GMR
The Original

A STUDY TO DETERMINE THE PREVALENCE OF PRURITUS IN PREGNANT WOMEN AND ITS CORRELATION WITH OBSTETRICS CHOLESTASIS IN PREGNANCY AND ITS FETOMATERNAL OUTCOMES

Dr. Shanmathi K.A[1*], Prof.Dr.Meena T.S[2], Dr. Jasmine Kavitha Washington[3]

[1*]Final year Postgraduate, Department of Obstetrics and Gynaecology, Sree Balaji Medical College and Hospital, Chennai, Tamil Nadu, India, Email: shanmathikiran@gmail.com, ORCID iD: 0009-0006-8421-4648
[2]Head of the Department and Professor, Department of Obstetrics and Gynaecology, Sree Balaji Medical College and Hospital, Chennai, Tamil Nadu, India, Email: meenats@gmail.com, ORCID iD : 0009-0000-7879-6254
[3]Assistant Professor, Department of Obstetrics and Gynaecology, Sree Balaji Medical College and Hospital, Chennai, Tamil Nadu, India, Email: drkavithawahington@gmail.com, ORCID iD : 0009-0005-3313-6494

ABSTRACT

Background: Pruritus is a common symptom during pregnancy and may represent the earliest clinical manifestation of intrahepatic cholestasis of pregnancy (ICP), a pregnancy-specific liver disorder associated with significant maternal and fetal complications. Early diagnosis is essential for improving pregnancy outcomes.

Methods: A hospital-based prospective observational study was conducted among 245 pregnant women presenting with pruritus at a tertiary care teaching hospital over 18 months. Detailed clinical evaluation, liver function tests, serum bile acid estimation, and obstetric assessment were performed. Participants were categorized into ICP and non-ICP groups based on clinical and biochemical findings and followed until delivery. Maternal and neonatal outcomes were compared using appropriate statistical tests, with a p-value of <0.05 considered statistically significant.

Results: Among the 245 participants, 60 women (24.5%) were diagnosed with ICP. The majority developed pruritus between 28 and 32 weeks of gestation (31.8%). Women with ICP showed significantly greater involvement of the palms and soles, generalized pruritus, elevated liver enzymes, and abnormal serum bile acid levels. Maternal complications, including gestational diabetes mellitus (20.0%), preterm premature rupture of membranes (10.0%), preterm delivery (40.0%), and lower segment caesarean section (58.3%), were significantly more common among women with ICP. Neonatal outcomes such as meconium-stained liquor (43.3%), intrauterine growth restriction (16.7%), neonatal intensive care unit admission (35.0%), and Apgar score <7 at 5 minutes (13.3%) were also significantly higher in the ICP group.

Conclusion: Nearly one-fourth of pregnant women presenting with pruritus had intrahepatic cholestasis of pregnancy. ICP was significantly associated with adverse maternal and neonatal outcomes. Early recognition of persistent pruritus, prompt biochemical evaluation, and timely obstetric management are essential to reduce fetomaternal morbidity and improve pregnancy outcomes.

KEYWORDS: Intrahepatic cholestasis of pregnancy; Pruritus; Pregnancy; Serum bile acids; Fetomaternal outcomes; Preterm delivery; Neonatal intensive care unit; Liver function tests.

INTRODUCTION

Pregnancy is associated with profound physiological, hormonal, metabolic, immunological, and vascular adaptations that facilitate fetal growth and development while maintaining maternal homeostasis. These physiological alterations also increase susceptibility to several systemic disorders, including hepatobiliary diseases and pregnancy-specific dermatoses. Among the dermatological manifestations, pruritus is one of the most frequently encountered symptoms during pregnancy, affecting approximately 15–20% of pregnant women worldwide, making it a common reason for obstetric consultation. Although pruritus is often physiological and self-limiting, it may also represent the earliest manifestation of significant maternal disorders requiring prompt evaluation and management to prevent adverse pregnancy outcomes.[1]

Most cases of pruritus during pregnancy are related to physiological skin stretching, xerosis, hormonal changes, or pregnancy-specific dermatoses. However, a clinically important proportion is attributable to intrahepatic cholestasis of pregnancy (ICP), a pregnancy-specific cholestatic liver disorder characterized by generalized pruritus, elevated serum bile acid concentrations, and abnormal liver function tests in the absence of other identifiable liver diseases. The reported global prevalence of ICP ranges from 0.5% to 2% of all pregnancies, although considerably higher prevalence rates of 5–15% have been documented in certain geographical regions because of genetic susceptibility, environmental influences, and ethnic variations.[2]

ICP has emerged as one of the most clinically significant liver disorders unique to pregnancy because of its association with considerable maternal discomfort and increased fetal morbidity. The disease typically presents during the late second or third trimester, with intense nocturnal pruritus predominantly affecting the palms and soles before progressing to generalized itching. Unlike dermatological disorders, ICP usually presents without primary skin lesions, and excoriations

result only from persistent scratching. Early recognition is therefore challenging, emphasizing the importance of maintaining a high index of clinical suspicion among obstetricians.[3]

