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A Prospective Cohort Study to Determine the Incidence of IHCP and Pregnancy Outcome in Women with Cholestasis of Pregnancy
Type of article

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ABSTRACT

OBJECTIVE: This study was conducted to determine the incidence and outcomes of obstetric cholestasis in pregnancy.

STUDY DESIGN: This was a hospital-based, observational, prospective cohort study conducted among antenatal women in the late second trimester and third trimester (24 to 40 weeks of gestational age) attending an antenatal clinic at the Department of Obstetrics and Gynaecology, Base Hospital, Delhi Cantt, New Delhi. The study was conducted over two years, from June 2022 to November 2023, after obtaining approval from the institutional ethics committee and written informed consent from the participants.

RESULTS: Most participants (96.0%) had mild Intrahepatic cholestasis of pregnancy (IHCP), while 2.8% had moderate and 1.2% had severe IHCP. Gestational age at delivery significantly correlated with IHCP severity (p=0.023). Mild IHCP cases had a lower incidence of premature rupture of membranes (6.7%) compared to moderate to severe IHCP cases (20%), although the difference was not statistically significant. A significant difference was found between IHCP severity and the mode of delivery (p=0.023), with a higher proportion of term deliveries in mild IHCP cases (94.2%) compared to moderate to severe IHCP cases (70.0%). Although the occurrence of meconium staining was relatively higher among moderate to severe IHCP cases than mild IHCP cases (20% vs. 10%, respectively), the difference was not statistically significant. No significant association was observed between IHCP severity and postpartum hemorrhage (PPH).

CONCLUSION: IHCP predominantly affects pregnant women under the age of 35, with most cases presenting with mild severity. Maternal complications such as premature rupture of membranes and mode of delivery were found to vary based on IHCP severity, with term deliveries being more common among mild cases.

Keywords: Cholestasis of pregnancy; Intrahepatic cholestasis of pregnancy

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Introduction

Obstetric cholestasis is a liver disease unique to pregnancy. Once assumed to be a benign condition, its significance has been highlighted only recently due to associated maternal and perinatal morbidity and mortality. It is the most common cause of liver disease in pregnancy. Patients usually present with pruritus, especially on the palms and soles, as reported in studies by Anand et al (1). Studies by Corcoran et al reported that it can be detected with raised liver enzymes, bile acid, and serum bilirubin, and symptoms resolve rapidly after delivery (2). The etiology of cholestasis in pregnancy is not well understood. It is complicated and multifactorial and thus remains a subject of ongoing research and clinical debate. Emerging evidence suggests a genetic component to intrahepatic cholestasis of pregnancy (IHCP), with certain gene polymorphisms implicated in predisposing individuals to bile acid dysregulations. Additionally, hormonal changes during pregnancy, including. elevated estrogen and progesterone metabolism, may exacerbate cholestasis in susceptible individuals.

Environmental factors such as diet, exposure to toxins, and geographical variations also appear to influence the incidence and severity of IHCP. Impaired bile acid metabolism is considered a central mechanism in IHCP. Elevated serum levels of bile acids, particularly cholic acid and chenodeoxycholic acid, are characteristic of IHCP and are believed to contribute to the pruritus and liver injury observed in affected individuals. Disruption of hepatic bile acid transporters and impaired bile acid synthesis may cause this dysregulation.

The aim of the study is to determine the incidence of obstetric cholestasis and the outcome in women with cholestasis of pregnancy. It also aims to study the fetal outcome in pregnancies with cholestasis of pregnancy and to study the maternal outcome (primary) in terms of gestational age at the time of delivery and mode of delivery.

Material and Method

This was a hospital-based observational prospective cohort study conducted among antenatal women in the late second trimester and third trimester (24 to 40 weeks of gestational age) attending an antenatal clinic at the Department of Obstetrics and Gynaecology, Base Hospital Delhi Cantt, New Delhi. The study was conducted over two years, from June 2022 to November 2023, after obtaining approval from the institutional ethics committee and written informed consent from all participants. The study was conducted in accordance with the Declaration of Helsinki, and the Institutional Ethics Committee approval was obtained vide No: IEC-01/2022/11.

Inclusion Criteria: The antenatal women in late second trimester and third trimester (24 - 40 weeks of gestational age) attending the antenatal clinic, Base Hospital, Delhi Cantt. Selection of cases was based on clinical symptoms (Pruritus) and serum bile acid levels (level>10 micromole/L)

Exclusion Criteria: Positive serology for hepatitis A, B, and C; previous history of gallbladder disease or sonographic evidence of gallbladder disease; hypertension complicating pregnancy; and autoimmune diseases such as primary biliary cirrhosis and autoimmune chronic active hepatitis were considered exclusion criteria.

