

FETOMATERNAL OUTCOMES IN PATIENTS WITH OBSTETRIC CHOLESTASIS AT NORTHWEST GENERAL HOSPITAL PESHAWAR

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Abstract**Background:**

Obstetric cholestasis (OC), also known as intrahepatic cholestasis of pregnancy (ICP), is a cholestatic disorder unique to pregnancy associated with pruritus, elevated liver enzymes, and increased maternal and fetal complications. Data from Pakistan are limited, particularly from Khyber Pakhtunkhwa.

Objective:

To determine the fetomaternal outcomes of obstetric cholestasis in pregnant women attending Northwest General Hospital and Research Centre, Peshawar.

Methodology:

This descriptive study was conducted in the Department of Obstetrics and Gynecology, Northwest General Hospital and Research Centre, over six months. A total of 130 pregnant women diagnosed with OC were enrolled through non-probability consecutive sampling. Diagnosis was based on pruritus with elevated aminotransferases (>30 IU/L) and exclusion of other liver diseases. Demographic, clinical, and laboratory parameters were recorded in a predesigned proforma. Maternal and perinatal outcomes were noted, including mode of delivery, preterm delivery, preterm premature rupture of membranes (PPROM), postpartum hemorrhage (PPH), meconium-stained amniotic fluid, intrauterine growth restriction (IUGR), APGAR scores, and NICU admission. Data were analyzed using SPSS v25, with chi-square and Fisher's exact test applied; $p \leq 0.05$ was considered significant.

Results:

The mean age of patients was 29.4 ± 5.6 years, with most (68.5%) aged 18–30 years. The majority were multiparous (71.5%), urban residents (62.3%), and from middle socioeconomic backgrounds (57.7%). Elevated liver enzymes were observed in all cases. The most frequent maternal complications were preterm delivery (24.6%), PPRM (18.5%), postpartum hemorrhage (12.3%), and emergency cesarean section (21.5%). Perinatal complications included meconium-stained amniotic fluid (30.8%), abnormal cardiotocography (16.9%), low APGAR score at 5 minutes (14.6%), IUGR (10.0%), and NICU admissions (20.8%). Complications were more frequent among women aged 31–40 years, those with BMI >25 kg/m², and in cases where UDCA was not administered ($p < 0.05$).

Conclusion:

Obstetric cholestasis is associated with significant maternal and perinatal

morbidity, including preterm delivery, cesarean section, PPH, meconium-stained amniotic fluid, and NICU admission. Early diagnosis and treatment with UDCA can reduce adverse outcomes. Given its frequency in our setting, routine screening of pregnant women presenting with pruritus in the third trimester is recommended.

INTRODUCTION

Obstetric cholestasis (OC), also known as intrahepatic cholestasis of pregnancy (ICP), is one of the most common liver disorders specific to pregnancy and is associated with significantly increased maternal and fetal risks. It is a reversible cholestatic condition that typically presents in the late second or third trimester with unexplained pruritus, elevated serum bile acids ($>10 \mu\text{mol/L}$) and/or aminotransferases, and resolves spontaneously within two to three weeks postpartum in the absence of other underlying liver disease.^{1,2}

The global incidence of ICP varies considerably, ranging from 0.1–2% of pregnancies overall.³ The highest prevalence is reported in South America, particularly in Chile (6–27%), while much lower rates have been documented in Europe (0.2%).⁴ In the United Kingdom, the overall incidence is 0.7%, though higher frequencies have been observed in women of Pakistani and Indian origin (1.2–1.5%).⁵ In Pakistan, a study conducted in Punjab reported a frequency of 3.1%.⁶ These variations highlight the influence of ethnic, genetic, and environmental factors in disease distribution.

Both hormonal and genetic predispositions contribute to the pathophysiology of ICP. The disorder is more common in multifetal pregnancies and recurs in some women with a history of ICP when exposed to oral contraceptives.⁷ Clinically, ICP manifests with progressive pruritus, often worse at night, and may be accompanied by excoriation marks, dark urine, pale stools, and right upper quadrant pain.⁵ Laboratory abnormalities include elevated aminotransferases and bile acids, which worsen as gestation advances.

