

Neonatal jaundice in Algeria: Epidemiological, clinical, and prognostic insights from a retrospective study of 309 cases

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Neonatal jaundice is one of the most common conditions requiring hospitalization in newborns. While it's clinical patterns are well characterized in developed countries, limited data exist from North Africa, particularly Algeria. Identifying local risk factors and outcomes is crucial to guide neonatal care and prevention strategies. This retrospective study evaluated the clinical characteristics, etiologies, and risk factors of neonatal jaundice in 309 infants admitted to the Pediatric Department of Emir Abdelkader Oued-Zenati Public Hospital (Guelma, Algeria) between April 2019 and January 2023, based on epidemiological, clinical, and laboratory data. Within the cohort, 58.9% were male, with jaundice onset most frequently between day 2 and 7 of life (66.3%). Most cases (96.8%) involved term infants, although preterm neonates presented with higher bilirubin levels. The mean serum bilirubin was $166.47 \pm 46.36 \mu\text{mol/L}$, and the average hospital stay was 2.6 days. ABO incompatibility was identified in 19 cases, while Rh isoimmunization was observed in 19 cases, mainly involving Rh-negative mothers and Rh-positive infants. All neonates received phototherapy (82.7% conventional, 17.2% intensive). Significant associations were found between bilirubin levels and sex ($p = 0.000$), and between mode of delivery and infection ($p = 0.001$). Prolonged hospitalization was linked to cesarean delivery ($p = 0.002$) and leukocytosis ($p = 0.001$). Neonatal jaundice remains a prevalent condition in Algeria, with blood group incompatibility, Rh isoimmunization, and perinatal infections as major risk factors. Cesarean delivery and leukocytosis were predictive of longer hospital stay, underscoring the value of early risk stratification to improve neonatal outcomes.

Keywords: neonatal jaundice, hyperbilirubinemia, ABO incompatibility, Rh isoimmunization, phototherapy, hospital stay.

Introduction

Neonatal jaundice, clinically manifested by yellow discoloration of the skin and sclera due to elevated serum bilirubin levels, is one of the most common conditions encountered during the neonatal period, affecting approximately 60–80% of term and up to 80–90% of preterm infants during the first week of life¹. Although physiological jaundice is generally transient and self-limiting, a proportion of newborns develop severe hyperbilirubinemia, which may progress to acute bilirubin encephalopathy and kernicterus, leading to permanent neurological sequelae, including hearing impairment, cerebral palsy, and cognitive disabilities^{2,3}. Recent global evidence indicates that neonatal jaundice remains an

important contributor to neonatal morbidity, particularly in low- and middle-income countries (LMICs), where delayed recognition, inadequate monitoring, and limited access to effective treatment continue to contribute to adverse outcomes. Despite advances in neonatal care, severe hyperbilirubinemia remains responsible for a substantial burden of preventable bilirubin-induced neurological dysfunction worldwide^{2,4}.

The pathophysiology of neonatal hyperbilirubinemia is complex and multifactorial, involving increased bilirubin production due to accelerated erythrocyte turnover, immature hepatic uptake and conjugation, and enhanced enterohepatic circulation⁵. Several maternal and neonatal factors increase the risk of clinically significant hyperbilirubinemia, including prematurity, ABO or Rh isoimmunization, glucose-6-phosphate dehydrogenase (G6PD) deficiency, birth trauma, sepsis, inadequate breastfeeding, dehydration,

and excessive postnatal weight loss⁶⁻⁸. Additional risk factors, such as cephalohematoma and ethnicity-related genetic predisposition, have also been associated with an increased risk of severe hyperbilirubinemia⁸. Current international recommendations emphasize the importance of systematic bilirubin assessment before hospital discharge, risk stratification, and appropriate post-discharge follow-up to facilitate early identification and management of newborns at risk⁸.

