

# Neonatal Cholestasis - Single Centre Experience in Central India

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## ABSTRACT

**Background:** Neonatal cholestasis syndrome (NCS) is a major cause of morbidity and mortality in infants. The disorder has rarely been studied in centers from Central India. **Objectives:** To study the prevalence, clinical presentation and etiology of NCS at a tertiary referral center in Central India. **Materials and Methods:** The study was carried out at a tertiary referral center in Central India. The study is a descriptive study. The records of all patients with suspected NCS treated in the Department of Pediatrics from 2007-2012 were analyzed. **Results:** One hundred and sixty-eight children had a provisional diagnosis of NCS. The complete records of 100 children were available for the study. The median age of presentation was 78 days (range 15-270 days). The male:female ratio was 1.17:1. The clinical features noted were- jaundice (100/100,100%), failure to thrive (73,73%), organomegaly (68, 68%), acholic stools (38,38%), abdominal distention (52,52%) and poor feeding (29, 29%). The etiology as confirmed by investigations is as follows- neonatal hepatitis (20,20%), idiopathic neonatal hepatitis (18,18%), biliary atresia (41,41%), sepsis (14,14%) and others (7,7%). **Conclusions:** The proportion of NCS in our group of patients was 1.2 per 1000 patients. Jaundice, organomegaly and failure to thrive are the common presentations. Biliary atresia, neonatal hepatitis and idiopathic neonatal hepatitis were the common etiological factors at our center.

**Keywords:** Cholestasis, jaundice, neonatal, syndrome

## Introduction

*Jaundice- "Many infants are affected by this disease, some are even born with it, but it is rarely mentioned, though a great many die of it."*

Dr. John Cooke, 1769

Neonatal cholestasis syndrome (NCS) accounts for almost 30% of pediatric hepatobiliary diseases. It is defined as prolonged elevation of conjugated bilirubin beyond 14 days of life (i.e., the conjugated fraction >20% of total

bilirubin). Neonatal cholestasis includes a wide spectrum of clinical conditions ranging from congenital malformations of hepatobiliary tree, infections and inborn errors of metabolism.<sup>[1]</sup> NCS has been largely ignored in our country. It is diagnosed late and referral to tertiary care centers is delayed. Most children present with advanced disease and liver failure. There is scarcity of published (peer reviewed) data on NCS from India.<sup>[1]</sup> There is no data from Central India, on the etiology and clinical profile of neonatal

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**Cite this article as:** Jain M, Adkar S, Waghmare C, Jain J, Jain S, Jain K, et al. Neonatal cholestasis - Single centre experience in Central India. Indian J Community Med 2016;41:299-301.

### Access this article online

#### Quick Response Code:



#### Website:

www.ijcm.org.in

#### DOI:

10.4103/0970-0218.193331

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**Received:** 21-05-13, **Accepted:** 07-12-13

cholestatic disorders in this region. The objective of the study is to study the proportion, clinical presentation and etiology of NCS at a tertiary referral center in Central India.

## Materials and Methods

This descriptive study was carried out at Choithram Hospital and Research Centre, Indore. It is a tertiary referral center in Central India. Details of all patients treated as in patients or outpatients in the Department of Pediatrics from 2007 to 2012 were collected from the medical record section of the hospital.

### Inclusion criteria

The case records of all patients with NCS were collected by two methods-

Collection of details of all patients who underwent Hepatobiliary iminodiacetic (HIDA) scan for suspected neonatal cholestasis and then getting their detailed records from the record section.

Collection of case records of all patients treated in Department of Pediatrics with following International Classification of Diseases (ICD) codes: ICD 9 and 10 -k71.0 (toxic liver injury with cholestasis), k87 (disorders of gall bladder, biliary tract and pancreas in diseases classified elsewhere), k83.9 (unspecified diseases of biliary tract), R16 (hepatomegaly and splenomegaly) and R17 (unspecified jaundice).

All patients who had full records available formed the study group.

### Exclusion criteria

We excluded all patients whose records were incomplete or in whom a final diagnosis could not be made.

Case records of all patients presenting with NCS were studied. Detailed information including history, routine blood investigations, thyroid function tests and liver function tests was collected. Serological tests for toxoplasma, cytomegalovirus, rubella and herpes simplex were done in all patients. Specific tests like tandem mass spectrometry, serum ferritin and lip biopsies were done in suspected cases of congenital metabolic disorders. Data regarding abdominal imaging, HIDA scan and liver biopsies were collected.

The data was collected by two authors – one each from Departments of Gastroenterology and Pediatrics. It was entered in Microsoft excel sheet and analysed using appropriate statistical methods using SPSS software version 16.