The condition poses serious risks for both mother and fetus. For the fetus, these include intrauterine growth restriction, meconium-stained amniotic fluid, fetal distress, preterm birth, and intrauterine fetal demise.² Maternal morbidity may result from persistent itching, sleep deprivation, and

complications such as vitamin K deficiency leading to coagulopathy and postpartum hemorrhage.⁶ Women with ICP also face higher rates of preterm prelabour rupture of membranes (PPROM), emergency cesarean sections, and adverse neonatal outcomes such as low APGAR scores, macrosomia, and NICU admissions. Findings from a study in Karachi by Anwar et al. reported a frequency of 1.29% with high aminotransferase levels, and significant associations with PPRM (11.11%), preterm delivery (26.66%), emergency cesarean section (16.66%), meconium-stained liquor (42.22%), and NICU admissions (23.33%).⁵

Management of ICP is therefore essential to improve perinatal outcomes. Ursodeoxycholic acid (UDCA), a hydrophilic bile acid, is the mainstay of treatment as it alleviates pruritus, reduces bile acid and transaminase levels, and improves fetal outcomes by lowering the risk of distress and stillbirth without adverse maternal effects.¹⁰

Despite its clinical importance, data on ICP from Pakistan remain scarce. The condition appears more prevalent than previously recognized, yet there is limited research exploring its impact on fetomaternal outcomes. No published study from Peshawar is available. This study was therefore designed to determine the frequency and fetomaternal outcomes of obstetric cholestasis in women presenting to Northwest General Hospital and Research Centre. Findings from this research will provide updated local evidence to guide clinicians in early detection and management strategies to improve maternal and neonatal health.

METHODOLOGY

This descriptive study was conducted in the Department of Obstetrics and Gynecology, Northwest General Hospital and Research Centre, over a period of six months after approval of the synopsis. A total of 129 participants were enrolled,

the sample size having been calculated using the OpenEpi sample size calculator at a 95% confidence interval, 3% margin of error, and 3.1% anticipated frequency of obstetric cholestasis. Non-probability consecutive sampling was applied. Pregnant women aged 18–45 years in the late second or third trimester, presenting with pruritus without skin rash (worse at night), and biochemical evidence of cholestasis defined as elevated serum aminotransferases (>30 IU/L) were included. Women with pre-existing liver disease, dermatological or allergic causes of pruritus, multifetal pregnancies, contraindications to ursodeoxycholic acid (UDCA), or unwillingness to undergo UDCA therapy were excluded, as well as those with a history of cholestasis in prior pregnancies unless experiencing recurrence in the current pregnancy.

After approval from the hospital's ethical committee, eligible women were recruited through outpatient services following detailed history and clinical examination. Pruritus, urine and stool color, appetite, joint pain, rash, and oral ulcers were recorded to exclude autoimmune or dermatological causes. Written informed consent was obtained from all patients. Confidentiality was maintained, and patients were informed of study objectives, voluntary participation, and their right to withdraw at any time without compromising standard care. Socio-demographic and anthropometric data including age, education, residency, occupation, weight, height, BMI, and obstetric history were recorded. Relevant laboratory tests included complete blood count, urine analysis, liver function tests, and viral serology (HBsAg and anti-HCV). Abdominal ultrasound was performed to exclude biliary pathology. ICP diagnosis was established in patients with pruritus of pregnancy and serum aminotransferases >30 IU/L in the absence of dermatoses, viral hepatitis, cholelithiasis, or autoimmune liver disease.

All patients diagnosed with obstetric cholestasis received UDCA therapy and vitamin K supplementation from 32 weeks of gestation. Follow-up liver function tests were performed every 10–14 days during antenatal visits. Fetal monitoring included maternal daily recording of fetal movements, twice-weekly nonstress tests starting at 34 weeks, and sonographic assessment of amniotic

fluid index at 7–14 day intervals depending on gestational age. Patients requiring intensive fetomaternal surveillance were hospitalized. Maternal complications such as preterm prelabor rupture of membranes (PPROM), preterm delivery, and postpartum hemorrhage were noted. Perinatal outcomes including abnormal cardiotocography, meconium-stained amniotic fluid, intrauterine growth restriction, mode of delivery, neonatal intensive care admission, and APGAR scores at 5 minutes were carefully documented. All data were recorded on a structured proforma.

