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# Effect of Elevated Serum Bile Acid Levels in Intrahepatic Cholestasis of Pregnancy on Antenatal and Postnatal Outcomes; Prospective Cohort Study

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**Declaration**
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## ABSTRACT

**Study objective:** To evaluate the association of IHCP with antenatal and postnatal outcomes, aiming to reduce the disease-related morbidity and mortality.

**Design:** Prospective cohort study.

**Setting:** Gynaecology and Obstetrics unit of Patel hospital, Karachi.

**Material and Methods:** .Data were collected from pregnant patients with pruritus without rash, elevated liver enzymes, and serum bile acids ≥19 µmol/L. Disease severity was classified by bile acid levels. Management included ursodeoxycholic acid, antihistamines, and emollients, with follow-up testing after 7–14 days. Delivery decisions were based on symptoms, bile acid trends, and pregnancy risk factors. Maternal and neonatal outcomes were recorded using structured questionnaire. Studied parameters included timing of symptom onset, diagnosis of disease, time and mode of delivery, liquor colour, neonatal outcomes, birth weight and NICU admission.

**Results:** 36 patients were diagnosed with IHCP based on elevated serum bile acid levels. Most patients had singleton pregnancies (94.4%), with one twin and one triplet pregnancy. The mean maternal age was 26.14 years. Primigravida and multigravida women constituted 50% each, and 33.6% of multigravidas had a prior history of IHCP. Pruritus typically appeared between 29–34 weeks (median 32 weeks). ALT and AST elevation was noted between 30–36 weeks (median 33.5 weeks), while serum bile acids were elevated between 32–36 weeks (median 34.5 weeks). Based on bile acid levels, 61.1% had mild IHCP (19–39 µmol/L), 27.8% moderate (40–99 µmol/L), and 11.1% severe (≥100 µmol/L). The median gestational age at delivery was 37 weeks in mild and moderate IHCP and 36.3 weeks in severe cases. Delivery decisions were individualized. Vaginal delivery occurred in 36.1%, while 41.7% underwent elective and 22.2% emergency caesarean section. Induction of labour was performed in 13 patients, with non-progress of labour being the most common indication for emergency caesarean section. A total of 39 live-born neonates were delivered. The mean birth weight was 2.3 kg, with 58.9% weighing 2.5–3.5 kg. Meconium-stained liquor was observed in 25.6%, with no cases of meconium aspiration. NICU admission was required in 25.6%, primarily for transient tachypnea of the newborn and respiratory distress syndrome.

**Conclusion:** This study reinforces the importance of serum bile acid estimation as a primary diagnostic and prognostic tool in IHCP and highlights the benefits of structured monitoring and timely intervention in improving fetomaternal outcomes.

## INTRODUCTION

Intrahepatic cholestasis of pregnancy (IHCP) is a multifactorial liver disorder unique to pregnancy, characterized by maternal pruritus without rash, accompanied by elevated total serum bile acid levels, in the absence of any underlying dermatological or hepatobiliary disease. The condition is most commonly diagnosed in the late second trimester or early third trimester [3] and typically resolves spontaneously within four weeks postpartum, with normalization of serum bile acid levels.[2]

IHCP has a reported prevalence of approximately 1.2%–1.5% among women of Indian and Pakistani Asian origin,[1] while lower rates have been observed in Western populations. The etiology of IHCP is complex and is believed to involve a combination of genetic predisposition, hormonal influences, and environmental

factors. Familial clustering has been documented, particularly among first-degree relatives, and women with a history of IHCP are at increased risk of recurrence in subsequent pregnancies. [9-10]

According to the Royal College of Obstetricians and Gynaecologists (RCOG) guidelines of 2011, the diagnosis of IHCP was based on pruritus associated with deranged liver function tests (transaminases and gamma-glutamyl transferase) and/or raised bile acid levels. However, the updated RCOG guidelines of 2022 emphasize serum total bile acid concentration as the primary diagnostic marker, with a value of ≥19 µmol/L. Serum bile acids are now recognized as the most sensitive and specific marker for IHCP, while other liver enzymes such as alanine transaminase (ALT) and aspartate transaminase (AST) are not directly associated with adverse pregnancy outcomes. [5]

