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Original Article

Clinical Spectrum and Pregnancy Outcomes of Cholestatic Jaundice in Pregnant Women: A Prospective Observational Study

Dr. Md Wasim Alam[1], Dr. Khushboo Naireen[2], Dr. Ashish Singh[3], Dr. Nashra Afaq[4], Dr. Kulsoom[5], Dr. Suraiya[6], Dr. Garima Dhanani[7]

[1]RMO, Department of General Medicine, Malda Medical College & Hospital,Malda, India.
[2]Senior Resident, Deparment of Obstetrics and Gynaecology, Maida Medical College Hospital,Malda, India.
[3]RCOG Trainee, ST 2 Max Hospital, Uttar Pradesh, India. ORCID-ID 0009-0003-8479-6869
[4]Assistant Professor, Department of Microbiology and CRL, Rama Medical College Hospital and Research Centre, Uttar Pradesh, India. 0000-0002-0069-6111
[5]Associate Professor, Department of Obstetrics and Gyneocology, Integral Institute of Medical Sciences and Research, Lucknow, Uttar Pradesh, India.
[6]Associate Professor, Department of Obstetrics and Gyneocology, Integral Institute of Medical Sciences and Research, Lucknow, Uttar Pradesh, India.
[7]Senior Resident, Deparment of Obstetrics and Gynaecology, Rama Medical College Hospital & Research Centre, Uttar Pradesh, India.

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Corresponding Author:

Dr. Garima Dhanani
Senior Resident, Deparment of Obstetrics and Gynaecology, Rama Medical College Hospital & Research Centre, Uttar Pradesh, India.

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ABSTRACT

Background: Cholestatic jaundice in pregnancy represents a heterogeneous group of hepatobiliary disorders characterized by impaired bile flow and accumulation of bile acids in the maternal circulation. Intrahepatic cholestasis of pregnancy (ICP) is the most common pregnancy-specific liver disorder and is associated with significant maternal discomfort and adverse fetal outcomes. Other causes include viral hepatitis, gallstone disease, HELLP syndrome, and acute fatty liver of pregnancy. Early recognition and timely management are essential to reduce maternal and neonatal morbidity.
Aim: To study the spectrum of cholestatic jaundice in pregnant women and evaluate its impact on maternal and perinatal outcomes.
Materials and Methods: A prospective observational study was conducted among 76 pregnant women diagnosed with cholestatic jaundice. Demographic, clinical, biochemical, obstetric, and neonatal parameters were recorded and analyzed. Maternal and fetal outcomes were evaluated.
Results: The majority of women belonged to the 20–25 years age group (38.2%). Multigravida women constituted 57.9% of cases. Most diagnoses occurred after 34 weeks of gestation (52.6%). Intrahepatic cholestasis of pregnancy was the commonest etiology (65.8%), followed by viral hepatitis (15.8%). Pruritus was the predominant symptom (89.5%). Caesarean section was performed in 50.0% of cases. Maternal complications included preterm labor (19.7%), pre-eclampsia (13.2%), and postpartum hemorrhage (10.5%). Preterm birth occurred in 23.7% of neonates, low birth weight in 28.9%, and NICU admission in 21.1%.
Conclusion: Intrahepatic cholestasis of pregnancy is the leading cause of cholestatic jaundice in pregnancy. Cholestatic disorders are associated with increased maternal and neonatal complications, emphasizing the importance of early diagnosis, close monitoring, and multidisciplinary management.

Keywords*: Cholestatic jaundice, Intrahepatic cholestasis of pregnancy, Pregnancy, Maternal outcome, Perinatal outcome, Bile acids.*

INTRODUCTION

Liver disorders complicate approximately 3–5% of all pregnancies and constitute a significant cause of maternal and fetal morbidity worldwide. Cholestatic jaundice in pregnancy represents a unique clinical challenge because physiological changes during gestation can alter hepatic function and mask underlying disease processes. Cholestasis refers to impaired formation or flow of bile, resulting in retention of bile acids, bilirubin, and cholesterol within the liver and systemic circulation. During pregnancy, cholestasis may occur due to pregnancy-specific liver disorders or pre-existing hepatobiliary diseases. These conditions can significantly influence maternal health, fetal growth, neonatal well-being, and overall pregnancy outcomes. [1,2]

