

		ORIGINAL RESEARCH PAPER	Paediatrics
CLINICAL PROFILE AND OUTCOME OF NEONATAL CHOLESTASIS ADMITTED TO A TERTIARY HOSPITAL		KEY WORDS: neonatal cholestasis , biliary atresia	
Dr Spurti Patchipulusu*	Post Graduate MBBS MD Paediatrics Paediatrics Bangalore Medical College And Research Institute, Krishna Rajendra Road, Kalasipalya Bangalore 560002 *Corresponding Author		
Dr Sahana Devadas	Professor And HOD MBBS MD Pediatrics Paediatrics Bangalore Medical College And Research Institute Krishna Rajendra Road, Kalasipalya Bangalore 560002		
ABSTRACT	Objective: To assess the clinical profile, etiology, and outcomes of neonatal cholestasis in infants under three months at a tertiary care center. Methods: A retrospective study which included 15 infants diagnosed with neonatal cholestasis in Vani Vilas Hospital between November 2023 to April 2024 were evaluated- history and clinical findings were noted, which included jaundice, stool color, itching, abdominal distention, poor feeding, failure to thrive, constipation, etc and diagnosis was established by lab tests, radiological tests, liver biopsy and specific diagnostic tests. data was recorded and analysed Results: A total of 15 infants were included in this s study, it was found that 53.3% were males. The average age of presentation was 7 weeks. Te most common presentation being jaundice , hepatomegaly and high clored urine, while splenomegaly and ascites were least common. BILIARY ATRESIA, n=4 (26.6%) was the most common cause of neonatal cholestasis, followed by IDIOPATHIC NEONATAL HEPATTITIS, n=3(20%). Other causes being metabolic and infections. The most common cause of death, n=7(50%) in children with neonatal cholestasis was liver failure(71%). Conclusion: Biliary atresia was the most common and had a more favorable outcome than intrahepatic causes. Timely diagnosis and management are essential for improving outcomes in neonatal cholestasis cases.		
	INTRODUCTION Neonatal cholestasis is a serious liver disorder that presents with prolonged jaundice in infants, typically within the first weeks of life. Affecting approximately 1 in 2,500 live births worldwide, it has a significant prevalence in India, where it accounts for 19% to 33% of hepatobiliary cases presenting in tertiary hospitals ¹ . The condition results from impaired bile flow, which can be due to hepatocellular or obstructive causes. The most common etiologies include biliary atresia and idiopathic neonatal hepatitis, with other causes being metabolic disorders and infections. Infants with cholestasis often arrive at tertiary centers with advanced disease and liver failure due to delayed diagnosis and referral. This delay not only complicates treatment but also increases morbidity and mortality, emphasizing the need for prompt evaluation and management. Liver biopsy and HIDA scans play an essential role in diagnosing intrahepatic and extrahepatic causes, respectively, and are critical for effective treatment planning. This study aims to assess the clinical profile, etiology, and outcomes of neonatal cholestasis cases admitted to a tertiary care center. Conducted at Vani Vilas Hospital, BMCRI, Bangalore, the retrospective analysis includes data on 15 infants under three months with cholestasis. By examining demographics, clinical presentations, and diagnostic results, the study identifies biliary atresia as the leading cause, followed by idiopathic neonatal hepatitis. The findings underscore the importance of early intervention in reducing morbidity and improving outcomes for neonatal cholestasis, contributing to better management practices in similar healthcare settings. This study was a retrospective observational analysis conducted at Vani Vilas Hospital, BMCRI, Bangalore, aimed at understanding the clinical profile, etiology, and outcomes of infants presenting with neonatal cholestasis. The study focused on infants under three months of age who exhibited signs of prolonged jaundice lasting beyond 14 days, with a conjugated bilirubin fraction greater than 20%. Data collection spanned from November 2023 to April 2024.		
Study Population And Sampling		Data Collection After obtaining informed consent from the parents, demographic and clinical data were collected for each infant. This included age at diagnosis, sex, gestational age, birth weight, and delivery details (e.g., mode of delivery, any complications). Clinical presentations, such as jaundice duration, color of urine and stool, and any abdominal distension, were meticulously documented. Additionally, details on family medical history, feeding patterns, and any history of infections were recorded to understand potential contributing factors. Investigations And Diagnostics A range of laboratory investigations was conducted to comprehensively evaluate liver function and diagnose potential causes of cholestasis. The following diagnostic tests and evaluations were performed for each infant in the study ³ : Hemogram: This was conducted to assess the general health and detect signs of infections, anemia, or other blood disorders that may contribute to the condition. Liver Function Tests (LFTs): LFTs were performed to measure the levels of enzymes, proteins, and bilirubin in the blood, providing an indication of liver health and functionality. Elevated levels of liver enzymes and conjugated bilirubin were particularly significant for diagnosing cholestasis. Urine Analysis: Urine samples were analyzed to detect any abnormalities indicative of liver dysfunction or infections that could impact the biliary system. Coagulation Profile: Coagulation tests assessed the infants' blood clotting ability, as liver dysfunction can lead to coagulopathy. This information helped guide supportive care measures and interventions when	

