World Journal of Advanced Research and Reviews
eISSN: 2581-9615 CODEN (USA): WJARAI
Cross Ref DOI: 10.30574/wjarr
Journal homepage: https://wjarr.com/

(RESEARCH ARTICLE)

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# Prevalent causes and outcomes of unconjugated hyperbilirubinemia in neonates

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World Journal of Advanced Research and Reviews, 2025, 27(02), 1465-1473

Publication history: Received on 10 July 2025; revised on 17 August 2025; accepted on 19 August 2025

Article DOI: https://doi.org/10.30574/wjarr.2025.27.2.2964

## Abstract

**Background:** Early detection and prompt management of neonatal jaundice are critical in reducing neonatal morbidity and mortality. Effective treatment strategies include close monitoring, phototherapy, exchange transfusion, and addressing underlying causes. This study aimed to identify the prevalent causes of unconjugated hyperbilirubinemia in neonates and to assess their immediate clinical outcomes.

**Methodology**: This prospective hospital-based study was conducted at Ahmed Gasim Teaching Hospital from January to June 2022. A total of 103 neonates who met the inclusion criteria were enrolled. Data were analyzed using SPSS version 26.

**Results**: The study included 103 neonates, with a mean age of 7.6 ± 4.8 days (range: 1–28 days); 56 (54.4%) were male. The mean gestational age was 38.5 ± 1.9 weeks, with 91 (88.3%) being full-term and 12 (11.7%) being preterm. The mean age at onset of jaundice was 3.05 ± 1.8 days (range: 1–10 days). Mean total bilirubin was 14.4 ± 13.9 mg/dL, and mean direct bilirubin was 0.97 ± 0.60 mg/dL. The most common causes of unconjugated jaundice were sepsis (86, 83.5%), ABO incompatibility (25, 24.3%), dehydration (14, 13.6%), and Rh incompatibility (13, 12.6%). Treatments included phototherapy (72, 69.9%), medications (68, 66.0%), conservative management (32, 31.1%), and exchange transfusion (7, 6.8%). Most neonates (91, 88.3%) were discharged in good condition, while 12 (11.7%) were discharged against medical advice. No cases of kernicterus or mortality were reported.

**Conclusion:** Sepsis and ABO incompatibility were the leading causes of neonatal unconjugated hyperbilirubinemia. Most neonates responded well to treatment and were discharged in good condition.

**Keywords:** Causes; Outcomes; Unconjugated Hyperbilirubinemia; Neonates

## 1. Introduction

Neonatal jaundice is a common clinical sign in newborns, characterized by yellow discoloration of the skin and sclerae due to elevated serum bilirubin levels. This condition reflects the accumulation of bilirubin in tissues, including the skin and mucous membranes. Detection can be challenging in infants with darker skin tones, making examination of the sclerae a crucial aspect of clinical assessment [1].

Neonatal jaundice is a global health concern due to its significant contribution to neonatal morbidity and mortality. Approximately 60% of term infants and 80% of preterm infants develop jaundice within the first week of life, and up to 10% of breastfed infants may remain jaundiced for as long as one month. It accounts for nearly 70% of neonatal

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morbidity and 10% of neonatal mortality, with a substantial burden observed in South Asia and sub-Saharan Africa—regions where approximately 75% of neonatal deaths due to jaundice-related complications occur [2].

Physiological jaundice is the most common type, resulting from immature liver function and elevated levels of unconjugated bilirubin. In contrast, pathological jaundice is associated with conditions that either increase bilirubin production or impair its excretion. Major risk factors for neonatal unconjugated jaundice include prematurity and neonatal sepsis [3]. Other causes of neonatal bilirubinemia include breastfeeding or breast milk-related jaundice, perinatal infections, and hemolytic jaundice. The prevalence of these causes varies across different populations and regions. Hemolytic jaundice is further subdivided into Rh factor incompatibility, ABO blood group incompatibility, and jaundice due to glucose-6-phosphate dehydrogenase (G6PD) deficiency [1,4].