Based on serum bile acid levels, IHCP is classified into:

- **Mild:** 19–39 µmol/L
- **Moderate:** 40–99 µmol/L
- **Severe:** ≥100 µmol/L

IHCP is a major concern as it poses the pregnancy at risk of maternal and fetal complications such as preeclampsia, gestational diabetes mellitus, meconium-stained amniotic fluid, preterm birth, low birth weight babies, meconium aspiration, neonatal intensive care unit admissions, and stillbirth [4-8].

Given the transition from liver enzyme based diagnosis to bile acid based diagnosis and the limited local data correlating bile acid levels with fetomaternal outcomes, this study was conducted to assess the frequency of IHCP in our population and to evaluate its association with antenatal and postnatal outcomes, with the aim of reducing disease-related morbidity and mortality.

## MATERIAL AND METHODS

**Study Design and Setting:** This was a prospective cohort conducted at the Gynaecology and Endoscopy Unit, Patel Hospital, Karachi, from January 2024 to May 2025, following approval from the Institutional Ethical Review Committee

### Inclusion and Exclusion Criteria

For the assessment of frequency of disease and its obstetric and neonatal outcomes in our population, we included those pregnant patients in our study who complained of itching followed by raised alanine transaminase and aspartate transaminase along with raised serum bile acid concentration of 19micromol/L or more, without having any known dermatological or hepatobiliary pathology. If the bile acids were not sent despite of itching and raised liver enzymes, patient not included in study.

### Data Collection Procedure

Data collection started during antenatal visits of a patient who presented in opd with pruritus without rash, raised liver enzymes, and raised serum bile acid levels at or above 19micromole/L or more Patients were categorized into mild moderate and severe type as per bile acid values.

Based on investigations and clinical assessment, patients were treated, ursodeoxycholic acid, antihistamines and topical emollients. Repeat samples were advised for patients after 7-14 days depending on symptoms and severity of disease. Decision regarding further management including time and mode of delivery was based on worsening of symptoms and serial estimation of serum bile acid levels along with other risk factors in pregnancy. Afterwards the intrapartum and postnatal outcomes were recorded on a structured questionnaire after delivery.

### Data Collection Parameters

After fulfilling the inclusion and exclusion criteria, the parameters which were being studied includes, gestational age at which itching started, gestational age at which IHCP diagnosed on the basis of liver enzymes and serum bile acid, gestational age of delivery, mode of delivery, colour of liquor- clear or meconium stained, outcome of baby – alive or still birth, weight of the baby and whether baby needed post-delivery intensive care or not.

### Statistical Analysis

Statistical analysis was performed using SPSS version 20.0. Results were presented as mean and standard deviation, or median with IQR for quantitative variables ( age, parity). Frequency and percentage were calculated for qualitative variables (loq or standard). For quantitative variables-data following normality t- test was applied, while Mann Whitney test if data not following normality. For qualitative (categorical) variables Chi-square test was used. To check the confounding effect of current mode of delivery and gestational age at delivery with parity and previous mode of deliveries odds ratio was used, while for previous gestational age at delivery linear regression method applied. P value < 0.05 is significant

## RESULTS

There were 36 patients diagnosed with intrahepatic cholestasis of pregnancy on the basis of raised serum bile acid levels equal to or more than 19 micromole/L. Patients with bile acid <19 micromole despite of pruritis with raised ALT, AST levels or bile acid not sent and diagnosed on AST, ALT levels criteria were all excluded from the study.

The demographics shows among 36 IHCP patients 34 females were Singleton, 1 twin and 1 triplet pregnancies. The mean age of the patients was 26.14 year. 50% were primigravida and rest 50% were multigravida females. Out of these multigravidas 33.6% had a history of IHCP in previous pregnancies.