Pregnancy-specific dermatoses contribute substantially to maternal morbidity and reduced quality of life. Differentiating physiological pruritus from pathological conditions such as polymorphic eruption of pregnancy, atopic eruption, pemphigoid gestationis, and ICP is essential because only ICP carries a substantial risk of adverse fetal outcomes. Appropriate clinical examination combined with laboratory evaluation therefore plays a crucial role in establishing an accurate diagnosis and initiating timely intervention.[4]

The pathogenesis of ICP is multifactorial and involves a complex interaction between genetic predisposition, hormonal influences, impaired hepatocellular bile acid transport, and environmental factors. Elevated estrogen and progesterone metabolites impair bile acid secretion through hepatocytes, resulting in intrahepatic bile acid accumulation and increased maternal serum bile acid concentrations. These circulating bile acids stimulate peripheral nerve endings, producing the characteristic pruritus, while simultaneously crossing the placenta and exerting toxic effects on the fetus, thereby increasing the risk of adverse perinatal outcomes.[5]

According to the World Health Organization (WHO), nearly 295,000 women die annually from pregnancy-related complications, with the majority occurring in low- and middle-income countries. Early identification and appropriate management of high-risk pregnancy conditions remain fundamental strategies for reducing maternal and neonatal morbidity and mortality worldwide. Maternal liver disorders constitute an important component of comprehensive antenatal care because delayed diagnosis may significantly compromise fetal well-being.[6]

The WHO recommendations on antenatal care advocate a minimum of eight antenatal contacts during pregnancy, emphasizing comprehensive clinical assessment, early identification of maternal complications, appropriate laboratory investigations, and timely referral to improve maternal and neonatal outcomes. Women presenting with persistent pruritus should therefore undergo systematic clinical evaluation to exclude underlying pathological causes, including ICP.[7]

The Centers for Disease Control and Prevention (CDC) recognizes pregnancy-related complications as major contributors to maternal and neonatal morbidity. Timely recognition of medical disorders during pregnancy, particularly those associated with fetal compromise, remains essential for reducing preventable adverse outcomes. Hepatic disorders such as ICP require early biochemical evaluation because delayed diagnosis may increase the risk of fetal complications, including spontaneous preterm birth and stillbirth.[8]

The CDC further recognizes intrahepatic cholestasis of pregnancy as an important pregnancy-associated liver disease requiring prompt clinical suspicion, biochemical confirmation, close fetal surveillance, and appropriate obstetric management because elevated maternal bile acid concentrations have been consistently associated with fetal distress, meconium-stained liquor, neonatal respiratory complications, and intrauterine fetal death.[9]

The National Institute for Health and Care Excellence (NICE) recommends that all pregnant women presenting with unexplained pruritus should undergo serum bile acid estimation and liver function testing, even in the absence of jaundice, to facilitate early diagnosis of ICP. Repeated biochemical assessment is advised when symptoms persist despite initially normal investigations because biochemical abnormalities may develop later during the disease course.[10]

Similarly, the Royal College of Obstetricians and Gynaecologists (RCOG) recommends serial monitoring of liver function tests and serum bile acid concentrations, individualized fetal surveillance, and planned delivery according to disease severity. Women with serum bile acid levels exceeding 100 μmol/L have a substantially increased risk of stillbirth and require intensive monitoring with consideration of early delivery to optimize neonatal outcomes.[11]

The International Federation of Gynecology and Obstetrics (FIGO) emphasizes standardized evaluation, multidisciplinary management, and evidence-based clinical protocols for maternal medical disorders complicating pregnancy. Integration of obstetricians, hepatologists, neonatologists, and laboratory services is recommended to improve maternal safety and neonatal survival in pregnancies complicated by ICP.[12]

The American College of Obstetricians and Gynecologists (ACOG) also advocates individualized obstetric care, emphasizing early biochemical diagnosis, fetal surveillance, and appropriately timed delivery based on maternal clinical status and biochemical severity. Such strategies have significantly improved perinatal outcomes while minimizing unnecessary obstetric interventions.[13]

Emerging evidence suggests that women with ICP have an increased prevalence of metabolic disorders, particularly gestational diabetes mellitus, and may subsequently develop hepatobiliary disorders later in life. These findings highlight that ICP is not merely a pregnancy-specific hepatic disorder but may represent a broader metabolic disease requiring comprehensive maternal assessment and long-term follow-up.[14]

In India, maternal health continues to remain a national priority under various reproductive and maternal health initiatives. The Indian Council of Medical Research (ICMR) advocates evidence-based clinical protocols, standardized antenatal screening, and early diagnosis of high-risk pregnancy conditions to reduce maternal and neonatal morbidity and mortality. However, Indian data regarding the prevalence of pruritus and its association with ICP remain limited, particularly in tertiary care settings.[15]

Therefore, the present study was undertaken to determine the prevalence of pruritus among pregnant women, evaluate its correlation with intrahepatic cholestasis of pregnancy using clinical and biochemical parameters, and assess the associated fetomaternal outcomes in a tertiary care hospital. The findings are expected to contribute to improved early diagnosis, standardized clinical management, and better maternal and neonatal outcomes.