Severe unconjugated hyperbilirubinemia—defined as a total serum bilirubin (TSB) level exceeding 20 mg/dL (342.1 μmol/L)—affects less than 2% of term infants but significantly increases the risk of kernicterus. Kernicterus, a chronic form of bilirubin encephalopathy, results in permanent neurodevelopmental disabilities. Due to its hydrophobic nature, bilirubin can cross the blood-brain barrier, leading to bilirubin-induced neurological dysfunction (BIND). The severity of BIND ranges from mild language processing delays to severe encephalopathy, kernicterus, and even death. Globally, approximately 24 million neonates are at risk of complications from unconjugated hyperbilirubinemia each year. Despite being preventable with timely intervention, the condition causes an estimated 114,000 infant deaths annually and leaves more than 63,000 children with permanent neurological impairment [5,6].

Given its potentially severe, life-threatening consequences—particularly involving the nervous system—neonatal hyperbilirubinemia demands thorough investigation. This study aims to explore the prevalent causes and short-term outcomes of neonatal jaundice among infants admitted to Ahmed Gasim Specialized Hospital for Children in Khartoum, Sudan, between January 2022 and June 2022. Specifically, the study seeks to identify the common causes of neonatal unconjugated jaundice at this facility and assess the short-term clinical outcomes among the affected neonates.

## 2. Methodology and materials

A prospective hospital-based study was conducted from January 2022 to June 2022 at Ahmed Gasim Teaching Hospital for Children in Khartoum State, Sudan. This hospital serves as a major secondary-level referral center for pediatric care and includes an intensive care unit with 7 beds, a high-dependency unit with 8 beds, and 7 long-stay wards totaling 110 beds.

The study focused on neonates aged ≤28 days who were admitted with either conjugated or unconjugated jaundice. A total of 103 participants were enrolled. Inclusion criteria included neonates diagnosed with jaundice whose caregivers provided informed consent. Neonates whose caregivers declined participation were excluded.

### 2.1. Sample Size

A convenience sampling method was used, and the final sample size was 103 neonates.

### 2.2. Variables

Dependent Variable: Neonatal unconjugated hyperbilirubinemia

Independent Variables: Demographic characteristics (age, gestational age, gender, residence), admission details, causes of jaundice, treatment methods, and clinical outcomes

### 2.3. Data Collection and Technique

Data were collected using a structured questionnaire administered through direct interviews with caregivers and supplemented by information extracted from medical records.

### 2.4. Data Analysis and Presentation

Collected data were entered into Microsoft Excel and analyzed using SPSS version 26. Descriptive statistics were used: continuous variables were expressed as mean ± standard deviation (SD), while categorical variables were presented as frequencies and percentages [n (%)]. Results were displayed using univariate and bivariate tables (cross-tabulations), pie charts, and histograms. The Chi-square test was used to determine associations between variables, with statistical significance set at $p < 0.05$.

### 2.5. Ethical Clearance

Ethical approval was obtained from the Ministry of Health in Khartoum, Sudan, the hospital's administrative authority, and relevant institutional ethical committees. Written informed consent was obtained from all caregivers. Anonymity and data confidentiality were maintained through the use of coded serial numbers.

## 3. Results

103 neonates met the inclusion criteria and were included in the study. Data analysis was performed using SPSS version 26, and the following findings were obtained:

### 3.1. Demographic and Clinical Characteristics

The mean age of the patients was 7.6 ± 4.8 days, with a range of 1 to 28 days. Most neonates (n = 82, 63.1%) were 7 days old or younger, while 48 (35.9%) were older than 7 days. Of the neonates, 56 (54.4%) were male, and 47 (45.6%) were female. The mean gestational age was 38.5 ± 1.9 weeks, with the majority being full-term (n = 91, 88.3%) and the remainder preterm (n = 12, 11.7%). A family history of neonatal jaundice was reported in 21 cases (20.4%) [Table 1]. The most common maternal illness was infection during pregnancy, affecting 25 cases (24.3%). Other maternal conditions included premature rupture of membranes (PROM) in 6 cases (5.8%), home vaginal delivery in 5 cases (4.9%), and preeclampsia in 3 cases (2.9%) [Table 2].

### 3.2. Clinical Features and Causes of Jaundice

The mean age at onset of jaundice was 3.05 ± 1.8 days (range: 1–10 days). Most cases (n = 49, 47.6%) developed jaundice between days 2 and 3 of life, while 34 cases (33%) developed jaundice after day 3 [Table 3]. The mean birth weight was 2.8 ± 0.7 kg (range: 1–6 kg). A majority (n = 78, 75.7%) had a birth weight between 2.5 and 4 kg, and 23 (22.3%) weighed less than 2.5 kg [Table 4].