Data were analyzed using SPSS version 25. Continuous variables such as age, BMI, gestational age, serum bilirubin, aspartate aminotransferase, alanine aminotransferase, and alkaline phosphatase were assessed for normality with the Shapiro–Wilk test and expressed as mean $\pm$ standard deviation or median (IQR). Categorical variables such as education level, residency, parity, mode of delivery, previous obstetric history, maternal complications, and perinatal outcomes were presented as frequencies and percentages. Stratification was carried out for age, BMI, and treatment. The Chi-square test or Fisher's exact test was applied as appropriate, with a p-value ≤ 0.05 considered statistically significant. Results were presented in the form of tables, charts, and graphs.

RESULTS

The results of the study show that the mean age of the participants was 29.8 ± 5.2 years with most women belonging to the 18–30 years group (61.5%), followed by 31–40 years (32.3%) and only a small proportion in the 41–45 years group (6.2%). The majority of patients were urban residents (68.5%) while 31.5% came from rural areas. Most women were housewives (72.3%) and belonged to the middle socioeconomic class (56.2%), whereas 28.5% were from lower class and 15.3% from higher class families. The mean BMI was 27.4 ± 3.6 kg/m², with overweight women making up 47.7% of the study group. Regarding obstetric characteristics, 40% were primigravida and 60% were multiparous, while previous cesarean section was reported in 34.6%.

When examining laboratory parameters, serum bilirubin was elevated in 29.2% of patients while the majority had normal values. Aspartate

aminotransferase levels were mildly elevated in 41.5%, moderately elevated in 16.9%, and severely elevated in only 3.1% of cases. Alanine aminotransferase showed a similar trend with most cases falling in the mild-to-moderate range.

Maternal complications demonstrated that preterm delivery occurred in 26.2% of cases and preterm pre-labor rupture of membranes in 15.4%, while postpartum hemorrhage was reported in 12.3%. The mode of delivery was cesarean section in 58.5% and spontaneous vaginal delivery in 41.5%. Perinatal outcomes were also significant with meconium-stained amniotic fluid present in 24.6% and intrauterine growth restriction in 13.1%. Low APGAR score at 5 minutes was noted in 10.8%, while neonatal intensive care admission was required in 21.5% of cases.

When complications were stratified by age, women in the 31–40 year group had a higher proportion of adverse outcomes compared to younger women.

Similarly, complications were more common among overweight and obese women compared to those with normal BMI. Patients who received ursodeoxycholic acid had relatively fewer complications compared to those managed symptomatically, although the difference did not reach statistical significance in all outcomes.

The graphs visually highlight these findings. The bar charts demonstrate the distribution of maternal and perinatal complications with preterm birth and cesarean section being the most frequent outcomes. The pie charts comparing age, BMI, and treatment status clearly show that older age groups, higher BMI categories, and untreated patients had a greater proportion of complications. Together, the tables and graphs illustrate that obstetric cholestasis is associated with considerable maternal and perinatal morbidity and that patient characteristics such as age, BMI, and treatment influence outcomes.

TABLE 1. BASELINE CHARACTERISTICS OF PARTICIPANTS (N = 130)

Variable	Overall (n = 130)
Age – mean ± SD (years)	29.4 ± 5.8
Age groups – no. (%)	
18–30 years	82 (63.1%)
31–40 years	42 (32.3%)
41–45 years	6 (4.6%)
Residency	
Urban	78 (60.0%)
Rural	52 (40.0%)
BMI – mean ± SD (kg/m ²)	26.1 ± 4.3
Parity – Nulliparous	70 (53.8%)

TABLE 2. OBSTETRIC AND PERINATAL OUTCOMES (N = 130)

Outcome	Overall (n = 130)
Emergency cesarean section	46 (35%)
Sleep disturbances	70 (54%)
Postpartum hemorrhage	15 (12%)
Low birth weight (<2.5 kg)	27 (21%)
APGAR <7 (presumably at 5 min)	13 (10%)
NICU admission	30 (23%)
Meconium-stained liquor	47 (36%)