Despite the availability of effective therapeutic interventions, including intensive phototherapy and exchange transfusion, severe hyperbilirubinemia remains a significant public health concern, particularly in LMICs, where limited healthcare resources, delayed diagnosis, insufficient access to bilirubin measurement, and restricted availability of specialized neonatal care contribute to preventable morbidity and mortality^{4,8}. The burden is particularly high in Africa and South Asia, where neonatal jaundice accounts for a disproportionate number of cases of bilirubin-induced neurological dysfunction compared with high-income countries^{2,4,9}. These persistent disparities highlight the need to strengthen neonatal screening programs, improve early diagnosis, and ensure timely access to appropriate treatment strategies.

In Algeria, epidemiological data regarding neonatal jaundice remain limited, resulting in an incomplete understanding of its regional burden, etiological profile, clinical characteristics, and outcomes. Furthermore, few hospital-based studies have comprehensively assessed the underlying causes, therapeutic approaches, and prognosis of affected neonates. Therefore, the present retrospective study conducted at the Pediatric Department of Guelma Hospital (Northeastern Algeria) aimed to characterize the epidemiological features, clinical presentation, etiologies, management strategies, and outcomes of neonatal jaundice, thereby providing region-specific evidence to support improvements in neonatal screening, early diagnosis, and clinical management in Algeria.

Materials and methods

This retrospective study was conducted at the Pediatric Department of Emir Abdelkader Public Hospital (EPH), Oued-Zenati, located in Guelma, Algeria. The study covered a four-year period from April 2019 to January 2023 and included a total of 309 neonates diagnosed with neonatal jaundice. The

study population consisted of medical records of newborns admitted with clinical signs of neonatal jaundice.

All neonates diagnosed with jaundice and admitted to the pediatric department during the study period were included. We excluded cases with incomplete medical records, newborns lost to follow-up, or those transferred to other medical facilities.

This study was conducted in accordance with the ethical standards of the institutional review board. All data were anonymized to ensure patient confidentiality.

Data collection was carried out through the review of hospitalization records, from which a range of demographic and clinical variables were extracted. These included the patient's age at admission, sex, length of hospital stay, prematurity status, and mode of delivery (vaginal or cesarean section). Clinical data also encompassed total and direct (conjugated) serum bilirubin levels, white blood cell (WBC) count, ABO and Rh blood group, as well as the use of phototherapy as part of the therapeutic management. Hospital survival time was defined as the time from hospital admission to discharge.

Statistical analysis

Data were entered and analyzed using IBM SPSS Statistics version 25.0 (IBM Corp., Armonk, NY, USA) and Microsoft Excel 2013. Qualitative variables were expressed as frequencies and percentages, while quantitative variables were summarized as means $\pm$ standard deviations (SD). Comparisons of means between two groups were conducted using the independent samples t-test, while comparisons among more than two groups were assessed using one-way analysis of variance (ANOVA).

Associations between categorical variables were evaluated using the Chi-square test (χ^2). For non-parametric correlations, Spearman's rank correlation coefficient was applied. A p-value of less than 0.05 was considered statistically significant, with significance thresholds interpreted as follows: $p < 0.05$ (significant), $p < 0.01$ (highly significant), $p < 0.001$ (very highly significant), and $p > 0.05$ (not significant).

For the analysis of hospitalization duration, Kaplan–Meier survival analysis was performed to estimate time-to-discharge probabilities. Differences between survival curves across categorical groups (e.g., mode of delivery, leukocyte classification) were assessed using the log-rank test. This approach

allowed for the evaluation of prognostic factors potentially associated with prolonged hospital stay.

Results

Demographic and perinatal profile of jaundiced neonates

Among the 309 neonates admitted for jaundice, a male predominance was observed, with 182 males (58.9%) and 127 females (41.1%), yielding a male-to-female sex ratio of 1.43. Regarding the timing of onset, the condition was most frequently observed between the second and seventh day of life, accounting for 205 cases (66.3%). Jaundice was less common in the first 24 hours (33 cases, 10.7%) and after the eighth day of life (71 cases, 23%). In terms of gestational age, the vast majority of affected neonates were born at term (≥ 38 weeks), comprising 299 cases (96.8%), while only 10 neonates (3.2%) were preterm. Vaginal delivery was the predominant mode of birth in this cohort, reported in 279 cases (90%), compared to 30 neonates (10%) delivered by cesarean section. These findings suggest that neonatal jaundice in this population primarily affects full-term, male infants delivered vaginally, with onset typically occurring between the second and seventh day of life (Table 1).