Moro reflex was present in 100 neonates (97.1%) and absent in 3 (2.9%) [Figure 5]. Abdominal examination revealed abnormalities in 8 neonates (7.8%); among these, 5 (62.5%) had abdominal distension, and 3 (37.5%) had hepatomegaly. Only one patient (1%) had an abnormal head examination, specifically, cephalohematoma [Table 5].

### 3.3. Laboratory Findings

The laboratory results showed the following mean values: hemoglobin 14.3 ± 2.5 g/dL, total white blood cell count 12.3 ± 4.5 × $10^9$/L, red blood cell count 4.33 ± 0.52 × $10^{12}$/L, mean corpuscular volume 92.5 ± 15.5 fL, platelet count 247.8 ± 99.8 × $10^9$/L, and reticulocyte count 3.94 ± 2.6%. The mean total bilirubin level was 14.4 ± 13.9 mg/dL, and the mean direct bilirubin level was 0.97 ± 0.60 mg/dL. The mean C-reactive protein (CRP) level was 23.93 mg/L [Table 6].

The most common blood group was O+ (n = 52, 50.5%), followed by A+ (n = 29, 28.2%), B+ (n = 16, 15.5%), and AB+ (n = 4, 3.9%) [Table 7]. The most frequent cause of unconjugated hyperbilirubinemia was sepsis, present in 86 cases (83.5%). Other causes included ABO incompatibility (n = 25, 24.3%), dehydration (n = 14, 13.6%), and Rh incompatibility (n = 13, 12.6%) [Table 8].

### 3.4. Treatment and Outcomes

The mean duration of hospital admission was 4.67 ± 4.6 days (range: 1–24 days). Most neonates (n = 48, 46.6%) were admitted for fewer than 7 days, while 46 (44.7%) stayed for 7 to 14 days [Table 9].

Treatment modalities included phototherapy (n = 72, 69.9%), medications (n = 68, 66.0%), conservative therapy (n = 32, 31.1%), and exchange transfusion (n = 7, 6.8%) [Table 10].

Regarding outcomes, 91 neonates (88.3%) were discharged in good condition, while 12 (11.7%) were discharged against medical advice. No cases of kernicterus or mortality were reported [Table 11].

**Table 1** Demographic and Clinical Characteristics of neonates with unconjugated hyperbilirubinemia

| **Parameter** | **Value** |
|---|---|
| Mean Age (days) | 7.6 ± 4.8 (range: 1–28 days) |
| Age Distribution | |
| - Aged 7 days or younger | 82 (63.1%) |
| - Older than 7 days | 48 (35.9%) |
| Sex Distribution | |
| - Male | 56 (54.4%) |
| - Female | 47 (45.6%) |
| Mean Gestational Age (weeks) | 38.5 ± 1.9 |
| Gestational Age | |
| - Full-term | 91 (88.3%) |
| - Preterm | 12 (11.7%) |
| Family History of Jaundice | 21 (20.4%) |

**Table 2** Maternal illness of neonates with unconjugated hyperbilirubinemia

| **Maternal illness** | **Frequency** | **Percent** |
|---|---|---|
| Infection (during pregnancy) | 25 | 24.3 |
| PROM | 6 | 5.8 |
| NVD at home | 5 | 4.9 |
| preeclampsia | 3 | 2.9 |
| Umbilical cord around baby's neck | 3 | 2.9 |
| Non | 61 | 59.2 |
| Total | 103 | 100.0 |

**Table 3** Day of jaundice onset among neonates with unconjugated hyperbilirubinemia

| **Day of Jaundice Onset Mean ±SD (3.05±1.8 days)** | **Frequency** | **Percent** |
|---|---|---|
| 1 day | 20 | 19.4 |
| 2-3 days | 49 | 47.6 |
| >3 days | 34 | 33.0 |
| Total | 103 | 100.0 |

**Table 4** Birth weight among neonates with unconjugated hyperbilirubinemia

| Birth weight | Frequency | Percent |
|---|---|---|
| <2.5kg | 23 | 22.3 |
| 2.5-4kg | 78 | 75.7 |
| >4kg | 2 | 1.9 |
| Total | 103 | 100.0 |