Pruritus was commonly seen in between 29 to 34 (median 32) weeks of gestation, Alanine Aminotransferase(ALT) was raised between 30 to 36 (median 33.5) weeks and bile acids were found to be raised between 32 to 36 (median 34.5) weeks of pregnancy

**Table 1**

*Demographic Profile (n =36)*

| | |
|---|---|
| **Age (yr); Mean ± SD** | 26.14±5.23 |
| **Parity** | |
| Prim gravida | 18(50%) |
| Para 1 | 10(27.8%) |
| Para 2 | 4(11.1%) |
| Para 3 | 2(5.6%) |
| Para 4 | 0 |
| Para 5 | 2(5.6%) |
| **History** | |
| Yes | 6(33.3%) |

| | |
|---|---|
| No | 12(66.6%) |
| **No. of pregnancy** | |
| Singleton | 34(94.4%) |
| Twin | 1(2.8%) |
| Triplet | 1(2.8%) |
| **Gestational age of pruritus; Median (IQR)** | 32(29-34) |
| **Gestational Age of raised ALT; Median (IQR)** | 33.5(30-36) |
| **ALT Median (IQR)** | 171(108-294) |
| **Gestational age of raised bile acid; Median (IQR)** | 34.5(32-36) |
| **Bile acid; Median (IQR)** | 35.85(25.6-50.4) |

Table 2 shows the distribution of patients in mild moderate and severe categories i.e. 21 (61.1%) patients had initial bile acid levels between 19-39 µmol/L, 10 (27.8%) patients between 40-99 µmol/L and only 4 (11.1%) patients had levels =/>100 µmol/L.

**Table 2**

| Type of IHCP (Serum Bile Acid Levels) | Number of Patients | Percentage |
|---|---|---|
| MILD (19-39 umol/L) | 22 | 61.1% |
| MODERATE (40-99 umol/L) | 10 | 27.8% |
| SEVERE (>100 umol/L) | 4 | 11.1% |

Table 3 shows correlation between S. bile acid levels with time and mode of delivery. Time and mode of delivery was decided on the basis of individual patient's profile, either by induction of labour or caesarean section for other obstetric indications.

The timing of delivery is 37(36-38) weeks of gestation in mild and moderate whereas 36.3(35.4-36.6) weeks in severe IHCP.

Out of 36 patients, 13 were vaginal deliveries, 15 were elective caesarean sections and 8 were emergency caesarean sections. Out of 13 vaginal deliveries, 2 were instrumental vaginal deliveries both due to fetal distress, rest spontaneously delivered. Induction of labour was done in 13 patients, due to IHCP, followed by SVD in 7 patients, rest 6 had EM-LSCS, 4 due to non progress of labour (NPOL), and 2 due to Failed induction . The indications for ELLSCS and EMLSCS are mentioned in table 3C, with the most common for ELLSCS was previous 2 caesarean (25%) and EMLSCS was NPOL following induction of labour due to IHCP (44.4%).

**Table 3A**

*Maternal Outcome*

| | |
|---|---|
| **Delivery mode** | |
| Svd | 4(11.1%) |
| Svd With IOL | 7(19.4%) |
| Ellscs | 15(41.7%) |
| Emlscs | 8(22.2%) |
| Instrumental | 2(5.6%) |

**Table 3B**

| | Mild | Moderate | Severe | P-value |
|---|---|---|---|---|
| **Delivery time** weeks; Median (IQR) | 37(36-38) | 37(36-38) | 36.3(35.4-36.65) | 0.504[c] |
| **Delivery mode** | | | | |
| Svd | 2(9.1%) | 1(10%) | 1(25%) | |
| Svd With IOL | 6(27.3%) | 1(10%) | 0 | |
| Ellscs | 7(31.8%) | 5(50%) | 3(75%) | 0.62[b] |
| Emlscs | 6(27.3%) | 2(20%) | 0 | |
| Instrumental | 1(4.5%) | 1(10%) | 0 | |