Clinical course and hospitalization profile

Table 2 presents the clinical evolution of neonatal jaundice within the studied cohort. The majority of cases (89.3%) exhibited a self-limiting course with resolution within 14 days, consistent with typical patterns of physiological jaundice. Only 10.7% of

neonates experienced prolonged jaundice beyond two weeks, warranting further diagnostic evaluation for underlying pathological causes.

Regarding hospitalization duration, the average length of stay was 2.57 ± 1.23 days. Most neonates were discharged within two days, with 43% hospitalized for 2 days and 21.7% for a single day, reflecting favorable clinical outcomes and effective early management. However, a smaller proportion (4.2%) required extended hospitalization of 7 days or more, possibly indicative of more complex or severe presentations (Table 2).

Stratification of hyperbilirubinemia by clinical and etiological characteristics

As detailed in Table 3, the mean total serum bilirubin level among the cohort was 166.47 ± 46.36 $\mu\text{mol/L}$. Most neonates (69.26%) presented with mild hyperbilirubinemia (<180 $\mu\text{mol/L}$), while 30.42% fell within the moderate range (180–340 $\mu\text{mol/L}$). Only one case (0.32%) exhibited bilirubin levels >340 $\mu\text{mol/L}$, indicating the rarity of critical hyperbilirubinemia in this cohort.

The mean level of direct (conjugated) bilirubin was 12.80 ± 15.17 mg/dL, with the majority (89.6%) remaining within normal limits (≤ 20 mg/dL), suggesting a predominantly unconjugated pattern of hyperbilirubinemia. Indeed, 99.7% of cases were confirmed as unconjugated hyperbilirubinemia, while only one case presented with a mixed pattern (unconjugated bilirubin $<50\%$).

Etiological classification showed a clear predominance of physiological jaundice, accounting for 88.9% of cases, consistent with typical neonatal adaptation. Pathological forms were far less frequent, with hemolytic jaundice due to Rh incompatibility representing 6.1%, followed by non-hemolytic (2.8%) and viral hemolytic causes (2.2%).

Table 1 — Demographic and perinatal characteristics of jaundice neonates

Variable	Available data	% or Mean $\pm$ SD
Gender	309	Male 58.9% (n=182)
		Female 41.1% (n=127)
Day of life at hospital admission	309	2,57 $\pm$ 2,03 days 1 day 10.7% (n=33)
		2 to 7 days 66.3% (n=205)
		8 days or more 23% (n=71)
Gestational age	309	Full-term 96.8% (n=299)
		Premature 3.2% (n=10)
Mode of delivery	309	Cesarean 09.7% (n=30)
		Vaginal 90.3% (n=279)

Table 2 — Clinical evaluation of jaundice neonates

Variable	Available data	% or Mean $\pm$ SD
Duration of neonatal jaundice persistence	309	≤ 14 days 89.3% (n=276)
		15 days or more 10.7% (n=33)
Hospitalisation duration	309	2,57 $\pm$ 1,23 days
		1 day 21.7% (n=67)
		2 days 43% (n=133)
		3 days 20.7% (n=64)
		4 days 8.1% (n=25)
		5 days 1.0% (n=3)
		6 days 1.3% (n=4)
		≥ 7 days 4.2% (n=13)

Table 3 — Stratification of neonatal hyperbilirubinemia by gestational and clinical characteristics