Sample size: This is a prospective observational study. Sample size is calculated using the formula.

$$\text{Sample Size (n)} = Z_{1-\alpha/2}^{2}\, p\,(1-p)/\, d^{2}$$

Sample size was calculated on the basis of the proportion of obstetric cholestasis, 8.2% from the previous study by Padmaja et al, with an absolute precision of 5%. Using the formula n=4 pq/L2, the sample size is taken as 227 (3). Assuming a 10% non-responsiveness, the sample size is rounded to 250.

Statistical Methods

Data were entered in MS Excel and analyzed using SPSS software. Data was tabulated and analyzed using the software OpenEpi version 3.01 and Statistical Package for Social Sciences (SPSS) version 24 (IBM SPSS Statistics for Windows, Version 24.0. Armonk, NY, USA: IBM Corp.). Pearson's chi-square test and Fisher's exact test (used when the expected count in 20% of cells was less than 5) were employed for analytical statistics.

Results

When comparing IHCP severity with gestational age at delivery, 94.2% (226 individuals) of those with mild IHCP had term deliveries, while 5.8% (14 individuals) experienced preterm deliveries. On the other hand, among those with moderate to severe IHCP, 70.0% (7 individuals) had term deliveries, and 30.0% (3 individuals) had pre-term deliveries. The relatively higher rate of pre-term deliveries among moderate to severe IHCP cases compared to mild IHCP cases was found to be statistically significant, with a p-value of 0.023 (Table I).

On comparing IHCP severity with meconium staining (Table II), it was noted that one-tenth of cases diagnosed as mild IHCP (24/240 study participants, 10%) had meconium staining, whereas one-fifth (2/10 study participants, 20%) of cases diagnosed as moderate to severe IHCP had meconium staining. Though the occurrence of meconium staining was relatively higher among moderate to severe IHCP cases than mild IHCP cases, the difference was statistically not significant.

Table I: *Comparison of Intrahepatic cholestasis of pregnancy severity with gestational age at the time of delivery*

Gestational Age at the Time of Delivery	IHCP Severity		p
	Mild	Moderate to Severe	
Pre-term	**14**	3	0.023
	5.8%	30.0%	
Term	226	7	
	94.2%	70.0%	
Total	240	10	
	100.0%	100.0%	

IHCP: Intrahepatic Cholestasis of Pregnancy

Table II: *Comparison of intrahepatic cholestasis of pregnancy severity with meconium staining*

Meconium Staining	IHCP Severity		p
	Mild	Moderate to Severe	
No	216	8	0.279
	90.0%	80.0%	
Yes	24	2	
	10.0%	20.0%	
Total	240	10	
	100.0%	100.0%	

IHCP: Intrahepatic Cholestasis of Pregnancy

Among cases diagnosed as mild IHCP (Table III), 0.8% (2/240 study participants) had hemorrhage PPH, and none of the cases with moderate to severe IHCP had PPH. There was statistically no significant difference between IHCP severity and PPH.

On comparing IHCP severity with mode of delivery (Table IV), it was observed that among cases diagnosed as mild IHCP, the majority had vaginal delivery (72.1%), followed by LSCS (22.5%), and 5.4% of cases had assisted vaginal delivery. A similar trend was also seen in cases diagnosed as moderate to severe IHCP, wherein 70% of cases had vaginal delivery, 20% underwent LSCS, and 10% assisted vaginal delivery. There was statistically no significant difference between the severity of IHCP and the mode of delivery.

This compares the severity of IHCP with fetal distress (Table V). Among neonates born to cases diagnosed as mild IHCP, the majority (225 cases, 93.8%) did not have any fetal distress, and 6.3% of newborns had fetal distress. Whereas, among neonates born to patients categorized as having moderate to severe IHCP, none had fetal distress. There was statistically no significant difference between IHCP severity and fetal distress.