**Table 5** Clinical signs among neonates with unconjugated hyperbilirubinemia

| **Clinical signs** | | |
|---|---|---|
| Abdominal examination | Frequency | Percent |
| Normal | 95 | 92.2 |
| Abnormal | 8 | 7.8 |
| Total | 103 | 100.0 |
| Abnormality | | |
| Hepatomegaly | 3 | 37.5 |
| Abdominal distension | 5 | 62.5 |
| Total | 8 | 100.0 |
| Head examination | Frequency | Percent |
| Normal | 102 | 99.0 |
| Abnormal (Cephalohematoma) | 1 | 1.0 |
| Total | 103 | 100.0 |

**Table 6** Hematological parameter among neonates with unconjugated hyperbilirubinemia

| **Hematological parameter** | **Mean ±SD** | **Range** |
|---|---|---|
| Hb g/dl | 14.3±2.5 | 8-20 |
| TWBCs | 12.3±4.5 | 3-26 |
| RBCs | 4.33±0.52 | 2.8-5.5 |
| MCV | 92.5±15.5 | 8.6-116 |
| Platelets | 247.8±99.8 | 49-539 |
| Retics count | 3.94±2.6 | 1-14 |
| CRP | 23.93±13.3 | 0.4-200 |
| Total bilirubin | 14.4±13.9 | 1.9-42 |
| Direct bilirubin | 0.97±0.60 | 0.1-15.7 |

**Table 7** Blood groups of neonates with unconjugated hyperbilirubinemia

| Blood group | Frequency | Percent |
|---|---|---|
| O positive | 52 | 50.5 |
| A positive | 29 | 28.2 |
| B Positive | 16 | 15.5 |
| AB positive | 4 | 3.9 |
| O negative | 1 | 1.0 |
| B negative | 1 | 1.0 |
| Total | 103 | 100.0 |

**Table 8** Causes of jaundice among neonates with unconjugated hyperbilirubinemia

| Causes of jaundice | Frequency | Percent |
|---|---|---|
| Sepsis | 86 | 83.5 |
| ABO incompatibility | 25 | 24.3 |
| Dehydration | 14 | 13.6 |
| Rhesus incompatibility | 13 | 12.6 |
| Bruising | 0 | 0.0 |
| Other hemolytic disorder | 0 | 0.0 |
| Polycythemia | 0 | 0.0 |
| Breast milk | 0 | 0.0 |
| Undetermined | 7 | 6.8 |

**Note:** some patients had more than one cause, and the frequency exceeded the total number of patients.

**Table 9** Admission duration among neonates with unconjugated hyperbilirubinemia

| Duration of admission | Frequency | Percent |
|---|---|---|
| <7days | 48 | 46.6 |
| 7-14 days | 46 | 44.7 |
| 15-21days | 7 | 6.8 |
| >21 days | 2 | 1.9 |
| Total | 103 | 100.0 |

**Table 10** Unconjugated hyperbilirubinemia treatment modalities

| Treatment | Frequency | Percent |
|---|---|---|
| Phototherapy | 72 | 69.9 |
| Drugs | 68 | 66.0 |
| Conservative | 32 | 31.1 |
| Exchange transfusion | 7 | 6.8 |

**Table 11** Short-term outcome of neonates with unconjugated hyperbilirubinemia

| Outcome | Frequency | Percent |
|---|---|---|
| Discharge in good condition | 91 | 88.3 |
| Discharge against medical advice | 12 | 11.7 |
| Complicated (kernicterus) | 0 | 0.0 |
| Died | 0 | 0.0 |
| Total | 103 | 100.0 |

## 4. Discussion

This study included 103 neonates who met all inclusion criteria. The sociodemographic characteristics revealed that 56 (54.4%) were male, resulting in a male-to-female ratio of approximately 1.1:1. This finding aligns with studies by Abd Elmoktader et al. [7], Abbas SH et al. in Iraq [8], and others, which also reported a male predominance. This suggests that male neonates may be more susceptible to significant jaundice, although some studies have reported differing results.

The mean age at onset of jaundice was 3.05 ± 1.8 days, ranging from 1 to 10 days. Most cases (81.6%, n = 84) occurred before the fifth day of life, while 18.4% (n = 19) appeared between the fifth and tenth days. These findings are consistent with Abbas SH et al. [8], who noted that most neonates were admitted at ≥3 days of life, and with Akgül et al. [9], who reported a mean admission age of 4.4 ± 2.4 days. This timing may be explained by the physiological rise in bilirubin levels typically occurring after the first 72 hours of life.