Variable	Available data	% or Mean $\pm$ SD
Total serum bilirubin levels	309	166.47 $\pm$ 46.36 μ mol/L $< 180 \mu$ mol/L 69.26% (n=214) 180-340 μ mol/L 30.42% (n=94) $> 340 \mu$ mol/L 0.32% (n=1)
Gestational age	309	Full-term (n=299) 138.81 $\pm$ 67.78 μ mol/L $< 180 \mu$ mol/L 69.6% (n=208) 180-340 μ mol/L 30.1% (n=90) $> 340 \mu$ mol/L 0.3% (n=1) Premature (n=10) 167.43 $\pm$ 45.29 μ mol/L $< 180 \mu$ mol/L 60% (n=6) 180-340 μ mol/L 40% (n=4) $> 340 \mu$ mol/L 0% (n=0)
Direct (conjugated) bilirubin levels	309	12.80 $\pm$ 15.17 mg/dL ≤ 20 mg/dL 89.6% (n=277) > 20 mg/dL 10.4% (n=32)
Type of jaundice	309	Unconjugated bilirubin $> 50\%$ 99.7% (n=308) Unconjugated bilirubin $< 50\%$ 0.3% (n=1)
Etiological classification of neonatal unconjugated hyperbilirubinemia	309	Physiological jaundice 88.9% (n=274) Hemolytic jaundice virus 2.2% (n=7) Non-hemolytic jaundice 2.8% (n=8) Hemolytic jaundice RH 6.1% (n=19)
Treatment	309	Conventional phototherapy 82.2% (n=254) Intensive phototherapy 17.2% (n=53) Vitamin K 0.6% (n=2)

Regarding therapeutic interventions, conventional phototherapy was the primary modality used in 82.2% of cases, reflecting standard treatment practices for moderate hyperbilirubinemia. Intensive phototherapy was administered in 17.2% of neonates, likely in response to higher bilirubin levels or risk factors. Only two neonates (0.6%) received vitamin K, indicating its limited role in hyperbilirubinemia management in this population (Table 3).

Relationship between total serum bilirubin count and selected variables

A statistically significant difference in total serum bilirubin levels was observed between male and female neonates ($p = 0.000$), indicating a higher predisposition among males. In contrast, no significant associations were found between bilirubin levels and gestational age ($p = 0.870$) or prematurity status ($p = 0.456$), suggesting that these factors did not markedly influence bilirubin concentrations in this cohort (Table 4).

White blood cell (WBC) stratification by delivery mode and gestational Age

Table 5 summarizes the distribution of neonatal white blood cell (WBC) counts, with a mean WBC

Table 4 — Summary of the relationship between total serum bilirubin and selected variables

Variable	Groups compared	P-value
Sex	Male vs Female	0.000
Gestational age	Age groups	0.870
Prematurity	Preterm vs Term	0.456

level of $11.30 \pm 4.57 \times 10^9/L$ across the cohort. The majority of neonates (94.8%) demonstrated normoleukocytosis ($5-17.9 \text{ g/L}$), while leukopenia ($<5 \text{ g/L}$) and hyperleukocytosis ($\geq 18 \text{ g/L}$) were rare, observed in only 1% and 4.2% of cases, respectively.

When stratified by mode of delivery, vaginal delivery accounted for 90.3% of cases. Among these neonates, the mean WBC count was slightly lower ($10.87 \pm 4.44 \times 10^9/L$) compared to those born with cesarean section ($11.34 \pm 4.58 \times 10^9/L$). Notably, hyperleukocytosis was more prevalent in cesarean section neonates (13.3%) than in those delivered vaginally (7.2%). Leukopenia occurred exclusively in the vaginal group (6.8%).

Regarding gestational age, full-term neonates ($n=299$) showed a mean WBC level of $11.22 \pm 4.41 \times 10^9/L$, with normoleukocytosis in 87% of cases. Premature neonates ($n=10$), although a small

Table 5 — Stratification of neonatal WBC levels according to delivery method and gestational age

Variable	Available data	% or Mean $\pm$ SD
WBC classification	309	$11,30 \pm 4,57 \times 10^9/L$ Leukopenia (< 5 G/L) 1% (n=3) Normoleukocytosis (5-17.9 G/L) 94.8% (n=293) Hyperleukocytosis (≥ 18 G/L) 4.2% (n=13)
WBC according to mode of delivery	309	Vaginal (n=279) $10,87 \pm 4,44 \times 10^9/L$ Leukopenia (< 5 G/L) 6.8% (n= 19) Normoleukocytosis (5-17.9 G/L) 86.0% (n= 240) Hyperleukocytosis (≥ 18 G/L) 7.2% (n= 20) Cesarean (n= 30) $11,34 \pm 4,58 \times 10^9/L$ Leukopenia (< 5 G/L) 0.0% (n=0) Normoleukocytosis (5-17.9 G/L) 86.7% (n=26) Hyperleukocytosis (≥ 18 G/L) 13.3% (n=4)
WBC according to gestational age	309	Full-term (n=299) $11,22 \pm 4,41 \times 10^9/L$ Leukopenia (< 5 G/L) 6.4% (n=19) Normoleukocytosis (5-17.9 G/L) 87.0% (n=260) Hyperleukocytosis (≥ 18 G/L) 6.6% (n=20) Premature (n=10) $14,29 \pm 8,48 \times 10^9/L$ Leukopenia (< 5 G/L) 0.0% (n=0) Normoleukocytosis (5-17.9 G/L) 70% (n= 7) Hyperleukocytosis (≥ 18 G/L) 30% (n= 3)