Table III: *Comparison of Intrahepatic cholestasis of pregnancy severity with post-partum hemorrhage among Study*

PPH	Mild	Moderate to Severe	p
No	238	10	1.000
	99.2%	100.0%	
Yes	2	0	
	0.8%	0%	
Total	240	10	
	100%	100%	

PPH: Postpartum hemorrhage

Table IV: *Comparison of Intrahepatic cholestasis of pregnancy severity with mode of delivery*

Mode of Delivery	IHCP Severity		p
	Mild	Moderate to Severe	
Assisted	13	1	0.585
	5.4%	10.0%	
LSCS	54	2	
	22.5%	20.0%	
Vaginal	173	7	
	72.1%	70.0%	
Total	240	10	
	100.0%	100.0%	

IHCP: Intrahepatic Cholestasis of Pregnancy

Table VI delineates the distribution of clinical symptoms among the 250 study participants diagnosed with cholestasis of pregnancy. The reported symptoms include itching over palms and soles, itching all over the body, or a combination of both. A substantial 49.2% of participants (123 individuals) experienced itching specifically over their palms and soles, while 5.2% (13 individuals) reported itching all over their bodies. A considerable proportion, accounting for 45.6% (114 individuals), described experiencing both types of itching.

Discussion

In the present study, the incidence of IHCP was observed to be 6.57% (with 266 cases identified among 4050 deliveries at the study centre).

Corcoran et al. reported an incidence of 3.2% in their study among 1302 pregnant patients, which is lower than the prevalence observed in the present study (2). Similarly, studies by Pata et al. and Gardiner et al. reported lower incidence rates of 0.86% and 0.7%, respectively (4,5). Additionally, there are studies such as those by Arora et al. and Jamwal et al., which reported prevalence rates of 4.08% and 9.3%, respectively, which are relatively comparable to the prevalence observed in the present study (6,7).

The differences in prevalence and incidence rates across studies could be attributed to various factors, including differences in study design, diagnostic criteria, geographical variations, and especially the demographic characteristics of the study populations.

The demographic characteristics and obstetric profiles of the participants in the present study demonstrate some similarities and differences compared to the findings reported in studies by Nisha et al. and Anand et al. (1,8). The majority of the participants (238 cases, 95.2%) in the present study were in the age group of less than 35 years. The overall mean age of the participants was calculated to be 28.1 years, with a standard deviation of 3.8 years. Most participants were either primigravida (90 cases, 36.0%) or gravida two (99 cases, 39.6%). Anand et al. reported a higher proportion of primigravida participants (55%) compared to 36.0% in our study (1). Regarding parity, 45.6% of participants were para zero, 50.0% were para one, and 4.4% were para two, which aligns with the findings of Anand et al., who reported a recurrence rate of 61.1% among multiparous women (1). However, Nisha et al. reported a higher proportion of primigravida (60%), indicating potential differences in the obstetric profiles of the study populations (8).

In the present study, 49.2% of participants experienced itching specifically over their palms and soles, while 5.2% reported itching all over their bodies. A considerable proportion, accounting for 45.6%, described experiencing both types of itching. Additionally, only 2.0% exhibited excoriation of the skin, and jaundice was observed in just 0.4% of the participants.

Comparing these findings with previous studies, Naga et al reported that generalized pruritus was the most common symptom, appearing in 36.6% during the 2nd trimester and increasing to 83.3% in the 3rd trimester (9). Similarly, Ambros-Rudolph et al. and Anand et al. found pruritus to be a leading symptom in their respective studies, with high percentages of patients experiencing it (1,10). Dang et al. also reported pruritus as the leading symptom, further supporting the prevalence of itching seen in this study (11).

Table V: *Comparison of Intrahepatic cholestasis of pregnancy severity with foetal distress*

Mode of Delivery	IHCP Severity		p
	Mild	Moderate to severe	
No	225	10	1.000
	93.8%	100.0%	
Yes	15	0	
	6.3%	0.0%	
Total	240	10	
	100.0%	100.0%	

IHCP: Intrahepatic Cholestasis of Pregnancy

Table VI: *Distribution of study participants based on clinical symptoms*

Symptoms	Frequency	Percentage
Itching over palms and soles	123	49.2
Itching all over the body	13	5.2
Both	114	45.6
Total	250	100.0

Overall, the findings of the present study regarding the prevalence of itching in participants align with previous research, suggesting that pruritus is a common and prominent symptom in individuals with intrahepatic cholestasis of pregnancy across different studies.

The mean gestational age at the time of diagnosis in the present study was calculated to be 32.2 weeks, aligning with the advanced stages of pregnancy when cholestasis commonly manifests. Serum bile acids, an essential marker for cholestasis, displayed a mean level of 21.4 μmol/L, with findings falling within the spectrum reported by other studies.

Comparing these findings with existing literature, Corcoran et al. noted deranged liver function tests in 81% of patients, echoing the prevalent liver dysfunction observed in cholestasis cases (2). Anand et al. highlighted that most cases were diagnosed in the third trimester, similar to the gestational age at diagnosis observed in the present study (1). Dang et al. reported the onset of obstetric cholestasis around 31 weeks' gestation, consistent with the timing of diagnosis observed in the present study (11).

