

Fetomaternal Outcomes in Intrahepatic Cholestasis of Pregnancy at Tertiary Care Hospital in Lahore

Ambreen Nasir^{1,*}, Nazia Muneer¹, Arooj Butt¹, Sidra Hameed², Sidra Asif³, Muhammad Nasir Rana⁴

¹Department of Obstetrics and Gynecology, Rahbar Medical and Dental College/ PRTH, Lahore, Pakistan.

²Department of Obstetrics and Gynecology, CMH Institute of Medical College, Lahore, Pakistan.

³Department of Obstetrics and Gynecology, Avicenna Hospital and Medical College, Lahore, Pakistan.

⁴Department of Pediatrics Emergency Medicine, Children's Hospital, Lahore, Pakistan.

Abstract: Background: Intrahepatic cholestasis in pregnant women (ICP) is a liver disease that usually reported after 24 weeks of pregnancy with both maternal and fetal complications. ICP is common in general and especially in Pakistani-Asian populations. There is still very little information about fetomaternal outcomes related to ICP in the country.

Objective: The aim of this research is to evaluate the fetomaternal outcome of women with ICP in a tertiary health care hospital in Lahore.

Materials and Methods: A hospital-based single arm prospective observational study was conducted in the Department of Obstetrics & Gynecology PRTH/RMDC Lahore from September 1, 2024, to January 30, 2025 approval from institutional review Board (Ref no. 441/2024). 78 pregnant women in 2nd or 3rd trimester diagnosed with ICP were included. Diagnosis was based on clinical and laboratory findings. Information was gathered on the predesigned proforma. MS Excel 2007 and SPSS version 26 were used for data analysis.

Result: This study has 78 participants with a mean age of 26.42 years. The majority were aged 18-24 years (38.5%), and most had a BMI between 25-29 (42.3%). 64.1% were primigravida and 64.1% had completed primary education. 53.84% delivered full term (37-40 weeks), while 33.3% delivered between 34-36 weeks. The most common pregnancy complication was emergency caesarean section (38.46%), followed by preterm delivery (20.51%). There were 7 cases (8.97%) of spontaneous preterm delivery, 5 cases (6.41%) of intrapartum fetal death, and 1 stillbirth (2.5%).

Conclusion: The findings highlight that ICP predominantly affected younger, overweight primigravida with lower educational attainment. Furthermore, the study revealed significant neonatal complications, including low birthweight, respiratory distress, and meconium-staining.

Keywords: Intrahepatic cholestasis, Pregnancy complications, Emergency cesarean section, Preterm delivery, Birthweight.

INTRODUCTION

The diagnosis of ICP [Intrahepatic cholestasis of pregnancy] should be taken into consideration in a woman who has itching with no obvious jaundice and raised random total bile acid concentration of 19 micromole/L and above [1-4]. Furthermore, Cholestasis during pregnancy and acute fatty liver during pregnancy are both pregnancy-specific diseases [5]. Among all these possible liver disorders including pre-eclampsia, HELLP syndrome, hepatitis E infection, acute hepatitis, pre-existing chronic liver diseases; intrahepatic cholestasis is one of the most common pregnancy specific disorders related to hepatobiliary system [6]. Such patients also have altered immunity due to certain environmental influences, abnormal hormone metabolism, or genetic predisposition. Serum bile acid levels were not directly related to the intensity of itching [7].

Maternal complications include distress due to severe pruritus. Mothers with ICP are at greater risk of developing preeclampsia

or gestational diabetes. Therefore should have regular antenatal checkups. Fetal complications include premature deliveries, meconium aspiration, fetal distress, and stillbirth [8]. The risk of adverse outcomes is generally proportional to the severity of the disease and necessitates close monitoring and early delivery in severe cases. Main risk factor of ICP for fetus is still birth which cannot be predicted accurately even with available tests and resources, thus the derivative force of the study is the timely detection, early medication and patient education to control the adverse effects like still birth and improve fetomaternal outcomes [9].