subgroup, exhibited a markedly higher mean WBC count ($14.29 \pm 8.48 \times 10^9/L$) and a disproportionately elevated rate of hyperleukocytosis (30%). This may reflect an immature immune response or subclinical infection in preterm infants. No cases of leukopenia were observed in the preterm group.

These findings highlight distinct patterns of WBC distribution related to perinatal variables, with a potential link between prematurity and elevated leukocyte counts that merits further investigation (Table 5).

Association between WBC count and clinical variables

Table 6 summarizes the statistical associations between neonatal white blood cell (WBC) counts and selected perinatal variables. No significant difference was observed in WBC levels when stratified by mode of delivery (cesarean vs. vaginal; $p = 0.976$), suggesting that the delivery method does not influence neonatal leukocyte counts.

In contrast, a highly significant association was found between WBC count and gestational age ($p = 0.001$), indicating that preterm neonates exhibited markedly different leukocyte profiles compared to full-term counterparts. This likely reflects

Table 6 — Summary of the relationship between white blood cell (WBC) count and selected variables

Variable	Groups compared	P-value
Mode of delivery	Cesarean vs Vaginal	0.976
Prematurity	Preterm vs Full-term	0.001
Hospital stay duration	Days groups	0.002

immunological immaturity or a heightened inflammatory response in premature infants.

Furthermore, hospital stay duration was also significantly associated with WBC count ($p = 0.002$). This suggests that elevated or abnormal WBC levels may correlate with prolonged hospitalization, potentially due to underlying infections, clinical instability, or complications requiring extended monitoring.

These findings highlight the relevance of leukocyte counts as a potential marker for identifying neonates at risk of adverse outcomes, particularly among preterm infants and those requiring prolonged care (Table 6).

Distribution of jaundice neonates according to the etiologies of hemolytic jaundice

Distribution of jaundice neonates by ABO blood group incompatibility

ABO blood group incompatibility was identified in 19 neonates, accounting for 6.1% of the study

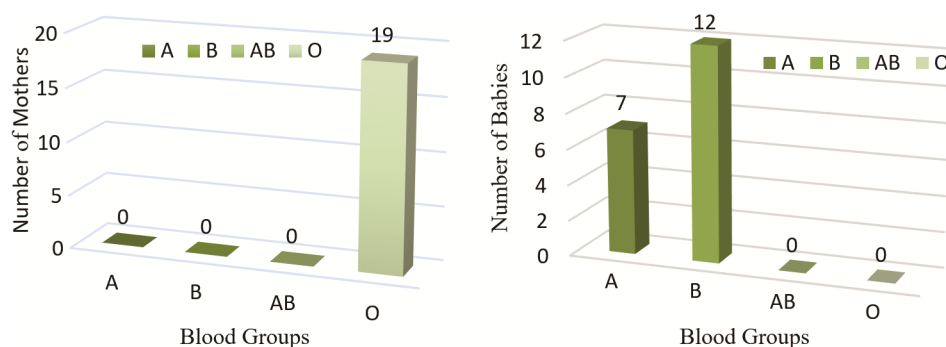


Fig. 1 — Blood groups of neonates and their mothers.

population, and was more frequent than Rh incompatibility. Among the affected neonates, blood group B was the most prevalent (63%), followed by blood group A (37%). In all cases of neonatal jaundice due to ABO incompatibility, the maternal blood group was O (Figure 1).