The mean gestational age was 38.5 ± 1.9 weeks, with 88.3% (n = 91) of neonates being full-term and 11.7% (n = 12) preterm. These results are similar to those of Asefa GG et al. [10], who found that 68.1% of their patients were term, and Abbas SH et al. [8], who reported a predominance of full-term neonates. In contrast, Kalita D. et al. [11] reported a higher proportion of preterm neonates (51.8%). The mean birth weight was 2.8 ± 0.7 kg; 75.7% of neonates weighed between 2.5 and 4 kg, while 22.3% weighed less than 2.5 kg. These findings align with an Egyptian study reporting a mean birth weight of 2.94 ± 0.39 kg. Asefa GG et al. [10], however, found that only 25% of jaundiced neonates had low birth weight. Term neonates with low birth weight or low gestational age remain at increased risk of jaundice and should be monitored closely before discharge.

Regarding the etiology of jaundice, neonatal sepsis was the most common cause, affecting 83.5% (n = 86) of cases, followed by ABO incompatibility (24.3%, n = 25), dehydration (13.6%, n = 14), and Rh incompatibility (12.6%, n = 13). These findings are consistent with studies from Egypt and other regions [7]. However, studies by Irshad et al. [12] and Kalita D et al. [11] reported lower rates of ABO incompatibility, likely due to differences in sample size and population characteristics. Some cases had undetermined causes, potentially due to metabolic or genetic conditions not routinely tested at the study facility.

The mean total bilirubin level was 14.4 ± 13.9 mg/dL, and the mean direct bilirubin level was 0.97 ± 0.60 mg/dL. These results align with data from Iraq and Akgül et al. [9], who reported similar bilirubin profiles. Other studies, such as Asefa GG et al. [10], observed slightly higher mean bilirubin levels. Variations may be attributed to differences in underlying etiologies, the timing of presentation, and access to early treatment.

Phototherapy and exchange transfusion were the primary treatment modalities for neonatal hyperbilirubinemia. Treatment thresholds vary across studies and settings. In this study, 69.9% (n = 72) of neonates received phototherapy, 66.0% (n = 68) were treated with medications, 31.1% (n = 32) received conservative therapy, and 6.8% (n = 7) underwent exchange transfusion. These findings differ slightly from Egyptian studies and that of Haq I et al. [13], where phototherapy was universally the first-line treatment and exchange transfusion rates varied based on jaundice severity.

In terms of outcomes, 88.3% (n = 91) of patients were discharged in good condition, while 11.7% (n = 12) were discharged against medical advice. Notably, no deaths were recorded during the study period. This contrasts with studies such as that of Tsao PC et al., which reported a kernicterus prevalence of 0.86% [14]. Globally, kernicterus-related mortality declined significantly between 1990 and 2019, with 2.8 million deaths recorded during this time. By 2019, mortality rates were as low as 4 per million live births in high-income countries (HICs) compared to 293 per

million in low-income countries (LICs), with 82% of deaths occurring in LICs and lower-middle-income countries. Annual mortality declined by 6.2% in HICs and 3.0% in LICs [15].

### 4.1. Study Limitations

This study was limited by a relatively small sample size and data being restricted to a single hospital, which may limit the generalizability of the findings.

## 5. Conclusion

The study found that most neonates were male, with a mean age at the onset of jaundice being 3.05 ± 1.8 days (range 1-10 days). Sepsis emerged as the most common cause of neonatal jaundice, followed by ABO incompatibility, dehydration, and rhesus incompatibility. The average duration of hospital admission was 4.67 ± 4.6 days. Most neonates received phototherapy, with some also treated with medications, conservative therapy, or exchange transfusion. Most patients were discharged in good condition, and there were no reported complications.

### *Recommendations*

Maternity hospitals should screen all newborns for hyperbilirubinemia before discharge and schedule follow-up appointments. Early breastfeeding and lactation support should be encouraged. Parents need to be educated on jaundice and the importance of timely follow-up. Anti-D immunoglobulin should be administered to Rh-negative mothers, and efforts should focus on preventing antenatal sepsis and ensuring timely treatment of early infections.

## Compliance with ethical standards

### *Acknowledgments*

The researchers independently funded this study.

### *Disclosure of conflict of interest*

The authors declare that they have no conflicts of interest.

### *Statement of informed consent*

Informed consent was obtained from all individual participants included in the study.

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