b: Fisher Exact test; c: Mann Whitney U test

**Table 3C**

*Indication for Induction of Labour and Caesarean Section*

| | |
|---|---|
| **Causes of Elective C/S** | |
| On demand | 2 (16.6%) |
| Twins | 1 (8.3%) |
| Previous 1 c/s with poor bishop | 2(16.6%) |
| Previous 2 c/s | 3(25%) |
| Previous 3 c/s | 2(16.6%) |
| Severe IHCP | 1(8.3%) |
| Vaginal varicosities | 1(8.3%) |
| **CAUSES OF EMLSCS** | |
| Failed induction of labour | 2(22.2%) |
| Non progress of labour | 4(44.4%) |
| Prev 2 In Labour | 1(11.1%) |
| Prev 1 In Labour | 0 |
| Absent diastolic flow | 1(11.1%) |
| Triplet In Labour | 1(11.1%) |

There were 39 neonates born to 36 mothers as there was 1 twin and 1 triplet delivery. All were alive babies, delivered with good apgar score and immediate cry. Mean weight was found to be 2.3kg, with 23 babies (58.9%) between 2.5-3.5kg, 10 babies(25.6%) 2-2.5kg, 3(7.6%) 1.5-2kg , 3(7.6%) 1-1.5kg and no baby below 1kg. 10(25.6%) babies had passed meconium, but no meconium aspiration reported in any of them. 10 babies were admitted In NICU, 7 babies with transient tachypnea of new born, and 3 babies due to respiratory distress syndrome

**Table 4A**

Fetal Outcome

| | |
|---|---|
| **Weight (Kg); Mean ± SD** | 2.3±0.52 |
| **Weight groups** | |
| 2.5-3.5kg | 23(58.9%) |
| 2-2.5 | 10(25.6%) |
| 1.5-2 | 3(7.6%) |
| 1-1.5 | 3(7.6%) |
| <1 | 0 |
| **Meconium** | |
| Msl 1 | 8(20.5%) |
| Msl 2 | 1(2.5%) |
| Msl 3 | 1(2.5%) |
| No Msl | 29(74.3%) |
| **Birth** | |
| Alive | 39(100%) |
| Still Birth | 0 |
| **NICU Admission** | |
| Yes | 10(25.6%) |
| No | 29(74.3%) |

**Table 4B**

| | Mild | Moderate | Severe | P value |
|---|---|---|---|---|
| **Weight (Kg); Mean ± SD** | 2.28±0.57 | 2.61±0.37 | 2.3±0.47 | 0.246[a] |
| **Weight groups** | | | | |
| 2.5-3.5kg | 16(64%) | 6(60%) | 1(25%) | |
| 2-2.5 | 4(16%) | 3(30%) | 3(75%) | |
| 1.5-2 | 2(8%) | 1(10%) | 0 | 0.258[b] |
| 1-1.5 | 3(12%) | 0 | 0 | |
| <1 | 0 | 0 | 0 | |
| **Meconium** | | | | |
| Msl 1 | 5(20%) | 2(20%) | 1(25%) | |
| Msl 2 | 0 | 1(10%) | 0 | 0.398[b] |
| Msl 3 | 0 | 1(10%) | 0 | |
| No Msl | 20(80%) | 6(60%) | 3(75%) | |
| **Birth** | | | | |
| Alive | 25(100%) | 10(100%) | 4(100%) | NA |
| Still Birth | 0 | 0 | 0 | |
| **NICU admission** | | | | |
| Yes | 6(24%) | 3(30%) | 1(25%) | 0.934[b] |
| No | 19(76%) | 7(70%) | 3(75%) | |

Sd: Standard deviation ; IQR: Inter-quartile ranges ; a: independent sample t test ; b: Fisher Exact test ; c: Mann Whitney U test

**Table 4C**

*Causes of Nicu Admission*

| | |
|---|---|
| Transient Tachypnea of Newborn | 7 (70%) |
| Respiratory Distress Syndrome | 3 (30%) |

## DISCUSSION

The median age of the patients in this study was 26.14years. The mean gestational age of delivery is 37 weeks, i.e. 37(36-38) weeks of gestation in mild and moderate whereas 36.3(35.4-36.6) weeks in severe IHCP. Mode of deliveries was 30.5% via SVD, 41.7% via ELLSCS, 22.2% via EMLSCS, and 5.6% via instrumental vaginal delivery.