The etiology was not obvious. Most popular theory is influence of increased estrogen and progesterone levels during pregnant females who are genetically predisposed [3, 10]. They have a slow release of bile excretion, leading to increased serum bile acid and liver enzymes. Pathophysiology of ICP involves the increased concentration of bile acids in the liver and bloodstream due to impaired excretion into bile ducts. The hallmark symptom of ICP is severe itching, which typically affects the palms, hands, and soles, but can involve other areas of the body. Pruritus can range from mild to severe. Other symptoms may include dark

* Address correspondence to this author at the Department of Obstetrics and Gynecology, Rahbar Medical and Dental College/ PRTH, Lahore, Pakistan. Email: doctorambreennasir@gmail.com

colored urine, pale stools and jaundice. Some mothers can have pruritus with ICP and normal LFTs.

ICP occurs due to change in metabolism of carbohydrates and renal and intestinal functions. Steatorrhea can decrease the levels of vitamin K-dependent clotting factors and PPH [1]. ICP leads to 1.5 times the chances of caesarean section rate and 8 times increase in hospital stay for > 10 days. There are chances of 3 times increase in induction of labor. Risks to fetus includes premature deliveries, intrauterine deaths, meconium aspiration and increased risk of neonatal respiratory distress syndrome [8, 11].

Mothers with mild itching were given local applicants resulting in tranquil effects on skin. If severity is greater, ursodeoxycholic acid [UDCA] can be administered at doses of 600-900mg/day for 3 weeks. It significantly decreases skin itching and relaxes patients. Addition of water-soluble vitamin k [10mg orally per day] can be started from 34 weeks but we are not in routine practice at our setup.

Regular antenatal checkups, detailed examinations, and investigations are important. Based on clinical examination, ultrasonography and CTG induction of labor maybe decided. Based on these findings, it is inferred that pregnancy can be continued and terminated at 38 weeks.

The diagnosis of ICP is based on clinical features and laboratory findings, including increased serum bile acid levels and deranged liver function tests. The management of ICP aims to relieve symptoms, minimize maternal and fetal complications, and ensure safe delivery.

MATERIALS AND METHODS

A hospital-based single arm prospective observational study was carried out in the Department of Obstetrics and Gynecology at PRTH/RMDC Lahore from September 1, 2024, to January 30, 2025 after obtaining approval from institutional review Board [Ref no. 441/2024]. PRTH is a tertiary care hospital receiving referrals from remote areas of Punjab thus providing an opportunity to study the disease pattern in a diverse population. The study involved 78 females who presented in the 2nd or 3rd trimester of pregnancy with pruritus and abnormal liver function tests. The sample size was determined using the WHO sample size calculator.

From admission to discharge, all cases underwent thorough observation. Information gathered included the mother's age, weight, height, pregnancy count, delivery history, delivery method [spontaneous or medicated], mode of childbirth, post-partum bleeding, and biochemical measurements. Body mass index was determined using pre-pregnancy maternal body measurements. Potential fetal complications encompass premature birth, amniotic fluid with meconium staining, fetal distress, and stillbirth. The likelihood of unfavorable outcomes generally correlates with the condition's severity, necessitating vigilant monitoring and early delivery in severe instances. Perinatal results were documented, including birth weight, preterm labor,

fetal viability, abnormalities in intrapartum cardiotocography, meconium staining, and the need for neonatal intensive care unit admission [2, 10, 12].

Essential data was gathered and documented, including clinical characteristics and conducted tests. A pre-designed, structured form was used to record all information and outcomes. Descriptive data was separately noted for presentation and discussion purposes. The study commenced after obtaining approval from the ethics committee and institutional board. Each case underwent individual analysis based on its merits. Anthropometric, clinical, and laboratory parameters were recorded. To measure levels of serum total bile acids, ALT, AST, and serum bilirubin, the blood sample was collected. When necessary, laboratory tests were repeated. From admission to discharge, all mothers were under close observation. Both maternal and fetal details and outcomes were documented. The sample size was calculated using the WHO Sample Size Calculator, based on an expected ICP incidence of 3-5% [13], a confidence level of 95%, and a margin of error of 5%, yielding a minimum sample size of 73. We enrolled 78 participants to account for potential dropouts.

The inclusion criteria were the pregnant women in the 2nd or 3rd trimester with pruritus and serum total bile acids equal or more than 19 $\mu\text{mol/l}$ that were confirmed by the Liver Function Test [LFT]. The exclusion criteria included patients with pre-existing hepatic conditions, hepatitis E, and those that refused to consent.