MATERIALS AND METHODS

This hospital-based prospective observational study was conducted in the Department of Obstetrics and Gynaecology, Sree Balaji Medical College and Hospital, Chennai, over a period of 18 months to determine the prevalence of pruritus

among pregnant women, evaluate its correlation with intrahepatic cholestasis of pregnancy (ICP), and assess the associated fetomaternal outcomes.

The study population comprised antenatal women of any gestational age presenting with complaints of pruritus to the outpatient and inpatient obstetric services during the study period. A total of 245 eligible pregnant women were recruited using a consecutive sampling technique after obtaining written informed consent. The sample size was calculated using the standard formula for prevalence studies, $n = Z^2PQ/d^2$, considering an expected prevalence of pruritus during pregnancy of 20%, a 95% confidence level, and an absolute precision of 5%, yielding a required sample size of 245 participants.

Pregnant women presenting with pruritus and willing to participate were included in the study. Women with pre-existing dermatological disorders, chronic liver disease, viral hepatitis, autoimmune liver diseases, or gallbladder diseases such as cholelithiasis and cholangitis were excluded to avoid confounding causes of pruritus.

After enrolment, detailed demographic information, obstetric history, gestational age, onset and distribution of pruritus, and associated clinical symptoms were recorded using a structured proforma. All participants underwent comprehensive clinical examination, including general physical, systemic, dermatological, and obstetric assessments. Laboratory evaluation included complete blood count, liver function tests comprising serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), total bilirubin, coagulation profile, and serum bile acid estimation. Additional investigations such as renal function tests, thyroid function tests, abdominal ultrasonography, and obstetric ultrasonography were performed whenever clinically indicated. Participants were subsequently categorized into ICP and non-ICP groups based on clinical presentation and biochemical findings and were followed prospectively until delivery. Maternal and neonatal outcomes were documented during the intrapartum and immediate postpartum periods.

The primary outcome of the study was the prevalence of intrahepatic cholestasis of pregnancy among pregnant women presenting with pruritus. Secondary outcome measures included maternal complications such as gestational diabetes mellitus, preeclampsia, preterm premature rupture of membranes, preterm delivery, and mode of delivery, along with fetal outcomes including meconium-stained liquor, intrauterine growth restriction, Apgar score at 5 minutes, neonatal intensive care unit admission, and intrauterine fetal death.

The collected data were entered into Microsoft Excel and analysed using the Statistical Package for the Social Sciences (SPSS). Continuous variables were expressed as mean ± standard deviation, whereas categorical variables were presented as frequencies and percentages. Comparisons between groups were performed using the Student's t-test for continuous variables and the Chi-square test for categorical variables. Logistic regression analysis was performed to identify predictors of adverse fetomaternal outcomes. A p-value of less than 0.05 was considered statistically significant.

The study protocol received approval from the Institutional Ethics Committee before commencement. Written informed consent was obtained from all participants prior to enrolment. Confidentiality of participant information was maintained throughout the study, and all procedures were carried out in accordance with institutional ethical standards and the principles of the Declaration of Helsinki.

RESULTS

Table 1. Baseline Clinical Characteristics of Pregnant Women with Pruritus (n=245)

Variable	Category	n	%
Gestational age at onset of pruritus	<24 weeks	28	11.4
	24–28 weeks	52	21.2
	28–32 weeks	78	31.8
	32–36 weeks	62	25.3
	>36 weeks	25	10.2
Mean maternal age (years)	Overall	26.3 ± 4.4	—
Gravidity	Primigravida	143	58.4
	Multigravida	102	41.6

Table 2. Prevalence of Intrahepatic Cholestasis of Pregnancy among Women with Pruritus

Diagnosis	**n**	**%**
ICP	60	24.5
Non-ICP	185	75.5
Total	245	100

Table 3. Clinical Characteristics of ICP and Non-ICP Groups

Variable	**ICP (n=60)**	**Non-ICP (n=185)**	**p value**
Mean age (years)	26.8 ±4.2	26.1 ±4.5	0.412

Primigravida	35 (58.3)	108 (58.4)	0.995
Third trimester presentation	38 (63.3)	100 (54.1)	0.214
Palms & soles involvement	60 (100.0)	40 (21.6)	<0.001
Abdominal pruritus	50 (83.3)	120 (64.9)	0.008
Generalized pruritus	42 (70.0)	95 (51.4)	0.015