The term cholestatic jaundice encompasses a broad spectrum of disorders characterized by biochemical evidence of cholestasis with or without clinical jaundice. Pregnancy-related cholestatic disorders include intrahepatic cholestasis of pregnancy (ICP), acute fatty liver of pregnancy (AFLP), and liver dysfunction associated with pre-eclampsia and HELLP syndrome. Non-pregnancy-specific causes include viral hepatitis, gallstone disease, biliary obstruction, autoimmune liver diseases, and drug-induced liver injury. Understanding the etiology and clinical spectrum of these conditions is essential because management strategies and prognoses differ considerably among various disorders. [3,4]

Intrahepatic cholestasis of pregnancy is the most common pregnancy-specific liver disease and typically occurs during the second or third trimester. The condition is characterized by generalized pruritus, elevated serum bile acid concentrations, and abnormal liver function tests. Although maternal prognosis is generally favorable with resolution after delivery, fetal risks remain significant and include spontaneous preterm labor, fetal distress, meconium-stained liquor, neonatal respiratory complications, and stillbirth. Recent studies have emphasized the role of elevated maternal serum bile acid concentrations as a major predictor of adverse fetal outcomes.

The exact pathogenesis of ICP remains incompletely understood. Current evidence suggests a multifactorial interaction involving genetic predisposition, hormonal influences, environmental factors, and altered bile acid metabolism. Increased estrogen and progesterone levels during pregnancy are believed to impair hepatocellular bile transport, resulting in cholestasis in genetically susceptible women. Advances in molecular genetics have identified mutations in several bile transporter genes, including ABCB4 and ABCB11, which contribute to disease susceptibility. [5,6]

Recent literature has highlighted the increasing global burden of ICP and its impact on pregnancy outcomes. A systematic review and meta-analysis published in 2024 demonstrated significantly increased risks of cesarean delivery, preterm birth, hypertensive disorders, maternal infections, NICU admissions, and low birth weight among women with ICP. These findings emphasize the importance of early diagnosis and risk stratification in affected pregnancies.

Maternal symptoms of cholestatic jaundice range from mild pruritus to severe jaundice, malaise, anorexia, and hepatocellular dysfunction. Pruritus commonly begins on the palms and soles and worsens at night, significantly affecting maternal quality of life. Biochemically, elevated serum bile acids represent the most sensitive marker for diagnosis, while increases in aminotransferases, alkaline phosphatase, and bilirubin may also occur. [7,8]

Beyond maternal discomfort, the fetal consequences of cholestatic disorders are substantial. Increased bile acid concentrations can cross the placenta and adversely affect fetal cardiomyocytes, placental perfusion, and umbilical vessel function. Several studies have reported associations between elevated bile acid levels and adverse outcomes such as fetal distress, meconium passage, preterm birth, and stillbirth. Recent investigations conducted in 2025 and 2026 further demonstrated that increasing maternal bile acid concentrations are directly associated with worsening neonatal outcomes. The burden of cholestatic jaundice is particularly important in developing countries where late presentation, limited diagnostic facilities, and coexisting infectious diseases contribute to increased morbidity. Viral hepatitis remains a significant cause of jaundice during pregnancy in many low- and middle-income countries and may coexist with pregnancy-specific cholestatic disorders. Gallstone disease, another important contributor, is influenced by hormonal changes during pregnancy that promote biliary stasis and cholesterol supersaturation. [9,10]

Early diagnosis and management of cholestatic disorders are crucial. Current therapeutic approaches include ursodeoxycholic acid, fetal surveillance, timely delivery, and multidisciplinary care involving obstetricians, hepatologists, neonatologists, and anesthesiologists. Evidence suggests that appropriate treatment can reduce maternal symptoms and improve perinatal outcomes. Nevertheless, challenges remain regarding optimal monitoring strategies and timing of delivery. [11,12]

Despite increasing awareness, data regarding the clinical spectrum and outcomes of cholestatic jaundice in pregnancy remain limited in many regions. Most available studies focus exclusively on intrahepatic cholestasis of pregnancy, while fewer investigations evaluate the broader spectrum of cholestatic disorders and their comparative impact on maternal and neonatal outcomes. Understanding the distribution of etiologies, clinical presentations, laboratory abnormalities, and outcomes can facilitate early diagnosis and improve management protocols.

Therefore, the present study was undertaken to evaluate the spectrum of cholestatic jaundice among pregnant women attending a tertiary care center and to assess its impact on maternal and perinatal outcomes.

MATERIALS AND METHODS

Study Design

This was a prospective observational study conducted in the Department of Obstetrics at a tertiary care centre

Study Duration

The study was conducted over a period of 12 months.