STATISTICAL ANALYSIS

Data analysis was performed using Microsoft Excel 2007 and SPSS version 26. Descriptive statistics, presented as mean, standard deviation, and percentages, were displayed in tabular format.

RESULT

The study included 78 participants. In terms of age bracket, the largest group consisted of 30 women (38.5%) aged 18-24 years, followed by 26 women (33.3%) in the 25-29 age range. Sixteen participants (20.5%) were 30-35 years old, and 6 women (7.7%) were above 35, with a mean age of 26.42 years. Regarding body mass index (BMI), 33 women (42.3%) fell within 25-29, 29 women (31.2%) were between 18.5-24, 11 women (14.1%) had a BMI under 18.5, and 5 women (6.4%) exceeded 30 (Table 1). In terms of pregnancy history, 50 women (64.1%) were experiencing their first pregnancy, 24 women (30.8%) had been pregnant before, and 4 women (5.1%) had multiple previous pregnancies. Education-wise, 50 participants (64.1%) had completed primary schooling, 22 women (28.2%) had attained secondary education, and 6 women (7.7%) were college graduates.

The duration of pregnancy varied among participants. The majority, comprising 42 women (53.84%), gave birth at full term between 37-40 weeks of gestation. A substantial number, 26 women (33.3%), delivered slightly earlier, between 34-36 weeks. Seven women (8.97%) experienced early preterm births

before 34 weeks, while 3 women (3.8%) had post-term deliveries after 40 weeks (Table 2).

Table 1. Socio-Demographic Variables.

Characteristics	Count	Percentage
Age		
18-24 years	30	38.5
25-29 years	26	33.3
30-35 years	16	20.5
>35 years	6	7.7
BMI		
<18.5	11	14.1
18.5-24	29	31.2
25-29	33	42.3
>30	5	6.4
Gravidity		
Primigravida	50	64.1
Multigravida	24	30.8
Grand multigravida	4	5.1
Educational status		
Primary	50	64.1
Secondary	22	28.2
Graduation	6	7.7
Weeks of pregnancy	Count (n= 78)	Percent
<34 weeks	7	8.97
34-36 weeks	26	33.3
37-40 weeks	42	53.84
>40 weeks	3	3.8

Table 2. Complications of Pregnancy.

Complications	Count (n = 78)	Percent
PPROM	5	6.4
Preterm delivery	16	20.51
PROM	9	11.53
Elective cesarean section	11	14.1
Emergency cesarean section	30	38.46
Postpartum hemorrhage	7	8.97

The table outlines the pregnancy complications experienced by the 78 participants. The most frequent complication was emergency caesarean section, affecting 30 women (38.46%). Preterm delivery occurred in 16 women (20.51%), while 11 women (14.1%) underwent planned caesarean sections. Early rupture of membranes was documented in 9 women (11.53%), and premature rupture of membranes before 37 weeks occurred in 5 women (6.4%). Furthermore, excessive bleeding after childbirth was observed in 7 women (8.97%). This table presents an overview of the types and frequencies of pregnancy-related

complications encountered in the study group.

The outcomes for newborns among the 78 participants varied significantly and were crucial (Table 3). Thirteen newborns (16.67%) had an APGAR score below 7 at 5 minutes, suggesting potential distress immediately after birth. Twenty-one infants (26.92%) weighed less than 2500 grams at birth, indicating low birth weight. Signs of fetal distress during labor were observed in 26 cases (33.3%), while 30 newborns (38.4%) had meconium-stained amniotic fluid, potentially indicating fetal stress during delivery. Spontaneous early delivery occurred in 7 cases (8.97%), and fetal death during labor was recorded in 5 cases (6.41%). One case (2.5%) resulted in a fresh stillbirth. This table provides a comprehensive summary of the health outcomes for newborns associated with the study participants. Table 4 shows the observed mean values of bile acids and transaminases that was reported in patients along with standard values.

Table 3. Neonatal Outcome.