Table 4. Laboratory Profile in ICP and Non-ICP Groups

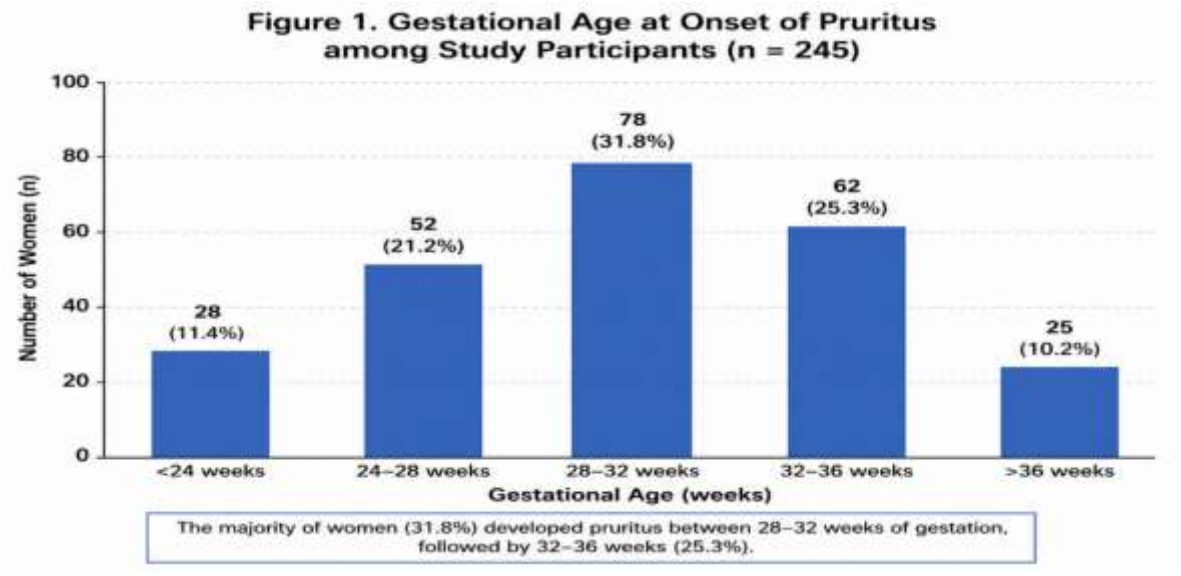
Investigation	**ICP (n=60)**	**Non-ICP (n=185)**	**p value**
Elevated ALT	60 (100.0)	12 (6.5)	<0.001
Elevated AST	60 (100.0)	10 (5.4)	<0.001
Elevated bilirubin	7 (11.7)	0	<0.001
Serum bile acid >40 µmol/L	**4 (6.7)**	**0**	**<0.001**