In our study, the majority of participants experienced term deliveries (93.2%), aligning with findings from various studies, such as those conducted by Corcoran et al. and Padmaja et al., who also reported predominantly term deliveries (2,3). In the present study, pre-term delivery was observed in 6.8% of participants, which was lower compared to some studies (1,8,9). Regarding maternal complications, premature rupture of membranes occurred in 7.2% of cases in our study, which is consistent with findings reported by Padmaja et al., who observed the same to be 8.9% (3). Additionally, meconium staining was observed in 10.4% of cases, which is comparable to the findings reported by Corcoran et al. (2) (7%), but lower than those reported by Bassi et al. (12) and Naga et al. (9), who observed incidences of 25.3% and 25%, respectively. Furthermore, we observed a postpartum hemorrhage rate of 0.8%, which is lower than the rates reported by Nisha et al. (8.75%) and Anand et al. (13.75%) (1,8).

In terms of the mode of delivery, 22.4% of participants in our study underwent LSCS, a rate comparable to that reported by Pegu et al. (13) (30.88%), but significantly lower than the rates observed in studies by Padmaja et al. (3), Jamwal et al. (7), and Anand et al. (1), where caesarean section rates ranged from 43.3% to 93.3%.

Most of the maternal complications observed in our study are either comparable to other studies or relatively lower. This may be because most of the patients attending our institute are either serving lady officers or spouses of military personnel who have a better understanding of the importance of maternal and fetal health during pregnancy. Our study contributes to the existing literature by providing insights into maternal complications associated with IHCP. The findings highlight the importance of vigilant monitoring and management of maternal health during pregnancy, particularly in cases of IHCP.

In our study, we observed that 6.0% of cases experienced fetal distress, which is in line with findings reported by Corcoran et al. and Naga et al., where fetal distress rates were reported at 7% and 9.5%, respectively (2,9). APGAR scores at 1 minute and 5 minutes in our study demonstrated favorable outcomes, with 98.4% of cases scoring 7 and above at 1 minute and 99.6% at 5 minutes. Similar to our findings, Corcoran et al. also observed a reduced APGAR score in 7% of newborns (2). Meconium aspiration was absent in all cases in our study, contrasting with findings from studies by Naga et al. (9) and Jamwal et al. (7), where meconium-stained amniotic fluid and meconium aspiration rates were higher (25% and 46.6%, respectively). Respiratory distress was observed in 2.8% of newborns in our study, and the incidence of neonatal jaundice and sepsis was also on the lower side (0.4% for both).

In our study, participants were categorized into three severity levels: mild (bile acid level <40 μmol/L), moderate (bile acid level between 40 - 100 μmol/L), and severe (bile acid level > 100 μmol/L). The majority of participants fell into the mild category (96%) of IHCP, with only a small proportion exhibiting moderate/severe IHCP (4%). Our study did not find a significant difference in IHCP severity and age group or onset of labor. However, our study did reveal a statistically significant association between IHCP severity and gestational age at the time of delivery, with a higher proportion of preterm deliveries observed among participants with moderate to severe IHCP (30% vs. 5.8%), a finding supported by Joutsiniemi et al. (14).

Interestingly, while the occurrence of meconium staining was higher in moderate to severe IHCP cases compared to mild IHCP cases, the difference was not statistically significant. Moreover, our study did not find a significant association between IHCP severity and postpartum hemorrhage or mode of delivery, consistent with the conclusions drawn by Arora et al. and Pegu et al (6,13). However, in our study, none of the neonates born to patients with moderate to severe IHCP experienced fetal distress.

Limitations: The differences in prevalence and incidence rates could be attributed to various factors, including differences in study design, diagnostic criteria, geographical variations, and especially to the demographic characteristics of the study population. A larger population size is required for more accurate results and comparisons.

Conclusion

IHCP predominantly affects pregnant women under the age of 35, with most cases presenting with mild severity. Maternal complications such as premature rupture of membranes and mode of delivery were found to vary based on

IHCP severity, with term deliveries being more common among mild cases. While maternal and foetal outcomes differed between IHCP severity groups, no significant associations were observed for certain parameters such as postpartum haemorrhage and meconium staining. These insights contribute to a better understanding of IHCP management and highlight the importance of tailored approaches to address the diverse clinical manifestations and outcomes associated with this condition during pregnancy. In addition to the observed variations in maternal and foetal outcomes based on IHCP severity, our study emphasizes the importance of early detection and intervention in mitigating adverse pregnancy outcomes associated with this condition. The prompt initiation of UDCA and close monitoring of liver function parameters and bile acid levels can play a crucial role in managing IHCP and reducing the risk of complications for both mother and baby. Furthermore, our findings highlight the need for multidisciplinary care involving obstetricians, hepatologists, and neonatologists to optimize the management of IHCP and improve pregnancy outcomes.