Distribution of jaundice neonates according to Rh incompatibility

In our study, all neonates who developed jaundice due to Rh incompatibility were Rh-positive, whereas all their mothers were Rh-negative (Figure 2).

Survival analysis of hospital stay duration

Although all patients were eventually discharged and no censoring was present in the dataset, survival analysis was performed to compare the distribution of hospital stay durations between groups. In this context, the Kaplan-Meier method represents the cumulative probability of hospital discharge over time.

Figure A shows the overall Kaplan-Meier survival curve based on the hospitalization duration of neonates with jaundice. A steep decline is observed within the first few days, indicating that most neonates are discharged early. This is consistent with descriptive data in Table 2, where the majority of neonates were hospitalized for 1 to 3 days. Figure B compares survival curves by gestational age. Although preterm neonates appear to have a slightly earlier discharge trend, this observation should be interpreted cautiously due to their low representation in the sample. Still, the general pattern aligns with the dataset, confirming that jaundice-related hospitalization is typically short, regardless of gestational age. In conclusion, these findings suggest that the hospitalization duration for neonates with jaundice is generally brief and similar across different gestational ages, despite the small number of preterm infants in the study (Figure 3).

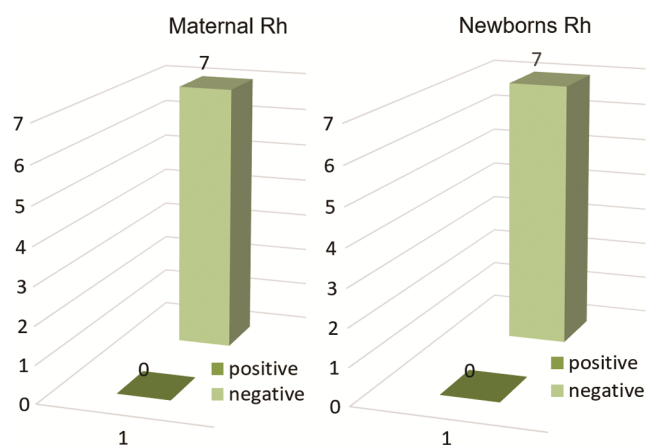


Fig. 2 — Rh status of neonates and their mothers.

Figure A shows the overall Kaplan-Meier survival curve based on the hospitalization duration of neonates with jaundice. A marked decline in the survival function occurs in the first few days, reflecting a generally short hospital stay. This aligns with the descriptive data, which indicate that most neonates were hospitalized for only a few days. Figure B compares survival curves based on the mode of delivery. The curves for vaginal and cesarean births are largely similar; suggesting that mode of delivery does not significantly impact the duration of hospitalization for jaundiced neonates. However, this interpretation should be made cautiously given the small number of neonates born via cesarean section. In conclusion, these results indicate that the length of hospital stay for neonates with jaundice is generally short and appears to be independent of the mode of delivery (Figure 4).

Discussion

This retrospective study aimed to characterize the epidemiological profile, etiological spectrum, risk factors, and clinical outcomes of neonatal jaundice among newborns admitted to the pediatric department

