Original Article

Clinical and Laboratory Profile of Hyperbilirubinemia in Infants Up to Nine Weeks of Age: A Retrospective Study from Oradea, Romania

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Abstract

Background: Hyperbilirubinemia is one of the most common clinical problems encountered during the neonatal and early-infant period. Although it is frequently benign, significant bilirubin elevation may lead to acute bilirubin encephalopathy and kernicterus, and its clinical interpretation depends on postnatal age, gestational maturity, feeding, hemolysis, and other risk factors. However, hospital-based data describing the demographic, perinatal, clinical, laboratory, and hospitalization characteristics of affected young infants remain limited in some settings. This study aimed to describe these characteristics among infants with hyperbilirubinemia admitted to a pediatric hospital in Oradea, Romania. **Material and Methods:** The records of 30 infants up to 9 weeks of age who were admitted to the hospital between July 2020 and December 2021 were retrospectively reviewed. Variables were age, sex, parity, birth order, weight, method of birth, APGAR score, maternal age, place of residence, gestation period, feeding pattern, signs/symptoms at delivery, abnormal laboratory findings which were selected, and length of hospital stay. Because the available data were in aggregated form, descriptive analysis was undertaken. 95% Wilson confidence intervals were used to report proportions with known denominators. **Results:** 17 of 30 (56.7%) infants were boys, 25 of 30 (83.3%) had physiologic pregnancies and 19 were from rural locations. Twenty-three (76.7%) were term, 18 (60.0%) were exclusively breastfed, and 18 (60.0%) had a birth weight of 3–4 kg. Infants aged 3–4 weeks formed the largest age group (14/30, 46.7%). Of 24 babies with actually known scores, 20 (83.3%) obtained a score of 9. The most common isolated presentation was vomiting (5 cases, 16.7%). Twenty-three infants (76.7%) had elevated indirect bilirubin, 12 (40.0%) had elevated gamma-glutamyl transferase. The average length of stay in the hospital was about 7 days based on source data. **Conclusion:** This small hospital-based series included a predominant number of infants with a term delivery, normal birth weight, and breastfed infants; the most common laboratory abnormality was elevation of indirect bilirubin. The results are descriptive and hypothesis-generating and should not be interpreted as estimates of population risk or evidence of causal associations.

Keywords: Hyperbilirubinemia; neonatal jaundice; bilirubin; infants; breastfeeding.

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Introduction

Hyperbilirubinemia is one of the most frequent clinical problems encountered in neonates and young infants. Most cases are those of unconjugated bilirubin attributable to increased bilirubin production, immature hepatic conjugation and enhanced enterohepatic circulation. It is important to assess the patient's bilirubin level promptly, as bilirubin encephalopathy and kernicterus can occur if the level is elevated.[1,2] Bilirubin interpretation is influenced by the following factors: feeding, hemolysis, risk factors and postnatal age, and gestational maturity.[1,3-6] We therefore reviewed a hospital-based series of infants with hyperbilirubinemia to describe their demographic, perinatal, clinical, laboratory, and hospitalization characteristics.

Materials and Methods

Study Design and Setting: We conducted a retrospective descriptive review of hospital records from a pediatric hospital in Oradea, Romania. Records from July 1, 2020, through December 31, 2021, were reviewed. The source thesis included 30 infants with hyperbilirubinemia aged up to nine weeks. Because some participants were older than 28 days, the term "infants" is used throughout rather than applying the neonatal designation to the entire cohort.

Study Population and Variables: Variables extracted from the source records included age in weeks, sex, pregnancy course (physiologic or pathologic as recorded), birth weight category, mode of delivery, Apgar score, maternal age category, residence (rural or urban), gestational age (term or preterm), feeding pattern (exclusive breastfeeding, formula feeding, or mixed feeding), presenting symptoms, selected laboratory abnormalities, and length of hospitalization.

Laboratory Assessment: Available records included hematologic measures and biochemical tests, including red-cell

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indices, hemoglobin/hematocrit, total and indirect bilirubin, alanine aminotransferase, aspartate aminotransferase, gamma-glutamyl transferase, and creatinine. Laboratory completeness was variable; therefore, laboratory findings are presented as reported in the source dataset and should not be interpreted as complete-case prevalence estimates.

Statistical Analysis: Because only aggregate counts were available for this analysis, statistical assessment was restricted to descriptive methods. Categorical variables are summarized as counts and percentages. For major proportions with a known denominator of 30, 95% confidence intervals were calculated using the Wilson method. No comparative hypothesis tests, odds ratios, regression models, or predictive analyses were performed because there was no comparator group and individual-level data were unavailable.

Results

Cohort Characteristics:

Thirty infants with hyperbilirubinemia were included. Seventeen (56.7%) were male, 25 (83.3%) followed pregnancies recorded as physiologic, and 19 (63.3%) were from rural areas. Twenty-three (76.7%) were term, 18 (60.0%) were exclusively breastfed, and 18 (60.0%) had a birth weight of 3–4 kg. Infants aged 3–4 weeks formed the largest age group (14/30, 46.7%). The main demographic and perinatal characteristics are shown in [Table 1 and Figure 1].