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needed.

5. Specific Diagnostic Tests:

Hepatobiliary Iminodiacetic Acid (HIDA) Scan²:
 A non-invasive diagnostic imaging test performed on six infants to assess biliary atresia. The HIDA scan, which uses a radioactive tracer, helps visualize bile flow from the liver into the small intestine. Among the six HIDA scans performed, four (66%) indicated biliary atresia, making it a valuable diagnostic tool in determining the primary cause of cholestasis in these cases.

Liver Biopsy³:
 Conducted for selected patients to obtain detailed histopathological data. This invasive procedure allowed for the microscopic examination of liver tissue, which helped in identifying intrahepatic causes of cholestasis such as idiopathic neonatal hepatitis or progressive familial intrahepatic cholestasis (PFIC). In this study, four patients underwent liver biopsy, with results showing three cases of neonatal hepatitis and one case consistent with PFIC.

Data Analysis
 The demographic and clinical characteristics, including age, sex, and key symptoms, were summarized to provide a profile of the affected population. The results of diagnostic tests, such as liver function tests, urine analysis, coagulation profiles, liver biopsies, and HIDA scans, were analyzed to determine the primary etiology in each case. Biliary atresia and idiopathic neonatal hepatitis were identified as the two leading causes, which informed further breakdown of outcomes and mortality rates.

Ethical Considerations
 Ethical approval for this study was obtained from the institutional ethics committee. Informed consent was obtained from the parents or guardians of each infant included in the study. The confidentiality and anonymity of all participants were maintained, with personal health information kept secure and accessible only to the research team. Any invasive procedures, such as liver biopsies, were performed following standard clinical guidelines and with parental consent.

RESULTS
 This study evaluated 15 infants diagnosed with neonatal cholestasis admitted to Vani Vilas Hospital, BMCRI, Bangalore. The findings provided insights into the demographic characteristics, clinical presentations, diagnostic findings, and outcomes associated with neonatal cholestasis.

Demographics And Clinical Presentation
 Among the 15 infants, the mean age of presentation was 7 weeks, with a slight male predominance. Key clinical features included prolonged jaundice persisting beyond the typical neonatal period, with conjugated bilirubin levels exceeding 20%. Other common symptoms observed were dark urine, pale or acholic stools, and abdominal distension, all indicative of impaired bile flow. A significant proportion of the infants had low birth weight and were born preterm, highlighting potential contributing factors for neonatal cholestasis.

Table 1: Based On Gender Distribution

	EXTRA HEPATIC	INTRA HEPATIC
	4(26.6%)	11 (73%)
MALE	2(50%)	5(45.4)
FEMALE	2(50%)	6(54.5%)

Etiology And Diagnostic Findings
 The primary etiologies identified were biliary atresia and idiopathic neonatal hepatitis. Biliary atresia, affecting 4 infants (26.6%), emerged as the most frequent cause, aligning with similar studies where extrahepatic cholestasis often

results from obstructive causes. This was followed by idiopathic neonatal hepatitis, observed in 3 cases (20%), representing the most common intrahepatic cause of cholestasis.