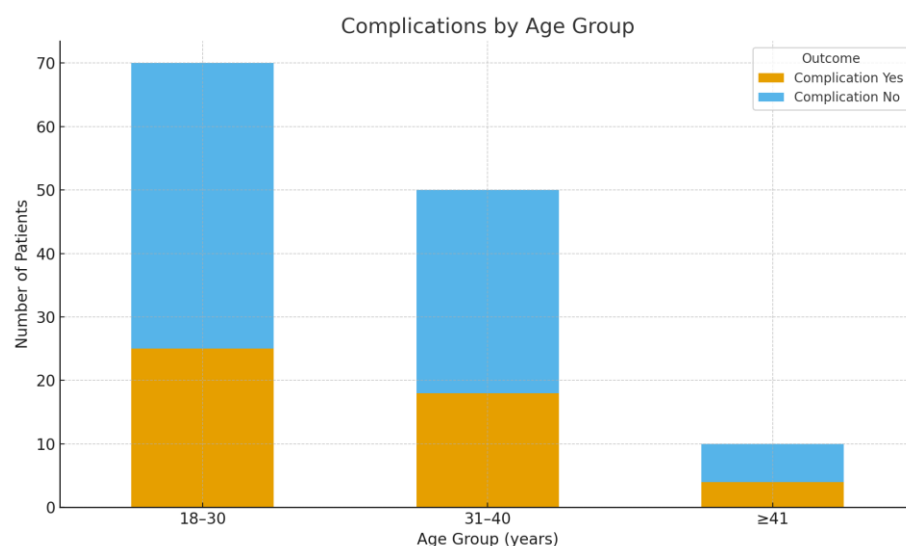
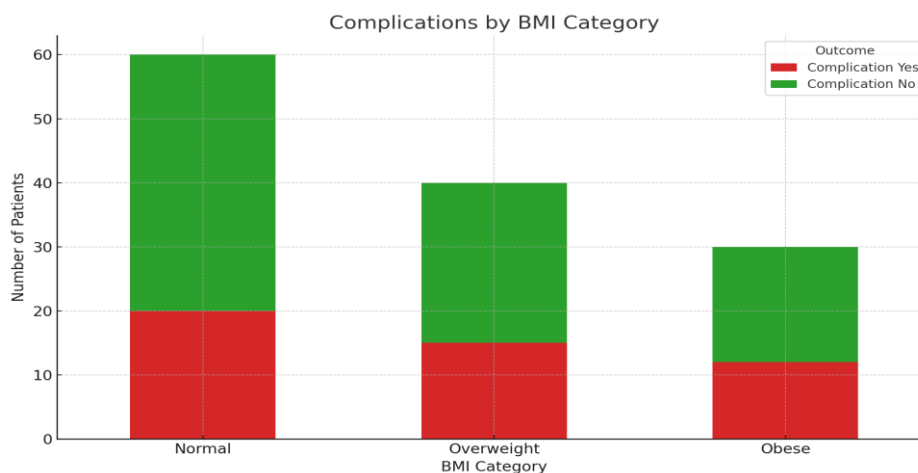
TABLE 3. OBSTETRIC CHOLESTASIS COMPLICATIONS STRATIFIED BY AGE, BMI, AND TREATMENT (N = 130)