Table 1: Demographic and Perinatal Characteristics

Note: Percentages are based on the full cohort of 30 infants.

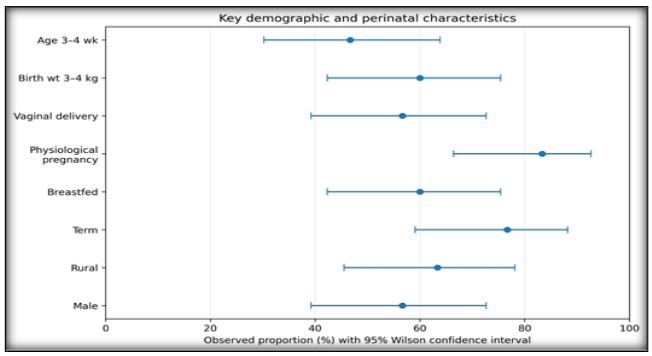

Figure 1: Key demographic and perinatal characteristics. Points show observed proportions and 95% Wilson confidence intervals.

Apgar Score and Maternal Age: Apgar information was available for 24 of the 30 infants. Among these 24, three had a score of 7, 20 had a score of 9, and one had a score of 10. Thus, 20/24 (83.3%) of infants with available information had an Apgar score of 9. The original thesis reported this as 66.6% when the full cohort denominator of 30 was used. Maternal age was distributed as five teenage mothers, 12 mothers in their twenties, 10 in their thirties, and three in their forties.

Clinical Presentation: Presenting symptoms were heterogeneous. Vomiting alone was recorded in five infants (16.7%), dyspnea with cough in four (13.3%), and cough with rhinorrhea in four (13.3%). Three infants each had nasal obstruction with dyspnea, fever alone, vomiting with fever and diarrhea, or fever with cough. Two infants had apnea and two presented primarily with skin changes. One infant had vomiting with dyspnea [Figure 2].

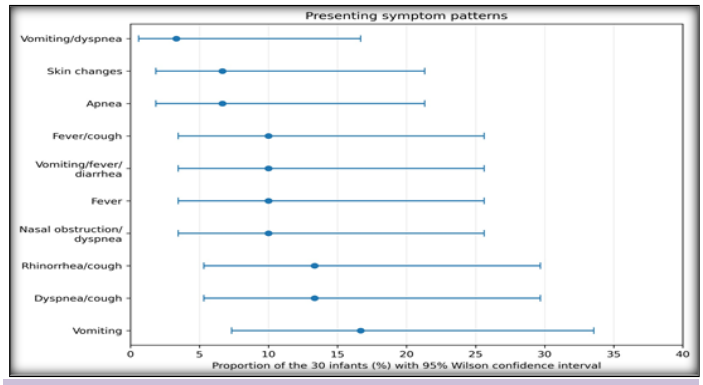

Figure 2: Presenting symptom patterns. Points and 95% Wilson confidence intervals are based on the reported counts of mutually exclusive symptom categories.

Laboratory Findings: Laboratory data were incomplete across the cohort. The source thesis reported anemia in 10 infants, polycythemia in nine, increased total bilirubin in almost all infants, elevated indirect bilirubin in 23, increased creatinine in seven, elevated alanine aminotransferase in five, elevated aspartate aminotransferase in five, and elevated gamma-glutamyl transferase in 12. Indirect bilirubin elevation was therefore the dominant reported biochemical abnormality (23/30, 76.7%), followed by increased gamma-glutamyl transferase (12/30, 40.0%). Because the denominator for each laboratory test was not separately documented, these percentages should be interpreted cautiously.

Hospitalization: Two infants were discharged within one day, seven remained for 2–3 days, five for 4–5 days, eight for seven days, four for 9–10 days, three for 11–13 days, and one for 19 days. The source thesis reports an average hospitalization duration of approximately seven days. Because individual hospitalization durations were unavailable, a precise mean, median, interquartile range, and standard deviation could not be independently recalculated [Figure 3].

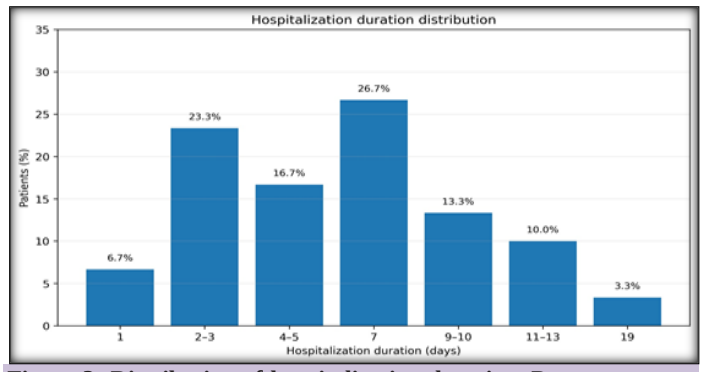

Figure 3: Distribution of hospitalization duration. Percentages are calculated from the 30-infant cohort using the duration categories reported in the source dataset.