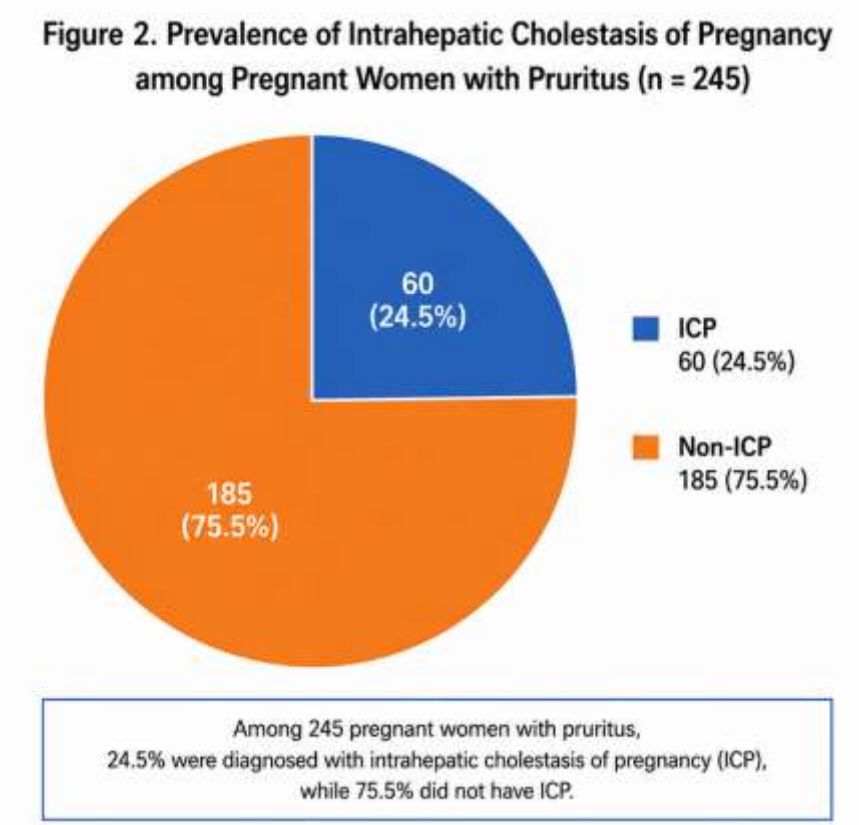
Table 5. Maternal Outcomes

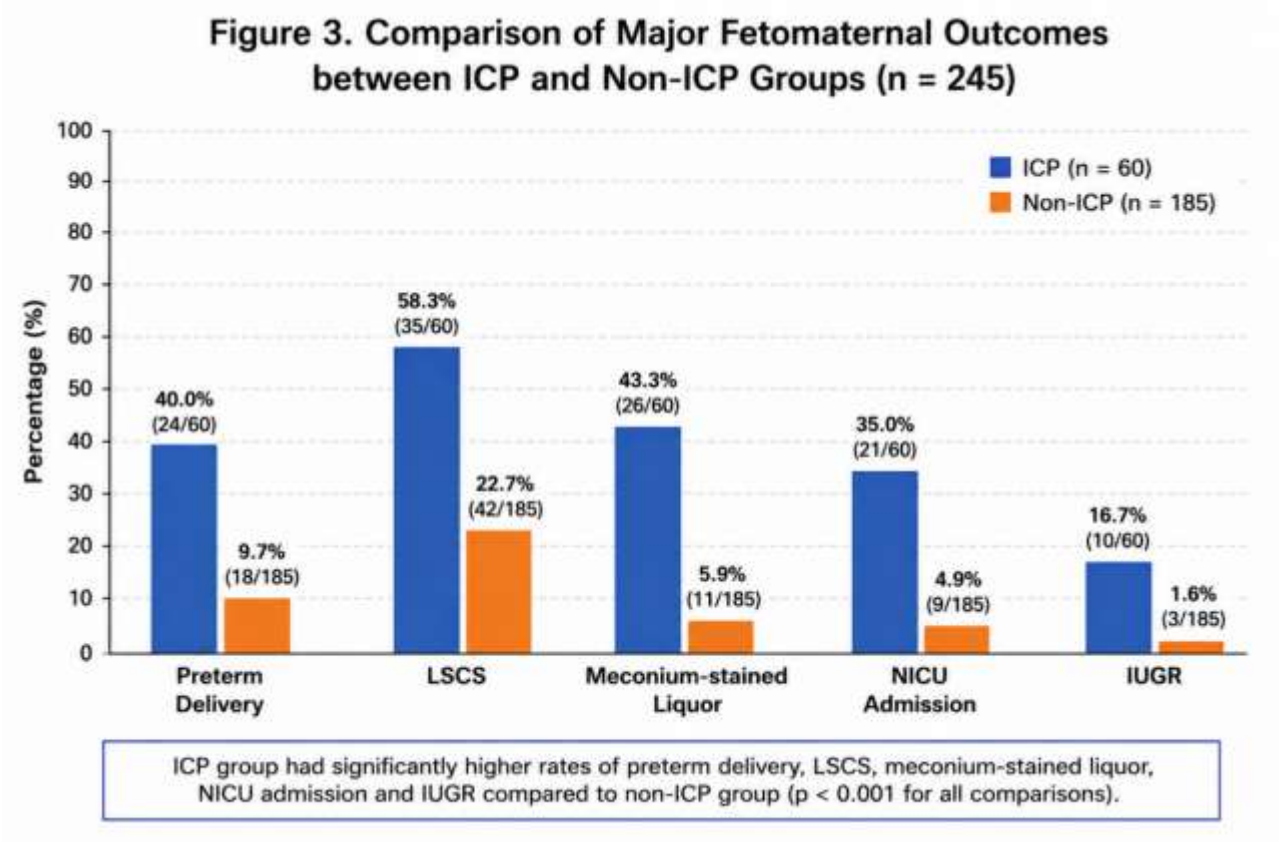
Outcome	**ICP (n=60)**	**Non-ICP (n=185)**	**p value**
Gestational diabetes mellitus	12 (20.0)	20 (10.8)	0.048
Preeclampsia	10 (16.7)	18 (9.7)	0.112
PPROM	6 (10.0)	3 (1.6)	0.002
Preterm delivery	24 (40.0)	18 (9.7)	<0.001
LSCS	35 (58.3)	42 (22.7)	<0.001

Table 6. Neonatal Outcomes

Outcome	**ICP (n=60)**	**Non-ICP (n=185)**	**p value**
Meconium-stained liquor	26 (43.3)	11 (5.9)	<0.001
IUGR	10 (16.7)	3 (1.6)	<0.001
NICU admission	21 (35.0)	9 (4.9)	<0.001
Apgar <7 at 5 min	8 (13.3)	5 (2.7)	0.003







DISCUSSION

The present prospective observational study included 245 pregnant women presenting with pruritus, among whom 60 women (24.5%) were diagnosed with intrahepatic cholestasis of pregnancy (ICP). The majority of participants developed pruritus between 28 and 32 weeks of gestation (31.8%), and most were primigravidae (58.4%). Women with ICP had significantly greater involvement of the palms and soles (100%), abdominal pruritus (83.3%), and generalized pruritus (70.0%). Biochemically, all women with ICP demonstrated elevated serum ALT and AST levels, while elevated bilirubin (11.7%) and serum bile acid levels >40 μmol/L (6.7%) were observed in severe disease. Maternal complications, including gestational diabetes mellitus (20.0%), PPROM (10.0%), preterm delivery (40.0%), and LSCS (58.3%), were significantly