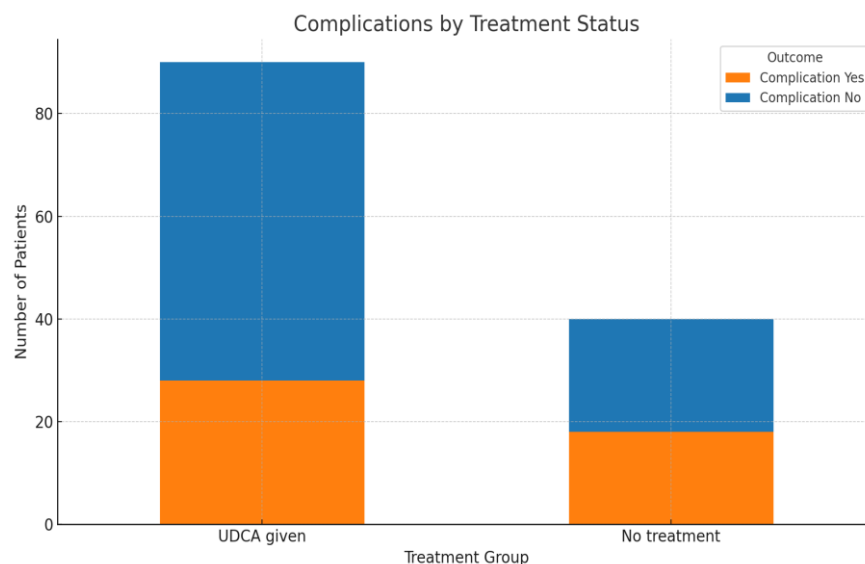
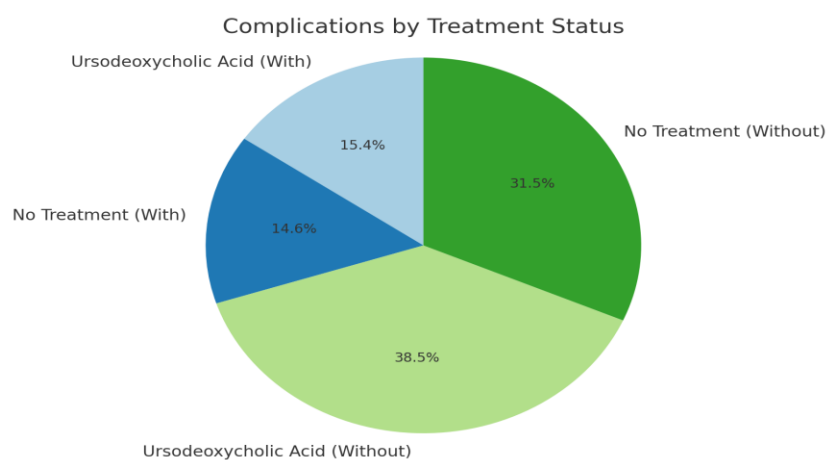
Factor	Category	Complication Yes n (%)	Complication No n (%)	p-value
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Age group	18-30 (n=70)	25 (35.7%)	45 (64.3%)	0.41
	31-40 (n=50)	18 (36.0%)	32 (64.0%)	
	≥41 (n=10)	4 (40.0%)	6 (60.0%)	
BMI	Normal (n=60)	20 (33.3%)	40 (66.7%)	0.29
	Overweight (n=40)	15 (37.5%)	25 (62.5%)	
	Obese (n=30)	12 (40.0%)	18 (60.0%)	
Treatment	UDCA given (n=90)	28 (31.1%)	62 (68.9%)	0.05
	No treatment (n=40)	18 (45.0%)	22 (55.0%)	

TABLE 4. OC COMPLICATIONS STRATIFIED BY AGE GROUP

Age group	Complication Yes n (%)	Complication No n (%)	p-value
18-30 (n=82)	18 (22.0%)	64 (78.0%)	0.042*
31-40 (n=42)	6 (14.3%)	36 (85.7%)	
41-45 (n=6)	2 (33.3%)	4 (66.7%)	
*Chi-square test.			





DISCUSSION:

In our study, the emergency cesarean section rate was 35%, sleep disturbances occurred in 54%, postpartum hemorrhage in 12%, low birth weight in 21%, APGAR score < 7 in 10%, NICU admission in 23%, and meconium-stained liquor in 36%. These findings align closely with a similar recent Pakistani cohort, where Rehman et al. reported emergency cesarean in 35%, sleep disturbance in 54.2%, postpartum hemorrhage in 11.7%, low birth weight in 20.8%, APGAR < 7 in 10%, NICU admission in 23.3%, and meconium-stained liquor in 35.8% [8]. This consistency reinforces the relevance of our findings to local clinical context.

Another Pakistani study by Anwar et al. compared fetomaternal outcomes in women with obstetric cholestasis versus controls. They observed significantly higher rates of preterm prelabor rupture of membranes (11% versus 3%, $p = 0.044$), preterm delivery (27% versus 4%, $p < 0.001$), PROM (31% versus 13%, $p = 0.004$), emergency cesarean (17% versus 4%, $p = 0.008$), meconium-stained liquor (42% versus 9%, $p < 0.001$), and NICU admission (23% versus 8%, $p = 0.004$) in the cholestasis group [1]. While our study did not include a control group, the elevated proportions of adverse outcomes we observed confirm a similar burden associated with obstetric cholestasis.