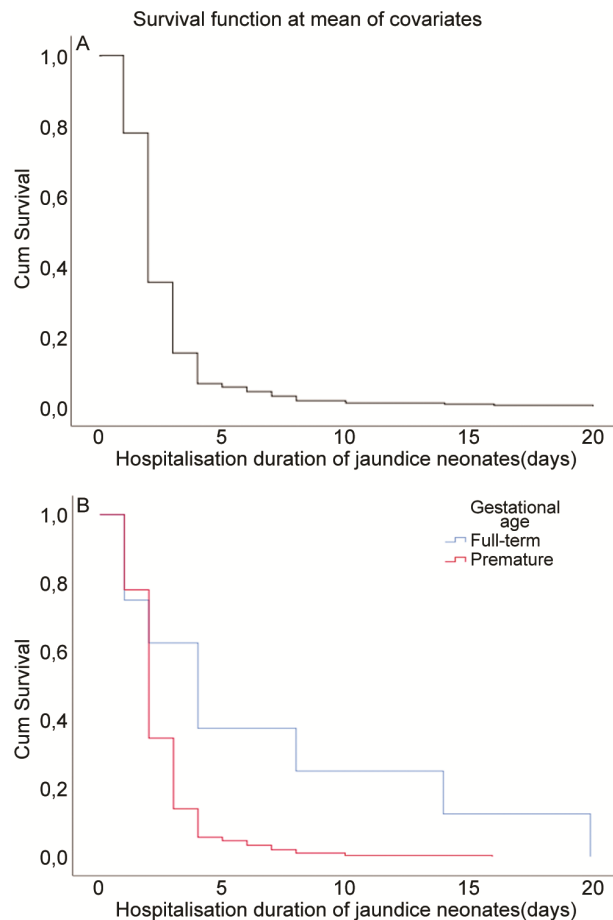


Fig. 3 — Kaplan–Meier survival analysis of hospitalisation duration among neonates with jaundice: A, overall survival function at the mean of covariates; B, survival curves according to gestational age (full-term vs premature).

of the Emir Abdelkader Oued-Zenati Public Hospital (EPH), Guelma, Algeria. A total of 309 neonatal jaundice cases were identified between April 2019 and January 2023, providing valuable regional data in a context where epidemiological information on neonatal hyperbilirubinemia remains limited.

Neonatal jaundice, defined as a yellow discoloration of the skin and mucous membranes resulting from increased serum bilirubin levels, represents the most common clinical condition encountered during the neonatal period. It primarily reflects the physiological imbalance between bilirubin production and elimination due to increased erythrocyte turnover, immature hepatic conjugation mechanisms, and enhanced enterohepatic circulation in newborns^{5,10}. Although most cases are benign and self-limiting, severe hyperbilirubinemia remains a major concern because of its potential progression to acute bilirubin encephalopathy and kernicterus,

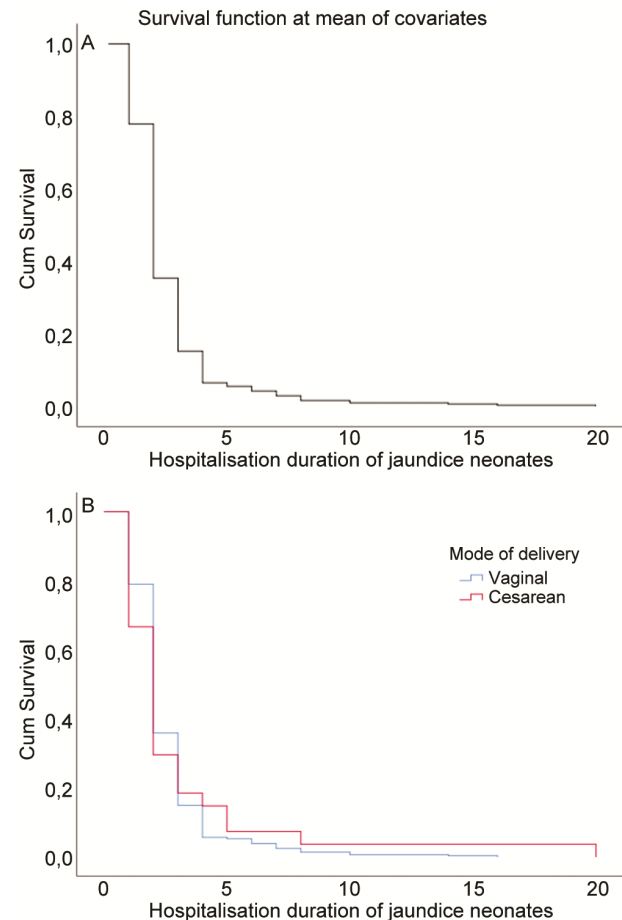


Fig. 4 — Kaplan–Meier survival plots of hospitalisation duration in jaundiced neonates. A: Survival function at the mean of covariates. B: Survival function according to mode of delivery (vaginal vs cesarean).

particularly when diagnosis and treatment are delayed^{2,3,11}. Worldwide, neonatal jaundice affects approximately 60–85% of term infants during the first week of life and remains a significant cause of neonatal healthcare utilization, including hospital readmissions for phototherapy and monitoring^{1,2,4}.