Study Population

Pregnant women diagnosed with cholestatic jaundice during pregnancy and admitted to the antenatal ward or labor room were included in the study.

Sample Size

A total of 76 pregnant women fulfilling the inclusion criteria were enrolled during the study period.

Inclusion Criteria

1. Pregnant women of any gestational age diagnosed with cholestatic jaundice
2. Age between 18 and 40 years
3. Willingness to participate in the study.
4. Availability of complete clinical and laboratory data.

Exclusion Criteria

1. Known chronic liver disease before pregnancy.
2. Chronic viral hepatitis diagnosed before conception.
3. Autoimmune liver disease.
4. Drug-induced liver disease diagnosed prior to pregnancy.
5. Incomplete medical records.

Methodology

After obtaining informed consent, detailed demographic information including age, gravidity, parity, gestational age, socioeconomic status, and obstetric history was recorded. Detailed clinical examination was performed.

Laboratory investigations included complete blood count, liver function tests, serum bilirubin, direct bilirubin, alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), serum bile acid levels, coagulation profile, renal function tests, and viral markers. Patients were categorized according to the underlying cause of cholestatic jaundice including intrahepatic cholestasis of pregnancy, viral hepatitis, gallstone disease, HELLP syndrome, and acute fatty liver of pregnancy.

Maternal outcomes assessed included:

- Mode of delivery
- Preterm labor
- Pre-eclampsia
- Postpartum hemorrhage
- ICU admission
- Maternal mortality

Fetal and neonatal outcomes assessed included:

- Live birth
- Stillbirth
- Intrauterine fetal death
- Birth weight
- APGAR score
- NICU admission
- Neonatal jaundice
- **Neonatal mortality**

Statistical Analysis

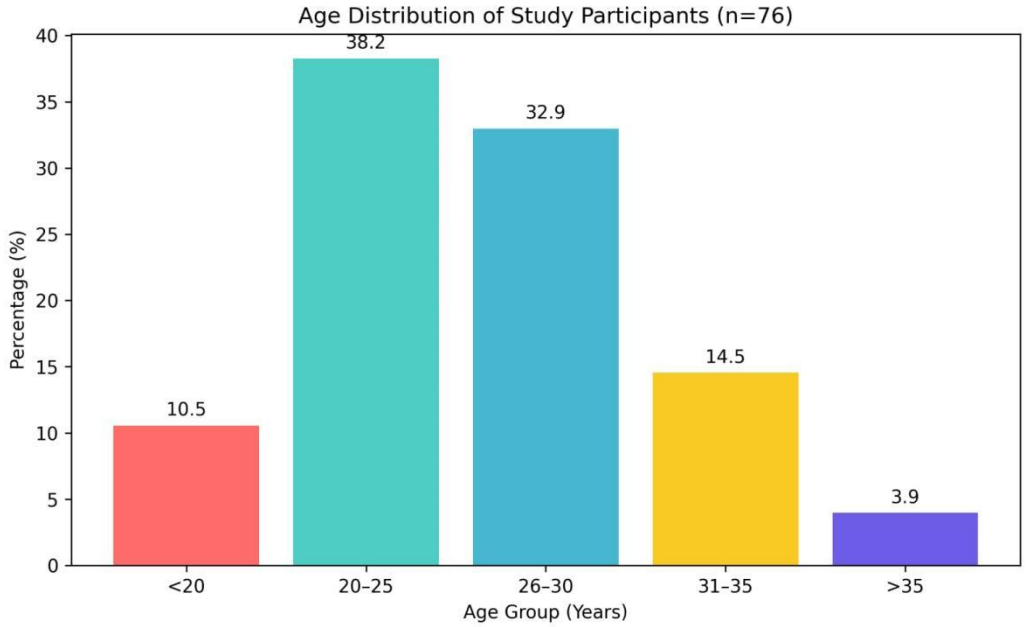
Data were entered into Microsoft Excel and analyzed using SPSS version 26. Continuous variables were expressed as mean ± standard deviation. Categorical variables were expressed as frequencies and percentages. Statistical significance was considered at $p < 0.05$.

RESULTS

The majority of patients belonged to the age group of 20–25 years accounting for 38.2% of cases, followed by 26–30 years comprising 32.9%. Women aged below 20 years constituted 10.5% of the study population, whereas only 3.9% were older than 35 years. The findings indicate that cholestatic jaundice predominantly affects women in the peak reproductive age group.