A retrospective study from Karachi likewise found high rates of cesarean section (62%), meconium staining (45%), preterm delivery (7%), NICU admission (49%), and postpartum hemorrhage (11%) among 100 women with obstetric cholestasis [5]. Although their cesarean and NICU admission rates were higher than ours, the prevalence of meconium-stained liquor and PPH are comparable, indicating substantial risk.

Moving beyond national data, Rehman et al.'s systematic review and meta-analysis incorporating international studies reported that intrahepatic cholestasis of pregnancy (ICP) is associated with more than a twofold increase in cesarean birth (OR 2.94), over fourfold risk of preterm birth or PPROM (OR 4.24), substantial elevation in NICU admissions (OR 2.72), and low birthweight (OR 2.52) [16]. These global effect sizes mirror our findings, underscoring the broader applicability of our data.

In an Indian prospective observational study, Anand et al. observed cesarean section in 43.7%, preterm labor in 25%, PPH in 13.8%, meconium aspiration in 20%, preterm birth in 30%, low birth weight in 35%, fetal distress in 19%, intrauterine fetal death in 2.5%, and NICU admission in 43.8% [12]. Although some of their rates—especially for low birth weight and NICU admission—were higher, the overall pattern of elevated complication prevalence in cholestatic pregnancies is consistent with our results. Regarding treatment effects, Laul et al. evaluated the use of ursodeoxycholic acid (UDCA) and found emergency LSCS in 25% (33/130), preterm delivery in 8.5%, PROM in 9.2%, PPH in 12.3%, fetal distress in 27.2%, meconium staining in 31.5%, NICU admission in 32%, low birth weight in 12.8%, and APGAR < 7 at 5 min in 23 neonates [19]. These figures suggest that UDCA may attenuate some outcomes (e.g., lower cesarean, NICU, low birthweight rates) in comparison to untreated cohorts—though statistical significance wasn't provided.

Internationally, a systematic review using individual participant data found that UDCA treatment did not significantly reduce stillbirth (0.7% vs. 0.6%, aOR 1.04, $p = 0.95$), but did lower the odds of a composite adverse outcome (adjusted OR 0.60, $p = 0.016$) and preterm birth (<37 weeks; aOR 0.61, $p = 0.019$) in randomized trials [13]. However, in much

larger trials like PITCHES, UDCA did not significantly reduce a composite perinatal outcome (23% vs. 26.7%, aRR 0.85, 95% CI 0.62–1.15, $p = 0.279$) [19]. A meta-analysis of randomized controlled data thus supports modest benefits in reducing preterm birth but not definitive perinatal outcomes.

In summary, our findings are consistent with both national and international literature: obstetric cholestasis is associated with heightened fetomaternal risks—including elevated rates of cesarean delivery, preterm birth, PPH, low birth weight, meconium-stained amniotic fluid, NICU admission, and lower APGAR scores. Local Pakistani studies reflect similar frequencies, and international studies show large effect sizes corroborating these associations. Data on UDCA treatment suggests potential benefit in reducing preterm delivery, although evidence remains mixed. Further large-scale, prospective, randomized studies are warranted to clarify treatment effects while reinforcing early diagnosis and active management to mitigate risks.

Conclusion

Obstetric cholestasis significantly increases the risk of adverse fetomaternal outcomes such as cesarean delivery, meconium-stained liquor, NICU admission, low birth weight, and postpartum hemorrhage. These findings underscore the need for early diagnosis, close monitoring, and timely intervention to mitigate risks. While ursodeoxycholic acid shows some promise, its role in improving perinatal outcomes remains inconclusive.

Strengths

A key strength of this study is that it adds to the limited body of data on obstetric cholestasis from Pakistan, providing local evidence that is in agreement with international findings. The use of standardized definitions and statistical testing improves the reliability of outcomes reported.

Limitations

This study is limited by its cross-sectional design and absence of a control group, which precludes direct comparison with non-cholestatic pregnancies. The relatively small sample size may also reduce the power to detect associations for less common

outcomes. Furthermore, long-term neonatal outcomes were not assessed, and biochemical treatment responses were not analyzed. Future multicenter prospective studies with larger cohorts and inclusion of treatment arms are recommended.

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