more frequent in the ICP group. Similarly, adverse neonatal outcomes such as meconium-stained liquor (43.3%), NICU admission (35.0%), intrauterine growth restriction (16.7%), and low Apgar score at 5 minutes (13.3%) were significantly higher among women with ICP than those without ICP, highlighting the considerable fetomaternal impact of this disorder.
Our study demonstrated that women diagnosed with ICP had significantly elevated liver enzymes and experienced substantially higher rates of adverse maternal and neonatal outcomes compared with women without ICP. Specifically, 40.0% underwent preterm delivery, 58.3% required lower segment caesarean section, 43.3% had meconium-stained liquor, and 35.0% of neonates required NICU admission. These findings are in agreement with the recommendations of the Society for Maternal-Fetal Medicine (SMFM), which advocate early serum bile acid estimation, liver function testing, individualized fetal surveillance, and timely delivery to minimize pregnancy complications in women with suspected ICP.[16] The close agreement between our findings and the SMFM recommendations emphasizes the importance of early biochemical diagnosis and standardized obstetric management in improving fetomaternal outcomes.
In the present study, women with ICP experienced significantly higher rates of preterm delivery, operative delivery, and adverse neonatal outcomes than women without ICP. These observations are comparable with the updated RCOG Green-top Guideline by Girling et al., which recommends serial biochemical monitoring and individualized timing of delivery according to serum bile acid concentrations because severe ICP is associated with increased fetal morbidity and stillbirth risk.[17] The similarities between our findings and the RCOG recommendations further reinforce the need for close antenatal surveillance and appropriate timing of delivery in pregnancies complicated by ICP.
Our study found that all women with ICP presented with pruritus involving the palms and soles, while generalized pruritus was observed in 70.0% of cases. Beuers et al. reported that cholestatic pruritus results from a complex interaction between bile acids, lysophosphatidic acid, autotaxin, endogenous opioids, and inflammatory mediators rather than bile acid accumulation alone.[18] The characteristic distribution of pruritus observed in our study closely resembles their observations and supports the current understanding of the neurobiological mechanisms responsible for cholestatic itching.
In the present study, 100% of women with ICP showed elevated ALT and AST levels, indicating significant hepatocellular dysfunction associated with the disease. Xiao et al. demonstrated that genetic susceptibility, hormonal influences, and impaired hepatocellular bile acid transport collectively contribute to the molecular pathogenesis of ICP.[19] Although molecular analysis was not performed in our study, the biochemical abnormalities observed among our participants are consistent with these pathogenic mechanisms, suggesting that disturbed bile acid transport underlies the clinical manifestations of ICP.
Our findings showed that the majority of women developed ICP during the third trimester, when hormonal activity reaches its peak. Abu-Hayyeh et al. reported that sulfated progesterone metabolites accumulate during late pregnancy and contribute to bile acid dysregulation and cholestatic pruritus.[20] The predominance of third-trimester disease in our study supports this hormonal hypothesis and demonstrates a similar temporal relationship between gestational age and disease onset.
In our study, conventional liver function tests and serum bile acid estimation effectively differentiated women with ICP from those without the disease. Kremer et al. demonstrated that serum autotaxin activity is a useful biomarker for diagnosing cholestatic pruritus and correlates with disease severity.[21] Although autotaxin estimation was not available in our setting, our findings indicate that routine biochemical investigations remain valuable diagnostic tools, particularly in resource-limited tertiary care hospitals.
The present study observed that palmar and plantar pruritus occurred in all women with ICP, supporting the characteristic clinical presentation of cholestatic itching. Experimental studies by Alemi et al. demonstrated that activation of the TGR5 receptor by circulating bile acids directly stimulates sensory neurons responsible for itch perception.[22] The clinical presentation observed in our study is therefore consistent with the biological mechanisms proposed by the authors.
Our study also demonstrated significantly higher rates of preterm delivery (40.0%), meconium-stained liquor (43.3%), NICU admission (35.0%), IUGR (16.7%), and low Apgar scores among women with ICP. These findings closely parallel the systematic review and meta-analysis by Ovadia et al., who reported that increasing maternal serum bile acid concentrations are associated with a progressive increase in spontaneous preterm birth, meconium-stained amniotic fluid, neonatal respiratory complications, NICU admission, and stillbirth.[23] The close similarity between our results and those of Ovadia et al. strengthens the evidence that ICP is associated with substantial neonatal morbidity and underscores the importance of timely diagnosis and intervention.
In the present study, women with intrahepatic cholestasis of pregnancy experienced significantly higher maternal and neonatal complications than women without ICP. Preterm delivery occurred in 40.0% of women with ICP, 58.3% underwent lower segment caesarean section, while 43.3% had meconium-stained liquor. Furthermore, 35.0% of neonates required NICU admission, 16.7% developed intrauterine growth restriction, and 13.3% had an Apgar score of <7 at 5 minutes. These findings indicate that ICP remains an important predictor of adverse pregnancy outcomes.
Our study demonstrated significantly increased rates of preterm delivery, meconium-stained liquor, NICU admission, and operative delivery among women with ICP. These findings closely resemble those reported by Geenes et al., who demonstrated that severe intrahepatic cholestasis of pregnancy is associated with substantially higher risks of spontaneous preterm birth, fetal compromise, operative delivery, and neonatal morbidity, particularly in women with elevated serum bile acid concentrations.[24] The similarities between the two studies suggest that worsening biochemical severity of ICP is consistently associated with poor perinatal outcomes irrespective of geographical differences.
In the present study, adverse neonatal outcomes were markedly increased among women with ICP despite appropriate obstetric care. Zhou et al., in a large cohort study, similarly reported that increasing severity of intrahepatic cholestasis of pregnancy was independently associated with higher incidences of preterm birth, fetal distress, neonatal intensive care admission, and other adverse perinatal outcomes.[25] Our findings are comparable with their observations, particularly

regarding the significantly higher frequency of preterm delivery and neonatal complications, emphasizing that disease severity remains an important determinant of pregnancy outcome.