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Authors' Contributions: Each author contributed to conception and design, data collection and analysis, experiments, writing the first draft, and supervision. Each author contributed to the writing of the paper and has read and approved the final manuscript.
Conflict of Interest: None

References

1. Anand RS, Khan N, Malik N, Aditya V, Singh R. Maternal and perinatal outcome in obstetric cholestasis- a prospective observational study. Int J Reprod Contracept Obstet Gynecol. 2021;10(2):653-7. Doi: 10.18203/2320-1770.ijrcog20210322
2. Corcoran A, Langan H. Obstetric Cholestasis: Investigation of a suspected high incidence in the West of Ireland. Eur J Obstet Gynecol Reprod Biol. 2022;269:114-7. Doi: 10.1016/j.ejogrb.2021.12.009. PMID: 34992033.
3. Padmaja M, Bhaskar P, Kumar GJ, Seetha R, Mahasweta C. A study of obstetric cholestasis. J Obstet Gynaecol India. 2010;60(3):225-31. Doi: 10.1007/s13224-010-0030-3. PMCID: PMC3394515.
4. Pata O, Vardarelı E, Ozcan A, Serteser M, Unsal I, Saruç M, et al. Intrahepatic cholestasis of pregnancy: correlation of preterm delivery with bile acids. Turk J Gastroenterol. 2011;22(6):602-5. Doi: 10.4318/tjg.2011.0427. PMID: 22287405.
5. Gardiner FW, McCuaig R, Arthur C, Carins T, Morton A, Laurie J, et al. The prevalence and pregnancy outcomes of intrahepatic cholestasis of pregnancy: A retrospective clinical audit review. Obstet Med. 2019;12(3):123-8. Doi: 10.1177/1753495X18797749. PMID: 31523268, PMCID: PMC6734627.
6. Arora S, Huria A, Goel P, Kaur J. Maternal and fetal outcome in intrahepatic cholestasis of pregnancy at tertiary care institute of North India. Indian Journal of Medical Sciences. 2020;73(3):335-9. Doi: 10.25259/IJMS_446_2020.
7. 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. Doi: 10.18203/2320-1770.ijrcog20212676.
8. Nisha N, Singh R, Archana K. Outcome of pregnancy complicated by obstetric cholestasis. J Evolution Med Dent Sci. 2019;8(48):3593-8. Doi: 10.14260/jemds/2019/776.
9. Naga VKM, Joseph B, Kallappa MS. Obstetric outcome in women with intrahepatic cholestasis: a 3-year study in a tertiary care hospital in Bengaluru. J South Asian Feder Obst Gynae. 2019;11(2):103-6 Doi: 10.5005/jp-journals-10006-1662.
10. Ambros-Rudolph CM, Glatz M, Trauner M, Kerl H, Müllegger RR. The importance of serum bile acid level analysis and treatment with ursodeoxycholic acid in intrahepatic cholestasis of pregnancy: a case series from central Europe. Arch Dermatol. 2007;143(6):757-62. Doi: 10.1001/archderm.143.6.757. PMID: 17576942.
11. Dang A, Agarwal N, Bathla S, Sharma N, Balani S. Prevalence of liver disease in pregnancy and its outcome with emphasis on obstetric cholestasis: An Indian scenario. J Obstet Gynaecol India. 2010;60(5):413-8. Doi: 10.1007/s13224-010-0068-2. PMCID: PMC3394613.
12. Bassi R, Gujral K, Mansukhani C, Khera N. Intrahepatic cholestasis of pregnancy: prevalence and perinatal outcome. The Ganga Ram Journal. 2012;2(2):73-8.
13. Pegu B, Mehrotra M, Yadav A, Sahoo PSK. Cholestasis of pregnancy: a prospective analysis from a South Andaman teaching hospital. International Journal of Reproduction, Contraception, Obstetrics and Gynecology. 2019;8(5):1895-8. Doi: 10.18203/2320-1770.ijrcog20191939.
14. Joutsiniemi T, Timonen S, Linden M, Suvitie P, Ekblad U. Intrahepatic cholestasis of pregnancy: observational study of the treatment with low-dose ursodeoxycholic acid. BMC Gastroenterol. 2015;15:92. Doi: 10.1186/s12876-015-0324-0. PMID: 26215400, PMCID: PMC4517361.