Table 2: Based On Etiology

ETIOLOGY	
Biliary atresia(BA)	4
Idiopathic neonatal hepatitis(INH)	3
Tyrosinemia	2
Sepsis	2
Congenital Hypothyroidism	1
Fatty acid oxidation defect(FAO)	1
Cytomegalovirus infection(CMV)	1

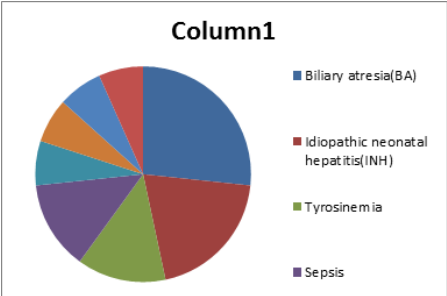


Figure 1: Distribution Based On Etiology

Liver Function Tests (LFTs) And Other Investigations
 The liver function tests revealed elevated levels of conjugated bilirubin and liver enzymes, consistent with cholestatic liver disease. All infants had abnormal liver function, with significantly increased levels of aspartate aminotransferase (AST) and alanine aminotransferase (ALT), markers indicative of liver cell damage.

Hepatobiliary Iminodiacetic Acid (HIDA) Scan: HIDA scans were conducted on 6 infants to diagnose biliary atresia. Among these, 4 infants (66%) were confirmed to have biliary atresia based on the imaging results. The scan proved effective in identifying obstructive cholestasis, with its high sensitivity aiding in early intervention planning for these infants.

Liver Biopsy: A liver biopsy was performed on 4 infants, offering histopathological insights into intrahepatic cholestasis. Three of these biopsies confirmed neonatal hepatitis, showing inflammatory changes in the liver consistent with this condition. One biopsy showed features compatible with progressive familial intrahepatic cholestasis (PFIC), a rare genetic disorder affecting bile flow.

Table 3: Based On Liver Function

		EXTRAHEPATIC	INTRAHEPATIC
Bilirubin	15.2	14.9	15.27
total direct	8.3(55%)	6.5	9.03
AST/ALT	312/321	454/515	260/250
GGT	79.4	94.7	73.8
INR	2.09	2.19	2.3
HB	6.8	12.15	9.27

Table 4: Based On Presentation

		EXTRA HEPATIC	
Jaundice	15(100%)	4(100%)	11(100%)
Dark urine	9(60%)	2(50%)	7(63%)
Acholic stools	7(46.6%)	2(50%)	5(45%)
Hepatomegaly	10(66.6%)	2(50%)	8(72%)
Splenomegaly	3(20%)	1(25%)	2(18%)

Ascites	5(20%)	0	5(45%)
Hypoglycemia	2(13.3%)	0	2(18%)

Outcomes And Mortality
 Of the 15 infants studied, 7 (50%) unfortunately succumbed to complications associated with neonatal cholestasis. Liver failure was the primary cause of death, accounting for 71% of the mortality cases. The outcomes varied significantly by etiology; infants with biliary atresia demonstrated relatively favorable outcomes compared to those with intrahepatic causes such as idiopathic neonatal hepatitis. The early identification of biliary atresia allowed some infants to undergo appropriate interventions, which likely contributed to their better prognosis.

Table 5: Based On Morbidity And Mortality

DISEASE	Morbidity	Mortality(50%)
Biliary atresia (4)	Failure to thrive-2(50%)	Sepsis-1(25%)
Idiopathic neonatal hepatitis (3)	Sepsis- 1 (25%)	Liver failure-2(66%)
Metabolic (4)	Liver cirrhosis-1 (25%)	Liver failure-2(50%)
Infections (3)	Chronic Liver disease-1 (33%)	MODS-1 Liver failure – 1 (66%)

The study highlighted the critical role of early diagnostic interventions, particularly liver biopsy and HIDA scans, in managing neonatal cholestasis. Liver biopsy was instrumental in confirming intrahepatic causes, while HIDA scans effectively identified cases of biliary atresia. These diagnostic tools provided clarity on the disease etiology, enabling targeted management and highlighting the need for timely referrals.

Table 6: Based On Outcome

	Extra hepatic	Intra hepatic
Total	4	11
Death	1(25%)	6(54%)
Improved	3(75%)	5(45%)

Comparative Analysis With Previous Studies
 The study's findings were consistent with similar research in the field. For example, previous studies from tertiary centers in India and Bangladesh also identified biliary atresia as the most common extrahepatic cause and idiopathic neonatal hepatitis as a leading intrahepatic cause. Such comparative insights affirm the study's findings and underscore the prevalence of biliary atresia in neonatal cholestasis cases in this region.

Summary
 This study reinforces that biliary atresia is a primary cause of neonatal cholestasis and, when diagnosed early, can lead to favorable outcomes. The high mortality rate from liver failure in cases of intrahepatic cholestasis underscores the need for early diagnostic measures and effective management strategies to improve patient outcomes in tertiary care settings.