Outcome	Number n=103	Percent
APGAR score less than 7 (5 minutes)	13	16.67
Birth weight less than 2500 grams	21	26.92
Intrapartum fetal distress	26	33.3
Meconium-stained liquor	30	38.4
Spontaneously delivered preterm	7	8.97
Intrapartum death of fetus	5	6.41
Fresh still birth	1	2.5

Table 4. Liver Function Test for the Study Population (N=78).

Liver Function Test	Normal Value	Observed Value (Mean ± S.E)
Total Bile Acids	10μmol/L	35.17±2.78
Alanine Transaminase	0-42U/L	42.82± 1.40
Aspartate Transaminase	0-32U/L	36.256±0.974
Serum Bilirubin	0-17 μmol/L	17.013±0.340

DISCUSSION

This study focused on the fetomaternal outcomes of ICP in patients. During the one-year study period there were 2260 women were admitted for delivery. 78 pregnant women with Intrahepatic Cholestasis of Pregnancy [ICP] were included in this study. Our study reveals the clinical and perinatal characteristics that are associated with ICP. This generally increases the risk of perinatal complications [14]. That in long term may contribute to effective monitoring and management of associated conditions.

The data showed that majority of the participants were young women that is approximately 71.8% under the age of 30. The mean age was found to be 26.4 years. However, another study suggested that this condition is more common in women over 30

years of age [15]. The incidence of ICP was found to be 3.45% in our hospital, which is almost double the incidence rate recorded earlier that is 1.46 [16].

We also found that significant percentage of subjects were overweight as majority had their BMIs between 25-29 kg/m². That shows the association between obesity, and overweight with ICP. Another study also had the similar results linking obesity with ICP [17]. In terms of the obstetric history, it was reported that around 64% of the women were primigravida which means it was their first time pregnancy. This is in line with other studies wherein 66% of the women with ICP cases were primigravida [18].

The 64% of the women only had primary education, which shows the high prevalence of ICP in lower educated subjects. It was also reported that 40% of the reported deliveries were pre term. The clinical decision may be backed to avoid prolonged exposure of bile acid and mitigate the fetal death risk. This is consistent with international practices [15].

Another maternal complication that was observed in the data was the emergency caesarian section that was 38.5% followed by 20.5% of preterm delivery and 14.1% of elective caesarian. The increase fetal distress causes complications that requires immediate support for the healthcare professionals. 9% of postpartum hemorrhage was also observed in our data. Study conducted earlier also showed that in patients with ICP, the C-section is frequent following complications [19] and in a meta-analysis study [13]. However, one study found no difference in C-section between women with ICP and without [20].

Regarding neonatal outcomes, a low APGAR score of <7 in 5 min was 16.67%, which is nearly the same as that reported by other researchers. The reason for this could be that 87% of unbooked ICP patients had a higher C-section rate. ICP in pregnant females have led to complications for both mother and fetus and increase the rate of caesarean section rates and discomfort due to pruritic [21]. The disease is related to a higher incidence of perinatal complications like 38.46% meconium staining, 42.27% and preterm delivery and fetal distress [22]. Intrapartum fetal distress and meconium staining are attributed to the fact that increased bile acids act as stimulants for the colonic motility of the fetus. In our study, the incidence of meconium staining was 38.46%.

We observed an intrauterine fetal death rate of 6.41%. This is because all five cases had IUD before their admission to the hospital. In our study, 41(52.56%) NICU admissions were due to higher intrapartum fetal hypoxia and a higher percentage of meconium aspiration (38.46%). Intrauterine death is often sudden and is usually due to anoxia or hypoxia. Recent studies have highlighted women with ICP have a significantly higher rate of IUD compared to women with normal pregnancies [23].

With respect to the biochemical profile, the mean total bile acid level was 35.17µmol/l which was above the normal levels of 19µmol/l. Other studies also found the similar results of higher

total bile acid levels in ICP patients [24]. Mild elevation was seen in transferases enzymes as well that suggests hepatic stress and is in line with the results of studies conducted prior [24, 25].