Our study also identified significantly increased neonatal morbidity among pregnancies complicated by ICP. Although our study primarily involved singleton pregnancies, Zhao et al. evaluated twin pregnancies complicated by intrahepatic cholestasis and reported that elevated maternal serum bile acid concentrations were associated with increased risks of preterm birth, fetal complications, and adverse neonatal outcomes.[26] Despite differences in study population, the increased neonatal morbidity observed in both studies indicates that ICP adversely affects fetal well-being irrespective of fetal number, although the magnitude of risk may be greater in multifetal gestations.

The present study demonstrated significantly higher rates of NICU admission, low Apgar scores, and meconium-stained liquor among neonates born to mothers with ICP. Similar findings were reported by Sarker et al., who showed that increasing severity of ICP was associated with neonatal morbidity extending beyond stillbirth, including respiratory complications, neonatal intensive care admission, and adverse neonatal adaptation.[27] The agreement between our findings and those of Sarker et al. highlights that neonatal morbidity remains a major clinical concern even when fetal demise is prevented through timely obstetric intervention.

In our study, adverse neonatal outcomes such as intrauterine growth restriction, NICU admission, and low Apgar scores were significantly more common in pregnancies complicated by ICP. Vasavan et al. demonstrated that elevated maternal bile acid concentrations may impair fetal cardiac function, thereby contributing to fetal compromise and poor neonatal outcomes.[28] Although fetal echocardiographic assessment was not performed in the present study, the increased neonatal morbidity observed may partly reflect similar mechanisms of fetal cardiovascular dysfunction described in their study.

The present study further demonstrated that pregnancies complicated by ICP were associated with increased maternal complications, including gestational diabetes mellitus, along with significant neonatal morbidity. Papacleovoulou et al. reported that maternal cholestasis not only affects pregnancy outcomes but may also induce long-term metabolic alterations in offspring through fetal programming mechanisms.[29] While long-term neonatal follow-up was beyond the scope of our study, the observed increase in adverse neonatal outcomes supports the concept that ICP may have consequences extending beyond the immediate perinatal period and warrants continued follow-up of affected children.

Our findings also demonstrated a significantly higher incidence of spontaneous preterm delivery among women with ICP. You et al. proposed that dysregulated bile acid metabolism promotes inflammatory activation within the uterus and fetal membranes, thereby contributing to spontaneous preterm labour.[30] The significantly increased frequency of preterm delivery observed in our study is consistent with these proposed inflammatory mechanisms and provides further clinical evidence supporting the association between bile acid dysregulation and premature birth.

CONCLUSION

The present study demonstrated that nearly one-fourth (24.5%) of pregnant women presenting with pruritus were diagnosed with intrahepatic cholestasis of pregnancy (ICP), highlighting the importance of considering ICP in all pregnant women with persistent itching. Women with ICP had characteristic clinical features, including predominant involvement of the palms and soles and generalized pruritus, accompanied by significantly elevated liver enzymes and abnormal serum bile acid levels.

Pregnancies complicated by ICP were associated with significantly higher maternal complications, particularly gestational diabetes mellitus, preterm premature rupture of membranes, preterm delivery, and increased rates of lower segment caesarean section. Adverse neonatal outcomes, including meconium-stained liquor, intrauterine growth restriction, neonatal intensive care unit admission, and low Apgar scores, were also significantly more frequent among women with ICP compared with those without the condition.

These findings emphasize that pruritus during pregnancy should not be considered merely a physiological symptom but should prompt timely clinical evaluation and biochemical assessment to exclude ICP. Early diagnosis, close maternal and fetal surveillance, and appropriate obstetric management can substantially reduce fetomaternal morbidity and improve pregnancy outcomes. Further multicentric studies with larger sample sizes and long-term neonatal follow-up are recommended to strengthen the existing evidence and optimize management strategies for pregnancies complicated by intrahepatic cholestasis.

REFERENCES

1. Cunningham FG, Leveno KJ, Bloom SL, et al. Williams Obstetrics. 26th ed. New York: McGraw-Hill; 2022. Chapter: Liver disease in pregnancy.
2. Gabbe SG, Niebyl JR, Simpson JL, et al. Obstetrics: Normal and Problem Pregnancies. 8th ed. Philadelphia: Elsevier; 2021.
3. Jameson JL, Fauci AS, Kasper DL, et al. Harrison's Principles of Internal Medicine. 21st ed. New York: McGraw-Hill; 2022. Chapter: Cholestatic liver diseases.
4. Bolognia JL, Schaffer JV, Cerroni L. Dermatology. 4th ed. Philadelphia: Elsevier; 2018. Chapter: Dermatoses of pregnancy.
5. Sherlock S, Dooley J. Diseases of the Liver and Biliary System. 13th ed. Oxford: Wiley-Blackwell; 2018.
6. World Health Organization. Maternal health. Available from: https://www.who.int/health-topics/maternal-health
7. World Health Organization. WHO recommendations on antenatal care for a positive pregnancy experience. Available from: https://www.who.int/publications/i/item/9789241549912
8. Centers for Disease Control and Prevention. Pregnancy complications. Available from: https://www.cdc.gov/pregnancy/complications.html