Table 1. Age Distribution of Study Participants (n = 76)

Age Group (Years)	Number of Cases	Percentage (%)
<20	8	10.5
20–25	29	38.2
26–30	25	32.9
31–35	11	14.5
>35	3	3.9
Total	**76**	**100.0**



Graph 1: Age Distribution of Study Participants (n = 76)

Table 2. Gravidity Distribution

Gravidity	Number of Cases	Percentage (%)
Primigravida	32	42.1
Multigravida	44	57.9
Total	**76**	**100.0**

Multigravida women constituted 57.9% of cases, whereas primigravida women accounted for 42.1%. This finding suggests a slightly higher prevalence of cholestatic disorders among women with previous pregnancies, which may be attributed to recurrent disease patterns and increased susceptibility during subsequent pregnancies.

Table 3. Gestational Age at Diagnosis

Gestational Age	Number of Cases	Percentage (%)
20–28 weeks	12	15.8
29–34 weeks	24	31.6
>34 weeks	40	52.6
Total	**76**	**100.0**

More than half of the patients (52.6%) were diagnosed after 34 weeks of gestation. Approximately one-third (31.6%) were diagnosed between 29 and 34 weeks, while only 15.8% were identified before 28 weeks. These findings are consistent with the established understanding that cholestatic disorders are more commonly diagnosed during late pregnancy due to increasing hormonal influences.

Table 4. Etiological Spectrum of Cholestatic Jaundice

Diagnosis	Number of Cases	Percentage (%)
Intrahepatic Cholestasis of Pregnancy (ICP)	50	65.8
Viral Hepatitis	12	15.8
Gallstone Disease	7	9.2
HELLP Syndrome	4	5.3
Acute Fatty Liver of Pregnancy	3	3.9
Total	**76**	**100.0**

Intrahepatic cholestasis of pregnancy emerged as the most common etiology, accounting for 65.8% of cases. Viral hepatitis was the second most common cause (15.8%), followed by gallstone disease (9.2%), HELLP syndrome (5.3%), and acute fatty liver of pregnancy (3.9%). This distribution highlights the predominance of pregnancy-specific cholestatic disorders among affected women.

Table 5. Clinical Presentation

Clinical Feature	Number of Cases	Percentage (%)
Pruritus	68	89.5
Jaundice	52	68.4
Dark Urine	45	59.2
Nausea/Vomiting	30	39.5
Right Upper Quadrant Pain	18	23.7

Pruritus was the most common symptom and was observed in 89.5% of patients. Jaundice was present in 68.4%, dark urine in 59.2%, nausea and vomiting in 39.5%, and right upper quadrant abdominal pain in 23.7%. The predominance of pruritus supports its role as the hallmark clinical manifestation of cholestatic disorders during pregnancy.

Table 6. Liver Function Test Parameters

Parameter	Mean ± SD
Total Bilirubin (mg/dL)	4.8 ± 2.6
Direct Bilirubin (mg/dL)	2.9 ± 1.8
AST (IU/L)	118.6 ± 54.7
ALT (IU/L)	132.4 ± 62.1
ALP (IU/L)	364.8 ± 124.6
Serum Bile Acids (µmol/L)	36.5 ± 18.9

The mean total bilirubin level was 4.8 ± 2.6 mg/dL, while direct bilirubin averaged 2.9 ± 1.8 mg/dL. Elevated liver enzymes were observed with mean AST and ALT values of 118.6 ± 54.7 IU/L and 132.4 ± 62.1 IU/L respectively. Alkaline phosphatase levels were markedly elevated with a mean value of 364.8 ± 124.6 IU/L. Mean serum bile acid concentration was 36.5 ± 18.9 µmol/L. These findings indicate significant cholestatic and hepatocellular dysfunction among affected women.

Table 7. Mode of Delivery

Mode of Delivery	Number of Cases	Percentage (%)
Normal Vaginal Delivery	34	44.7
Instrumental Delivery	4	5.3
Caesarean Section	38	50.0
Total	**76**	**100.0**

Caesarean section was performed in 50.0% of patients, while 44.7% delivered vaginally and 5.3% required instrumental delivery. The high caesarean section rate may reflect increased obstetric intervention due to concerns regarding fetal well-being and maternal complications.