LIMITATIONS

There are some limitations of the study. The study was conducted on a relatively small sample size of 78 participants, which may limit the generalizability of the findings to the broader population. Larger studies are needed to validate these results. As the study was conducted at a single tertiary care hospital in Lahore, the results may not be representative of other regions or health-care settings in Pakistan. The study period of just over one year may not capture the full spectrum of ICP cases and outcomes, particularly long-term neonatal outcomes. The study focused on a few socio-demographic variables, potentially overlooking other important factors such as socioeconomic status, access to healthcare, and nutritional status, which could influence outcomes. Future research on intrahepatic cholestasis of pregnancy (ICP) should be involving larger multi-centric studies which will make the findings more generalizable. Longitudinal follow-up e.g. over the years, is needed to assess long-term impacts for both mothers and neonates, giving clues to if ICP has any lasting negative effects.

CONCLUSION

The findings highlight that ICP predominantly affected younger, overweight primigravida with lower educational attainment. Furthermore, the study revealed significant neonatal complications, including low birthweight, respiratory distress, and meconium-staining. These results underscore the importance of early detection and management of ICP to mitigate potential risks to both mother and child.

AUTHORS' CONTRIBUTION

Ambreen Nasir: Conceptualization, Study Design, Methodology, Data analysis and interpretation, Writing Draft, Critical review and revision the manuscript, Final approval, final proof to be published.

Nazia Muneer: Critical review and revision the manuscript.

Arooj Butt and Sidra Asif: Methodology, Data analysis and interpretation.

Sidra Hameed: Conceptualization.

Muhammad Nasir Rana: Conceptualization, Study Design, Methodology, Data analysis and interpretation, Final approval, final proof to be published.

ACKNOWLEDGEMENTS

Declared none.

ETHICAL DECLARATIONS

Data Availability Statement

Data are available upon reasonable request. The data used to support the findings of this study are available from the corresponding author upon request.

Ethical Approval

The study was performed with the institutional formal ethical approval (Ref no. 441/2024).

Consent to Participate

Informed consented.

Consent for Publication

All of the authors give consent for publication of this manuscript.

Conflict of Interest

Declared none.

Competing Interest/Funding

Declared none.

Use of AI-Assisted Technologies

The authors declare that no generative artificial intelligence (AI) or AI-assisted technologies were utilized in the writing of this manuscript, in the creation of images/graphics/tables/captions, or in any other aspect of its preparation.