Discussion

The aim of this retrospective series was to descriptively characterize 30 infants with hyperbilirubinemia treated at the Pediatric Hospital of Oradea, in the period of the study. The cohort included an over-representation of term infants, a birth weight of 3–4 kg, exclusively breast feeding, and an age at presentation of 3–4 weeks. Elevated indirect bilirubin was the most common biochemical abnormality, consistent with the predominance of unconjugated hyperbilirubinemia in the source dataset.

The age distribution is noteworthy because almost half of the infants were 3–4 weeks old, later than the peak period commonly emphasized in routine newborn jaundice surveillance. This may reflect the inclusion of infants up to nine weeks of age and the hospital-based nature of the cohort. The observed age distribution should therefore not be interpreted as an incidence curve for neonatal jaundice.

Most infants were term and had birth weights of 3–4 kg. Although late-preterm birth is recognized as an important risk factor for significant hyperbilirubinemia, this study was not designed to estimate relative risk because it included no non-hyperbilirubinemic comparison group. A prospective study by Sarici et al. reported a higher incidence of significant hyperbilirubinemia among near-term infants than among term infants and later peak bilirubin levels in the first week.[3]

Sixty percent of the cohort was exclusively breastfed. Breastfeeding should not be interpreted as a pathological exposure on the basis of these data. Early feeding difficulty and inadequate intake can increase enterohepatic circulation and contribute to breastfeeding-associated jaundice, whereas breast milk jaundice is a distinct late-onset phenomenon.[8] The present study cannot distinguish inadequate-intake-related jaundice from breast milk jaundice because detailed feeding adequacy, weight-loss trajectories, and lactation assessments were unavailable.

Twenty-three babies had elevated indirect bilirubin levels, further confirming that this series is mainly indirect (unconjugated) hyperbilirubinemia. When clinically indicated, appropriate hematologic evaluation should be performed to address hemolysis, which is an important cause of severe unconjugated hyperbilirubinemia.[5,6] Current guidance emphasizes age-specific bilirubin assessment and consideration of neurotoxicity risk factors rather than reliance on a single universal bilirubin threshold.[1]

Only two infants were recorded as presenting primarily with visible skin discoloration while numerous infants presented with respiratory or gastrointestinal symptoms. This represents a limitation of using the admission complaint as a proxy for jaundice severity because hyperbilirubinemia may be diagnosed during evaluation of another clinical complaint. When jaundice is suspected, the assessment of objective bilirubin should, therefore be the key focus.

The observed rural predominance should also be interpreted cautiously. The percentage of infants born in rural areas was high (63.3%) but the denominator of the rural population, referrals, distance to hospital, socioeconomic status, and access to primary newborn care were not measured. This proportion of rural residents therefore cannot be interpreted as evidence of increased population-level risk. The same applies to the observed proportions of physiologic pregnancies, vaginal deliveries, and term births; these are descriptive characteristics of infants who reached the hospital rather than causal predictors.

The major asset of the study is the linkage of the demographic, perinatal, feeding, symptom, laboratory, and hospitalization data into a clearly defined clinical context. Major limitations include the small sample size, retrospective design, absence of a comparator group, incomplete laboratory data, the lack of individual bilirubin trajectories, the lack of a standardized etiology classification, and the lack of individual-level data for adjusted analysis. Additionally, the study period coincided with the COVID-19 pandemic, which was cited as a potential explanation for the decrease in hospital visits. These limitations substantially restrict the generalizability of the findings.

The manuscript does not report p-values, odds ratios, regression coefficients, or predictive models because the available aggregate data are not suitable for such analyses. Future prospective studies should collect exact postnatal age in hours, total and direct bilirubin concentrations, gestational age in completed weeks, weight trajectory, feeding adequacy, blood-group incompatibility, direct antiglobulin testing, reticulocyte count, G6PD status where appropriate, treatment thresholds, and clinical outcomes. These data would permit more informative etiologic classification and appropriately adjusted analyses.

Conclusion

Hyperbilirubinemia occurred most frequently in infants between 3–4 weeks of age and was more common in term infants, those who were born between 3–4 kg, in rural areas, delivered by vaginal delivery, and being solely breastfed. Laboratory changes most often included elevation of the indirect bilirubin and hospitalization was typically for about one week. These results are descriptive; they should not be taken as proof that breastfeeding, the rural living environment, vaginal delivery, or other factors observed are associated with hyperbilirubinemia. The study's main purpose is to identify pattern that can be applied to larger prospective studies with full individual-level bilirubin and risk- factor information.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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