All patients who had full records available formed the study group. The study group was analysed on the basis of age, sex, presenting complaints and final etiological diagnosis of NCS.

## Results

During the study period, a total of 1,31,440 children attended outpatient and inpatient services at our center. One hundred and sixty-eight children had a provisional diagnosis of NCS. Thus, the proportion of NCS was 1.2 patients/1000. The complete records of 100 children were available for the study.

The median age of presentation was 78 days (range 15–270 days). The male: female ratio was 1.17:1. History of consanguinity was noted in nine cases and family history of neonatal jaundice was present in one case. The clinical features noted were- jaundice (100/100,100%), failure to thrive (73,73%), organomegaly (68, 68%), acholic stools (38,38%), abdominal distention(52,52%) and poor feeding (29, 29%). The etiology as confirmed by investigations is mentioned below [Table 1].

Patients with biliary atresia were advised for Kasai Portoenterostomy and liver transplantation as per the disease severity. Patients with sepsis, cytomegalovirus and herpes infection were managed with intravenous antibiotics, antifungals and antivirals. Hypothyroidism was managed with thyroid hormones supplementation. Patients with other causes were managed symptomatically and referred to higher centers for further management.

## Discussion

Neonatal cholestasis syndrome is a difficult diagnostic problem. Early diagnosis is important for proper management. Fat-soluble vitamin supplementation, nutritional support and early referral to centers where NCS can be managed are required.

**Table 1: Etiology of NCS**

	No. of cases	Percentage
Neonatal hepatitis (CMV/Toxoplasma/ Rubella/Herpes)	20(10/6/2/2)	20
Idiopathic neonatal hepatitis	18	18
Biliary atresia	41	41
Sepsis	14	14
Hypothyroidism	02	2
Down's syndrome	02	2
Others (Tyrosinemia/Progressive Familial Intrahepatic Cholestasis/ Hemochromatosis)	03(1/1/1)	3

In our study, the proportion of NCS patients was 1.2 per 1000 patients. The median age of presentation was 78 days (2.6 months) and male to female ratio was 1.17:1. Two major studies from India and Bangladesh reported the median age of presentation to be 3.5 months.<sup>[1,2]</sup> The male to female ratio in these studies was also similar to our patient group. The earlier presentation in our study may be secondary to increased awareness over the years.

The presenting clinical features in our patients were jaundice, failure to thrive and organomegaly. Ahmad *et al.*, from Rawalpindi reported jaundice, listlessness, organomegaly, failure to thrive and feeding difficulty as the main clinical presentations.<sup>[3]</sup> However, we found feeding abnormalities to be less common in our group.

In our study, biliary atresia was the commonest cause of NCS followed by neonatal hepatitis. Three studies from Indian subcontinent had noted neonatal hepatitis to be the major cause for NCS.<sup>[1,2,4]</sup> In a study by Bazlul Karim *et al.*, from Bangladesh, neonatal hepatitis (22; 35.5%–17 with TORCH), followed by biliary atresia (16; 25.8%) and idiopathic neonatal hepatitis (15; 24.2%), were the commonest causes of cholestasis. Ahmad *et al.*, from Rawalpindi reported biliary atresia to be commoner in their group of patients.<sup>[3]</sup> The difference in etiological spectrum in our study compared to other studies may be secondary to referral bias or lack of definitive diagnostic tests like liver biopsies in majority of the patients.

The present study is one of the few studies on neonatal cholestasis and represents a single-center experience over a period of 6 years. There has been uniformity in approach and use of diagnostic tests. Moreover, our center is one of the few centers in Central India where HIDA scan is available and hence, patients from other hospitals also get referred for imaging. However, with our collection method, it is highly likely that we might have missed a few cases of NCS at our center. We retrospectively traced the records and it is likely that a few patients in whom the ICD coding was not properly

entered or HIDA scan was not done could have been missed.

The study highlights the common etiological factors for NCS in Central India. Although complete work up was done in most patients, data on long-term outcome and follow-up is not available. We would like to suggest maintaining of national/regional registries of this disease to ascertain regional variations in etiological spectrum and standardize treatment.

## Conclusions

The proportion of patients of NCS at our center is 1.2 per 1000. The mean age of presentation and clinical features were similar when compared to other studies. However, we found biliary atresia to be the commonest cause of NCS at our center.

## Recommendations

Early referral of neonates with conjugated hyperbilirubnemia to centers with expertise and facilities for early diagnosis and treatment is important. We would like to recommend maintenance of national/regional registries of these cases to ascertain regional variation.

## Financial support and sponsorship

Nil.

## Conflicts of interest

There are no conflicts of interest.

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