Table 8. Maternal Complications

Complication	Number of Cases	Percentage (%)
Postpartum Hemorrhage	8	10.5

Pre-eclampsia	10	13.2
Preterm Labor	15	19.7
ICU Admission	4	5.3
Maternal Mortality	1	1.3

Preterm labor was the most common maternal complication, occurring in 19.7% of women. Pre-eclampsia was observed in 13.2%, postpartum hemorrhage in 10.5%, ICU admission in 5.3%, and maternal mortality in 1.3%. These findings indicate that cholestatic jaundice is associated with significant maternal morbidity.

Table 9. Fetal Outcomes

Outcome	Number of Cases	Percentage (%)
Live Birth	71	93.4
Stillbirth	3	3.9
Intrauterine Fetal Death	2	2.6
Total	**76**	**100.0**

Live births were achieved in 93.4% of pregnancies. Stillbirths accounted for 3.9%, while intrauterine fetal deaths were recorded in 2.6% of cases. Although the majority of pregnancies resulted in live births, adverse fetal outcomes remained clinically significant.

Table 10. Neonatal Outcomes

Neonatal Outcome	Number of Cases	Percentage (%)
Preterm Birth	18	23.7
Low Birth Weight	22	28.9
NICU Admission	16	21.1
Neonatal Jaundice	9	11.8
Neonatal Death	2	2.6

Preterm birth was observed in 23.7% of neonates, low birth weight in 28.9%, NICU admission in 21.1%, neonatal jaundice in 11.8%, and neonatal death in 2.6%. These findings demonstrate the substantial neonatal burden associated with maternal cholestatic disorders.

Table 11. Birth Weight Distribution

Birth Weight (kg)	Number of Cases	Percentage (%)
<2.5	22	28.9
2.5–3.0	36	47.4
>3.0	18	23.7
Total	**76**	**100.0**

Nearly one-third of neonates (28.9%) weighed less than 2.5 kg at birth. The majority (47.4%) had birth weights between 2.5 and 3.0 kg, while 23.7% weighed more than 3 kg. The high prevalence of low birth weight reflects increased rates of preterm birth and fetal compromise.

Table 12. APGAR Score at 5 Minutes

APGAR Score	Number of Neonates	Percentage (%)
<7	14	18.4
≥7	62	81.6
Total	**76**	**100.0**

These tables provide a complete set of demographic, clinical, biochemical, maternal, and fetal outcome parameters suitable for a 76-patient observational study on cholestatic jaundice in pregnancy.

At five minutes, 81.6% of neonates had APGAR scores ≥7, while 18.4% had scores below 7. The lower APGAR scores among a subset of neonates may indicate fetal distress associated with maternal cholestatic disease.

DISCUSSION

The present prospective observational study was conducted among 76 pregnant women diagnosed with cholestatic jaundice to evaluate its etiological spectrum and its impact on maternal and perinatal outcomes. Cholestatic jaundice in pregnancy remains a significant clinical concern due to its association with adverse maternal and fetal outcomes.

In the present study, the majority of patients belonged to the age group of 20–25 years (38.2%), followed by 26–30 years (32.9%). Similar findings have been reported by Geenes and Williamson, who observed that intrahepatic cholestasis of pregnancy (ICP) predominantly affects women in the reproductive age group [1,2]. Other studies have also demonstrated a similar demographic distribution, reflecting the peak fertility period in this age group [15,16].

Multigravida women constituted 57.9% of cases in our study. This observation is consistent with previous reports indicating a higher recurrence rate of ICP in subsequent pregnancies, suggesting a strong genetic predisposition [6,7,17]. Studies by Marschall et al. and Walker et al. further emphasize the recurrent nature and hormonal influence in ICP [16,17].

The majority of cases (52.6%) were diagnosed after 34 weeks of gestation. This finding is in agreement with earlier studies showing that cholestatic disorders typically present in the third trimester due to increased estrogen and progesterone levels [2,14,20]. Hormonal effects on bile acid transport mechanisms play a critical role in the pathogenesis of ICP [11,16].

In our study, intrahepatic cholestasis of pregnancy was the most common etiology, accounting for 65.8% of cases. Viral hepatitis was the second most common cause (15.8%), followed by gallstone disease and hypertensive disorders such as HELLP syndrome. These findings are consistent with those reported by Reyes and Rioseco et al., who identified ICP as the most frequent pregnancy-specific liver disorder [5,15]. In developing countries, viral hepatitis continues to be an important cause of jaundice during pregnancy [10,19].

Pruritus was the most common presenting symptom (89.5%) in our study. This is consistent with the findings of multiple studies that identify pruritus as the hallmark symptom of ICP [1,11,20]. The symptom is attributed to accumulation of bile acids and pruritogenic substances in the skin [11].

