%) of women presented to the hospital with hyperbilirubinemia after 28 weeks of gestation, a finding consistent with Negi LM *et al.* [12], where 89.7% of women presented after 28 weeks. The late presentation during the late second and third trimesters reflects the timing of manifestation of most liver ailments during pregnancy.

Pruritus emerged as the most common presenting complaint in 41.7% of the women, followed by yellowish discoloration of the skin (37%) and headache (32%). These symptoms are typical of cholestatic liver diseases, with intrahepatic cholestasis of pregnancy (ICP) being the most common cause of jaundice, as observed in this study. These findings align with similar research by Sharma S, *et al.*, Dsouza AS *et al.* [14], and Negi LM *et al.* [12]. Pregnancy-induced hypertension was prevalent in 32% of the women in this study, similar to the findings of Sharma S *et al.* The most common cause of jaundice was intrahepatic cholestasis of pregnancy (30%), followed by pre-eclampsia (20%), hepatitis (13.3%), and eclampsia and acute fatty liver of pregnancy (AFLP) in 8.3% of cases. This distribution is in agreement with Dsouza AS *et al.* [14] and Acharya N *et al.* [15], although viral hepatitis was less prevalent in this study.

Cholestatic jaundice, particularly intrahepatic cholestasis of pregnancy, emerged as the leading cause of liver dysfunction associated with pregnancy (30%), consistent with research conducted by Acharya N *et al.* [15] and Negi LM *et al.* [12]. The lower prevalence of hepatitis (13.3%) could be attributed to improved sanitation and infectious disease control measures, reducing the incidence of waterborne diseases.

In terms of pregnancy outcomes, the study reported that 61.7% had term deliveries, while 36.7% experienced preterm deliveries, with 1.6% resulting in abortion. These findings are in line with observations made by Negi LM *et al.* [12], Oladokun *et al.* [16], and R Fathima Hasan *et al.* [17].

The distribution between spontaneous and induced labor was balanced in this study, with 77.96% experiencing spontaneous onset and 47.5% having induced labor. The mode of delivery was predominantly vaginal (77.96%), while 20.3% underwent cesarean sections, consistent with Krishnamoorthy *et al.* [18], R Fathima Hasan *et al.* [17], and Negi LM *et al.* [12].

The study emphasized the maternal complications associated with jaundice during pregnancy, with 21.6% of patients requiring blood or blood component transfusions. Additionally, 8.47% of cases necessitated ICU admissions due to complications such as atonic postpartum hemorrhage (PPH), hepatorenal failure, and the presence of esophageal varices. The study noted a relatively low incidence of disseminated intravascular coagulation (DIC) at 1.69%. These findings align with similar research by Negi LM *et al.* [12] and Jyothi GS *et al.* [19], emphasizing the need for a comprehensive approach and the importance of proper medical facilities, including 24-hour blood banks.

This study further examined cases admitted to the ICU and

found that hepatorenal syndrome (40%) was the primary reason for admission. DIC was observed in cases of eclampsia, and encephalopathy was seen in patients with eclampsia (20%), highlighting the various complications related to liver diseases during pregnancy.

In terms of neonatal outcomes, the study reported that 93.2% of births were live births, with a stillbirth rate of 6.8%. These findings are in accordance with research conducted by R Fathima Hasan *et al.* [17], Negi LM *et al.* [12], Jyothi GS *et al.* [19], and Afshaan Ambreen *et al.* [20]. Furthermore, the study noted that 3.6% of neonates had an APGAR score of less than 7 at 5 minutes, a lower rate than in the study by Sunanda KM *et al.* [21]. Common neonatal complications in this study included low birth weight (41.8%), prematurity (40%), and hypoglycemia (9%). Neonatal mortality was found to be 1.8%, which occurred on the second day of life due to hypoxic ischemic encephalopathy. A significant percentage (47.2%) of neonates required admission to the neonatal intensive care unit (NICU), with neonatal hyperbilirubinemia being the most common reason (57.7%), followed by low birth weight (34.6%) and birth asphyxia (7.7%).

Limitations

A noteworthy limitation of this study is related to the sample size, as it was conducted during the challenging backdrop of the COVID-19 pandemic when there was a noticeable reduction in patient attendance at Dr. Rajendra Prasad Government Medical College. Consequently, the study could only include a limited sample of sixty patients. The restricted sample size was primarily a result of the reduced footfall in outpatient departments during the pandemic, thus warranting consideration when interpreting the findings and generalizing them to a broader population.

Conclusion

In conclusion, liver diseases in pregnancy exhibit a spectrum of clinical presentations, underscoring the need for comprehensive care at tertiary centers to mitigate maternal and fetal morbidity and mortality. Timely diagnosis and interventions, including postpartum hemorrhage prophylaxis and ensuring the availability of blood components for coagulopathy management, are imperative. Close monitoring of both mother and fetus is essential, necessitating a collaborative approach involving obstetricians, neonatologists, intensivists, hepatologists, and hematologists. This multidisciplinary teamwork is crucial for optimizing the care of expectant mothers and their infants. Ongoing research and enhanced clinical practices remain essential to further improve the management of liver diseases during pregnancy and enhance patient outcomes.

Conflict of Interest

Not available

Financial Support

Not available

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