9. Centers for Disease Control and Prevention. Cholestasis of pregnancy overview. Available from: https://www.cdc.gov
10. National Institute for Health and Care Excellence. Intrahepatic cholestasis of pregnancy. Available from: https://www.nice.org.uk
11. Royal College of Obstetricians and Gynaecologists. Obstetric Cholestasis. Green-top Guideline No.43. Available from: https://www.rcog.org.uk
12. International Federation of Gynecology and Obstetrics (FIGO). Guidelines on maternal conditions affecting pregnancy. Available from: https://www.figo.org
13. American College of Obstetricians and Gynecologists. Liver disease in pregnancy. Available from: https://www.acog.org
14. American Diabetes Association. Standards of Care in Pregnancy. Available from: https://diabetes.org
15. Indian Council of Medical Research. Maternal health guidelines. Available from: https://www.icmr.gov.in
16. Society for Maternal-Fetal Medicine (SMFM), Lee RH, Greenberg M, Metz TD, Pettker CM. SMFM Consult Series #53: Intrahepatic cholestasis of pregnancy. Am J Obstet Gynecol. 2021;224(2):B2-B9. doi:10.1016/j.ajog.2020.10.001. PMID:33197417.
17. Girling J, Knight CL, Chappell LC. Intrahepatic cholestasis of pregnancy: RCOG Green-top Guideline No.43. BJOG. 2022;129(13):e95-e114. doi:10.1111/1471-0528.17266. PMID:35975505.
18. Beuers U, Wolters F, Oude Elferink RPJ. Mechanisms of pruritus in cholestasis. Nat Rev Gastroenterol Hepatol. 2023;20(1):26-36. doi:10.1038/s41575-022-00679-0. PMID:36109643.
19. Xiao J, Li Z, Song Y, Sun Y, Shi H, Chen D, et al. Molecular pathogenesis of intrahepatic cholestasis of pregnancy. Can J Gastroenterol Hepatol. 2021;2021:6679322. doi:10.1155/2021/6679322. PMID:33884164.
20. Abu-Hayyeh S, Ovadia C, Lieu T, Jensen DD, Chambers J, Dixon PH, et al. Progesterone sulfates in intrahepatic cholestasis of pregnancy and pruritus. Hepatology. 2016;63(4):1287-1298. doi:10.1002/hep.28265. PMID:26426865.
21. Kremer AE, Bolier R, Dixon PH, Geenes V, Chambers J, Tolenaars D, et al. Autotaxin activity in intrahepatic cholestasis of pregnancy diagnosis. J Hepatol. 2015;62(4):897-904. doi:10.1016/j.jhep.2014.11.022. PMID:25457195.
22. Alemi F, Kwon E, Poole DP, Lieu T, Lyo V, Cattaruzza F, et al. TGR5 receptor mediates bile acid-induced itch. J Clin Invest. 2013;123(4):1513-1530. doi:10.1172/JCI64551. PMID:23524965.
23. Ovadia C, Seed PT, Sklavounos A, et al. Association of adverse perinatal outcomes of intrahepatic cholestasis of pregnancy with biochemical markers: a systematic review and meta-analysis. Lancet. 2019;393(10174):899-909. doi:10.1016/S0140-6736(18)31877-4. PMID:30773280.
24. Geenes V, Chappell LC, Seed PT, Steer PJ, Knight M, Williamson C. Association of severe intrahepatic cholestasis of pregnancy with adverse pregnancy outcomes. Hepatology. 2014;59(4):1482-1491. doi:10.1002/hep.26617. PMID:24115241.
25. Zhou Q, Yuan Y, Wang Y, He Z, Liang Y, Qiu S, et al. Severity of intrahepatic cholestasis of pregnancy and adverse outcomes: a large cohort study. BMC Pregnancy Childbirth. 2024;24(1):476. doi:10.1186/s12884-024-06585-3. PMID:39012345.
26. Zhao Y, Zhang Q, Sheng Y, Zhang M, He G, Liu X. Bile acids and pregnancy outcomes in twin pregnancies complicated by intrahepatic cholestasis. BMC Pregnancy Childbirth. 2025;25(1):588. doi:10.1186/s12884-025-07644-7. PMID:40389846.
27. Sarker M, Zamudio AR, DeBolt C, Ferrara L. Intrahepatic cholestasis of pregnancy severity and adverse neonatal outcomes beyond stillbirth. Am J Obstet Gynecol. 2022;227(3):517.e1-517.e7. doi:10.1016/j.ajog.2022.05.022. PMID:35568244.
28. Vasavan T, Deepak S, Jayawardane IA, Lucchini M, Martin C, Geenes V, et al. Fetal cardiac dysfunction in intrahepatic cholestasis of pregnancy. J Hepatol. 2021;74(5):1087-1096. doi:10.1016/j.jhep.2020.11.033. PMID:33245977.
29. Papacleovoulou G, Abu-Hayyeh S, Nikolopoulou E, et al. Maternal cholestasis programs metabolic disease in offspring. J Clin Invest. 2013;123(7):3172-3181.
30. You X, et al. Bile acid dysregulation and spontaneous preterm labor through inflammatory pathways.