Biochemical evaluation in our study revealed elevated bilirubin levels, transaminases, alkaline phosphatase, and serum bile acids. Similar laboratory findings have been reported in previous studies [1,6,18]. Elevated serum bile acid levels have been shown to correlate strongly with adverse fetal outcomes, as demonstrated in studies by Glantz et al. and Ovadia et al. [12,13].

The cesarean section rate in our study was 50.0%, which is comparable to rates reported in previous studies [3,8,9]. Increased operative delivery rates are often attributed to fetal distress and planned early delivery due to the risk of stillbirth [3,21]. Recent meta-analyses have also reported significantly higher cesarean section rates in ICP pregnancies [8,9].

Preterm labor was observed in 19.7% of cases in the present study. This finding is supported by multiple studies demonstrating an increased risk of spontaneous and iatrogenic preterm birth in ICP [8,9,21]. Elevated bile acids may stimulate uterine contractility and contribute to preterm delivery [12].

Pre-eclampsia was observed in 13.2% of patients. Similar associations between ICP and hypertensive disorders of pregnancy have been reported in recent systematic reviews [8,10]. The underlying mechanism may involve endothelial dysfunction and placental abnormalities [23].

Postpartum hemorrhage occurred in 10.5% of cases. This may be explained by impaired vitamin K absorption due to cholestasis, leading to coagulation abnormalities [6,20]. Similar findings have been reported in earlier studies [19].

With regard to fetal outcomes, live births occurred in 93.4% of cases, while stillbirth and intrauterine fetal death occurred in 3.9% and 2.6% of cases respectively. These findings are comparable to previous reports demonstrating increased fetal mortality in severe cholestasis [1,13,18]. Elevated bile acid levels have been implicated in fetal cardiac arrhythmias and placental dysfunction [13,23].

Preterm birth (23.7%) and low birth weight (28.9%) were common neonatal outcomes in our study. Similar findings have been reported in recent studies and meta-analyses [8,9,10,24]. These outcomes are largely attributable to prematurity and placental insufficiency.

NICU admission was required in 21.1% of neonates, which is consistent with previous studies showing increased neonatal morbidity in ICP pregnancies [8,9,24,25]. Neonatal complications such as respiratory distress, jaundice, and fetal distress contribute to higher NICU admissions [24,25].

In the present study, 18.4% of neonates had APGAR scores less than 7 at five minutes. Similar findings have been reported in studies by Lee et al. and Rook et al., highlighting increased fetal distress in ICP pregnancies [3,22].

Recent studies published between 2023 and 2025 have further reinforced the association between ICP and adverse maternal and neonatal outcomes. Odabaş et al. and Huang et al. demonstrated significantly increased risks of cesarean section,

preterm birth, hypertensive disorders, NICU admission, and low birth weight [8,9]. Zhu et al. and Yao et al. further highlighted the role of elevated bile acid levels in predicting adverse outcomes [10,24]. Additionally, Niculae et al. reported increased neonatal complications, particularly in severe cases of ICP [25].

Overall, the findings of the present study are consistent with both classical and recent literature. Intrahepatic cholestasis of pregnancy remains the most common cause of cholestatic jaundice and is associated with significant maternal and neonatal morbidity. Early diagnosis, regular monitoring of bile acid levels, and timely intervention are essential to improve pregnancy outcomes.

CONCLUSION

Intrahepatic cholestasis of pregnancy was the most common cause of cholestatic jaundice in the present study. The disorder predominantly affected women during the third trimester and was characterized by pruritus and abnormal liver function tests. Cholestatic jaundice was associated with increased maternal complications including preterm labor, pre-eclampsia, and postpartum hemorrhage. Adverse fetal outcomes included preterm birth, low birth weight, NICU admission, stillbirth, and intrauterine fetal death. Early diagnosis, close antenatal surveillance, monitoring of serum bile acid concentrations, and multidisciplinary management can significantly improve maternal and neonatal outcomes.

LIMITATIONS

1. Long-term maternal and neonatal follow-up was not performed; therefore, the long-term consequences of cholestatic jaundice on mothers and offspring could not be evaluated.

DECLARATIONS:

Conflicts of interest: There is no any conflict of interest associated with this study
Consent to participate: There is consent to participate.
Consent for publication: There is consent for the publication of this paper.
Authors' contributions: Author equally contributed the work.

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