All babies delivered were alive and healthy, mean weight of babies was 2.3kg, 10 babies needed NICU admission, 7 due to TTN and 3 due to RDS, but discharged with good health post treatment. 10 babies passed meconium but no meconium aspiration reported.

Comparing our data with other studies performed in Pakistan, regarding ihcp and its outcomes,

At hamdard university hospital Karachi in 2024 of 76 patients, the median age of the patients was 27.5 (23.0-33.7) years. Forty-eight (63.2%) ICP women had caesarean section delivery, 14 (18.4%) had post-partum haemorrhage, and 40 (52.6%) had itching after delivery. Whereas 54 (71.1%) neonates were preterm, 43 (56.6%) were of low birth weight, 18 (23.7%) had meconium-stained amniotic fluid, 23 (30.3%) had APGAR score <7 at 1 min, 8 (10.5%) had APGAR score <7 at 5 mins, 6 (7.9%) had NICU admission, 4 (5.3%) had still birth, and neonatal death was observed in 5 (6.6%) neonates. [13]

Another recent study done in Lahore, 2024-2025 which included 78 participants with a mean age of 26.42 years. 64.1% were primigravida. 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%). 5 cases (6.41%) of intrapartum fetal death, and 1 stillbirth (2.5%) [12]

One study conducted in 2016 involving 5 hospitals of Punjab, including of 1001 obstetric patients, 31(3.1%) had intrahepatic cholestasis of pregnancy. Pruritus was the main symptom in 25 (85%) patients followed by rash in 20 (65%). In 20 (64%) patients, labour was induced. Mode of delivery was Caesarean Section in 18 (58%) patients and 9 (29%) had postpartum haemorrhage. Regarding neonatal complications, 22 (70%) required admission to neonatal intensive care and 15 (48%) had meconium aspiration[7]

Regarding international studies, a study in Australia done in 2017 revealed prevalence rate of IHCP is 0.6%, the primary clinical outcomes of ihcp included a median age at delivery is 36.4 weeks, a low birth weight, and increase in special care nursery admissions [6].

Studies also conducted in India, recent in 2024 in Jodhpur showed a prevalence of 3.6% of IHCP, with significant weight difference between the birth weight in mild, moderate and severe categories. There was 1.32% rate of intrauterine death seen with moderate type of IHCP[11].

This study demonstrates the mean maternal age and gestational age at delivery align with regional and international studies. Notably, all neonatal outcomes in this cohort were favourable, with no stillbirths or neonatal deaths, likely reflecting timely diagnosis, close monitoring, and individualized obstetric management

Compared with other Pakistani studies, our cohort exhibited lower rates of preterm birth, stillbirth, and NICU admissions, suggesting that bile acid–based diagnosis and proactive management may contribute to improved outcomes. International studies similarly report lower prevalence rates in Western populations but comparable associations with preterm delivery and NICU admission.

## CONCLUSION

Overall, this study reinforces the importance of serum bile acid estimation as a primary diagnostic and prognostic tool in IHCP and highlights the benefits of structured monitoring and timely intervention in improving fetomaternal outcomes.