DISCUSSION
 The findings of this study reinforce neonatal cholestasis as a significant health concern in infants, with biliary atresia and idiopathic neonatal hepatitis being the predominant causes. Biliary atresia, observed in 26.6% of cases, was the leading extrahepatic cause, consistent with previous studies across tertiary centers in India and neighboring countries. Biliary atresia is often associated with a higher likelihood of successful intervention when diagnosed early, as surgical treatments like the Kasai procedure can restore bile flow in certain cases. This study underscores the importance of prompt diagnosis and intervention, which can alter outcomes for these infants, especially in cases of biliary atresia⁶.

Idiopathic neonatal hepatitis, identified in 20% of the cases, represented the most common intrahepatic cause. The presence of idiopathic hepatitis poses a diagnostic challenge due to its nonspecific clinical presentation, often requiring liver biopsy to confirm the diagnosis. This finding aligns with research indicating that idiopathic hepatitis remains a primary intrahepatic cholestatic condition in neonates, necessitating accurate histopathological evaluation to distinguish it from other metabolic and genetic causes of cholestasis.

The study highlights the value of liver biopsy and HIDA scans as diagnostic tools in managing neonatal cholestasis. Liver biopsy was particularly useful for diagnosing intrahepatic causes, allowing clinicians to confirm idiopathic hepatitis and identify rare cases of progressive familial intrahepatic cholestasis (PFIC). HIDA scans, which effectively confirmed biliary atresia in 66% of cases evaluated, remain an essential imaging technique for identifying obstructive causes. These findings emphasize that an integrated diagnostic approach—leveraging both histopathology and imaging—is crucial for effectively managing neonatal cholestasis.

The mortality rate in this study, primarily due to liver failure, points to the critical need for early identification and intervention. Infants with intrahepatic causes, particularly idiopathic hepatitis, showed higher mortality rates than those with biliary atresia. This may reflect the limited treatment options available for intrahepatic cholestasis, compared to the more direct surgical interventions possible for biliary atresia. These findings align with studies from other tertiary centers, which report better outcomes in cases of biliary atresia when early intervention is feasible.

Limitations
 The study's primary limitation is the small sample size of 15 infants, which restricts the generalizability of the findings. This limited cohort was due to the short data collection period and stringent inclusion criteria. A larger sample size over an extended period would provide more comprehensive data, potentially revealing additional causes of neonatal cholestasis not captured in this study. Furthermore, the study did not incorporate advanced diagnostic methods such as genetic testing, which could have identified rarer causes of cholestasis, especially for intrahepatic conditions like PFIC and other genetic metabolic disorders. The reliance on available diagnostic resources within the hospital setting may also have influenced the findings, as some etiologies could remain undetected without access to specialized testing.

Additionally, this study was retrospective in design, relying on medical records and previous diagnostic data, which may lack the standardization seen in prospective studies. Future research could benefit from a prospective design to ensure consistency in data collection and diagnostic testing protocols, potentially improving the reliability of findings related to clinical presentation and outcomes.

CONCLUSION
 Neonatal cholestasis remains a significant cause of morbidity and mortality among infants in tertiary care settings, with biliary atresia and idiopathic neonatal hepatitis identified as leading etiologies. Biliary atresia, the primary extrahepatic cause, has a more favorable prognosis when diagnosed early, enabling timely intervention through surgical procedures. In contrast, idiopathic neonatal hepatitis, the predominant intrahepatic cause, poses diagnostic and treatment challenges, often leading to poorer outcomes due to limited therapeutic options.

The study underscores the importance of a structured diagnostic approach, combining liver biopsy and HIDA scans, to distinguish between obstructive and hepatocellular causes of neonatal cholestasis effectively. Early diagnosis is critical

for improving outcomes, particularly in cases of biliary atresia, where surgical intervention can be life-saving. For intrahepatic causes, advances in genetic and metabolic testing may enhance diagnostic accuracy and potentially lead to novel therapeutic options in the future.

This research emphasizes the need for improved awareness, timely referral, and a standardized diagnostic approach for neonatal cholestasis in tertiary care settings. Larger, multi-center studies incorporating advanced diagnostic tools are warranted to expand on these findings, offering a broader understanding of the condition and optimizing care for affected infants.

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