REFERENCES

- [1] Girling J, Knight CL, Chappell L, the Royal College of Obstetricians and Gynaecologists. Intrahepatic cholestasis of pregnancy. BJOG: Int J Obstet Gynaecol 2022; 129(13): e95-e114.
- [2] Kenyon AP, Nelson Piercy C, Girling J, Williamson C, Tribe RM, Shennan AH. Obstetric cholestasis, outcome with active management: a series of 70 cases. BJOG: Int J Obstet Gynaecol 2002; 109(3): 282-8.
- [3] Reyes H, Sjövall J. Bile acids and progesterone metabolites in intrahepatic cholestasis of pregnancy. Ann Med 2000; 32(2): 94-106.
- [4] Meng LJ, Reyes H, Axelson M, Palma J, Hernandez I, Ribalta J, *et al.* Progesterone metabolites and bile acids in serum of patients with intrahepatic cholestasis of pregnancy: Effect of ursodeoxycholic acid therapy. Hepatology 1997; 26(6): 1573-9.
- [5] Birkness-Gartman J, Oshima K. Liver pathology in pregnancy. Pathol Int 2021; 72: 1-13.
- [6] Regunathan A, Srinivasan B. A study of intrahepatic cholestasis of pregnancy and its perinatal outcome in a tertiary care centre. J Evol Med Dent Sci 2001; 10(45): 3906-9.
- [7] Wang Y, Tang Y, Yang X, Xu J, Chen Y, Xu J, *et al.* Immune dysfunction mediated by the cerna regulatory network in human placenta tissue of intrahepatic cholestasis pregnancy. Front Immunol 2022; 13: 883971
- [8] Zecca E, De Luca D, Marras M, Caruso A, Bernardini T, Romagnoli C. Intrahepatic cholestasis of pregnancy and neonatal respiratory distress syndrome. Pediatrics 2006; 117(5): 1669-72.
- [9] Roediger R, Fleckenstein J. Intrahepatic cholestasis of pregnancy: Natural history and current management. Semin Liver Dis 2021; 41: 103-8.
- [10] Turunen K, Sumanen M, Haukilahti R-L, Kirkinen P, Mattila K. Good pregnancy outcome despite intrahepatic cholestasis. Scand J Prim Health Care 2010; 28(2): 102-7.
- [11] Madazli R, Yuksel MA, Oncul M, Tuten A, Guralp O, Aydin B. Pregnancy outcomes and prognostic factors in patients with intrahepatic cholestasis of pregnancy. J Obstet Gynaecol 2015; 35(4): 358-61.
- [12] Geenes V, Chappell LC, Seed PT, Steer PJ, Knight M, Williamson C. Association of severe intrahepatic cholestasis of pregnancy with adverse pregnancy outcomes: A prospective population-based case-control study. Hepatology 2014; 59(4): 1482-91.
- [13] Yu P, Zhang M, He C. Incidence of intrahepatic cholestasis of pregnancy and its impact on maternal and neonatal outcomes: A systematic review and meta-analysis. Clin Exp Obstet Gynecol 2025; 52(6): 37850.
- [14] Pulido-Cejudo A, Guzmán-Gutierrez M, Jalife-Montaña A, Ortiz-Covarrubias A, Martínez-Ordaz JL, Noyola-Villalobos HF, *et al.* Management of acute bacterial skin and skin structure infections with a focus on patients at high risk of treatment failure. Therap Advan Infect Dis 2017; 4(5): 143-61.
- [15] Heinonen S, Kirkinen P. Pregnancy outcome with intrahepatic cholestasis. Obstet Gynecol 1999; 94(2): 189-93.
- [16] Geenes V, Williamson C. Intrahepatic cholestasis of pregnancy. World J Gastroenterol: WJG. 2009; 15(17): 2049.
- [17] Valdovinos-Bello V, García-Romero CS, Cervantes-Peredo A, García-Gómez E, Martínez-Ibarra A, Vázquez-Martínez ER, *et al.* Body mass index implications in intrahepatic cholestasis of pregnancy and placental histopathological alterations. Ann Hepatol 2023; 28(1): 100879.
- [18] Kumari R, Raman RK, Kumari U. An observational study of pregnancy outcomes in patients with intrahepatic cholestasis of pregnancy in a tertiary care hospital. Int J Acad Med Pharm 2023; 5(5): 1728-32.
- [19] Kong C, Zhu Z, Mei F. Risk factors associated with cesarean

- section and adverse fetal outcomes in intrahepatic cholestasis of pregnancy. *Front Pediatr* 2023; 11: 1136244.
- [20] Shemer EAW, Thorsell M, Marschall H-U, Kaijser M. Risks of emergency cesarean section and fetal asphyxia after induction of labor in intrahepatic cholestasis of pregnancy: A hospital-based retrospective cohort study. *Sexual Reprod Healthc* 2013; 4(1): 17-22.
- [21] Jamwal D, Kour G, Mehta A. Maternal and perinatal outcome in pregnancy complicated by obstetric cholestasis: Study from a tertiary care centre in North India. *Int J Reprod Contracept Obstet Gynecol* 2021; 10(7): 2830-4.
- [22] Gallo DM, Romero R, Bosco M, Gotsch F, Jaiman S, Jung E, *et al.* Meconium-stained amniotic fluid. *Am J Obstet Gynecol* 2023; 228(5 Suppl): S1158-78.
- [23] Chen Y, Zhang H, Ning W, Chen Y, Wen C. The impact of intrahepatic cholestasis on pregnancy outcomes: A retrospective cohort study. *BMC Gastroenterol* 2023; 23(1): 16.
- [24] Wood AM, Livingston EG, Hughes BL, Kuller JA. Intrahepatic cholestasis of pregnancy: A review of diagnosis and management. *Obstet Gynecol Survey* 2018; 73(2): 103-9.
- [25] Mullally BA, Hansen WF. Intrahepatic cholestasis of pregnancy: Review of the literature. *Obstet Gynecol Survey* 2002; 57(1): 47-52.

Received: March 10, 2025

Revised: June 23, 2025

Accepted: June 25, 2025

© 2025. The Authors, National Journal of Health Sciences.

This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY- NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non- commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>.