## REFERENCES

1. Girling, J., Knight, C. L., & Chappell, L. (2022). Intrahepatic cholestasis of pregnancy. *BJOG: An International Journal of Obstetrics & Gynaecology*, *129*(13). https://doi.org/10.1111/1471-0528.17206
2. David, A. L., Kotecha, M., & Girling, J. C. (2000). Factors influencing postnatal liver function tests. *BJOG: An International Journal of Obstetrics & Gynaecology*, *107*(11), 1421-1426. https://doi.org/10.1111/j.1471-0528.2000.tb11659.x
3. Gupta, V., Rehman, A., Nimonkar, S., Chaudhari, P., & Saxena, N. (2023). Obstetric outcome of elevated total serum bile acid levels in women with intrahepatic cholestasis of pregnancy. *The New Indian Journal of OBGYN*, *9*(2), 302-307. https://doi.org/10.21276/obgyn.2023.9.2.22
4. Kenyon, A. P., Tribe, R. M., Nelson-Piercy, C., Girling, J. C., Williamson, C., Seed, P. T., Vaughan-Jones, S., & Shennan, A. H. (2010). Pruritus in pregnancy: A study of anatomical distribution and prevalence in relation to the development of obstetric cholestasis. *Obstetric Medicine*, *3*(1), 25-29. https://doi.org/10.1258/om.2010.090055
5. Ovadia, C., Seed, P. T., Sklavounos, A., Geenes, V., Di Ilio, C., Chambers, J., ... & Williamson, C. (2019). Association of adverse perinatal outcomes of intrahepatic cholestasis of pregnancy with biochemical markers: results of aggregate and individual patient data meta-analyses. *The Lancet*, *393*(10174), 899-909. https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(18)31877-4/fulltext
6. Gardiner, F. W., McCuaig, R., Arthur, C., Carins, T., Morton, A., Laurie, J., Neeman, T., Lim, B., & Peek, M. J. (2018). The prevalence and pregnancy outcomes of intrahepatic cholestasis of pregnancy: A retrospective clinical audit review. *Obstetric Medicine*, *12*(3), 123-128. https://doi.org/10.1177/1753495x18797749
7. Hafeez, M., Ansari, A., Parveen, S., Salamat, A., & Aijaz, A. (2016). Frequency of intrahepatic cholestasis of pregnancy in Punjab Pakistan: A single centre study. *J Pak Med Assoc*, *66*(2), 203-206.

8. Geenes, V., Chappell, L. C., Seed, P. T., Steer, P. J., Knight, M., & Williamson, C. (2014). Association of severe intrahepatic cholestasis of pregnancy with adverse pregnancy outcomes: A prospective population-based case-control study. *Hepatology*, *59*(4), 1482-1491. https://doi.org/10.1002/hep.26617
9. Turunen, K., Helander, K., Mattila, K. J., & Sumanen, M. (2013). Intrahepatic cholestasis of pregnancy is common among patients' first-degree relatives. *Acta Obstetricia et Gynecologica Scandinavica*, *92*(9), 1108-1110. https://doi.org/10.1111/aogs.12168
10. Pataia, V., Dixon, P. H., & Williamson, C. (2017). Pregnancy and bile acid disorders. *American Journal of Physiology-Gastrointestinal and Liver Physiology*, *313*(1), G1-G6. https://doi.org/10.1152/ajpgi.00028.2017
11. Jhirwal, M., Sharma, C., Shekhar, S., Singh, P., Meena, S. P., Kathuria, P., & Tak, A. (2022). Maternal and perinatal outcome in pregnancy complicated by Intrahepatic Cholestasis. *Cureus*. https://doi.org/10.7759/cureus.28512
12. Nasir, A., Muneer, N., Butt, A., Hameed, S., Asif, S., & Rana, M. N. (2025). Fetomaternal outcomes in Intrahepatic Cholestasis of pregnancy at tertiary care hospital in Lahore. *National Journal of Health Sciences*, *10*(2), 135-140. https://doi.org/10.21089/njhs.102.0135
13. Jamsheed, S., Samad, A., Khan, F., & Waleem, N. (2024). Maternal and fetal outcome in pregnancy complicated by intrahepatic cholestasis of pregnancy. *Journal of The Society of Obstetricians and Gynaecologists of Pakistan*, *14*(3), 310-315. https://www.jsogp.net/index.php/jsogp/article/view/744