In our cohort, neonatal jaundice was more frequently observed among male infants, with a male-to-female sex ratio of 1.43. This finding is consistent with several studies reporting a higher proportion of affected male neonates¹². Tague *et al.*¹³ (2022) and Oualid¹⁴ (2021) reported male-to-female sex ratios of 1.06 and 1.14, respectively, while Annisa *et al.*¹⁵ (2023) identified male sex as a potential risk factor for neonatal jaundice^{16–18}. Several mechanisms have been proposed to explain this association, including sex-related differences in bilirubin metabolism, a higher prevalence of Gilbert syndrome among males, and the increased occurrence of

X-linked disorders such as glucose-6-phosphate dehydrogenase (G6PD) deficiency, which may contribute to hemolysis and severe hyperbilirubinemia¹⁹⁻²¹. However, the relationship between sex and neonatal jaundice remains controversial, as some studies have failed to demonstrate a significant association. For example, Konaré²² (2017) reported either a balanced sex distribution or female predominance, suggesting that the observed sex differences may vary according to population characteristics, genetic background, prevalence of hemolytic disorders, healthcare-seeking behavior, and environmental factors.

In our study, the onset of jaundice occurred predominantly between the second and seventh days of life, accounting for 66.3% of cases, whereas only 10.7% of neonates presented with jaundice during the first 24 hours after birth. This temporal distribution is consistent with the expected pattern of physiological neonatal jaundice, which typically appears between the second and third days of life, reaches its peak intensity between the fifth and seventh days, and gradually resolves thereafter¹³. This pattern reflects the transient imbalance between bilirubin production and elimination during the early neonatal period, mainly related to increased erythrocyte turnover and the immaturity of hepatic bilirubin conjugation pathways. However, the occurrence of jaundice within the first 24 hours of life remains clinically significant, as it may indicate underlying pathological conditions, particularly hemolytic disorders, congenital infections, or other causes requiring early investigation.

Prematurity is a well-established risk factor for severe and prolonged neonatal hyperbilirubinemia due to immature hepatic function, reduced bilirubin conjugation capacity, and increased susceptibility to bilirubin accumulation. According to the World Health Organization (WHO)²³, approximately 15 million infants are born prematurely worldwide each year, with prematurity defined as birth occurring before 37 completed weeks of gestation²⁴. In our cohort, the vast majority of jaundiced neonates were born at term (96.8%; $n = 299$), whereas only 3.2% ($n = 10$) were premature. This finding is comparable to the study by Nzanza *et al.*²⁵ (2022), which reported a prematurity rate of 5% among neonates with jaundice²⁶. However, our observed prevalence was lower than that reported in previous studies, including Maïmouna²⁷ (1999), who found a prematurity rate of

22.2%, and Hounkponou *et al.*²⁴ (2017), who reported a prevalence of 17.89% among jaundiced newborns. These discrepancies may be explained by differences in population characteristics, referral patterns, neonatal care organization, maternal health conditions, and methodological approaches between studies. Furthermore, the relatively low proportion of preterm infants in our cohort may reflect the fact that our study population was recruited in a pediatric department rather than a neonatal intensive care unit, where premature infants and severe cases are more frequently managed.

Regarding the mode of delivery, vaginal delivery was predominant in our study, accounting for 90.3% of cases ($n = 279$), whereas cesarean delivery accounted for only 9.7% ($n = 30$). These findings differ from those reported by Zedini *et al.*²⁶ (2020), who observed a nearly equal distribution of vaginal (44.6%) and cesarean (53.9%) deliveries among jaundiced neonates. Similar variability was reported by Boskabadi *et al.*²⁸ (2020), who found that the proportion of vaginal deliveries among neonates with hyperbilirubinemia ranged from 16.7% to 75%, while approximately 40% were delivered by cesarean section. Such differences may be related to variations in obstetric practices, maternal and fetal indications for cesarean delivery, population characteristics, and referral patterns between healthcare settings. Although cesarean delivery has been associated in some studies with an increased risk of neonatal jaundice, potentially through delayed initiation of breastfeeding and differences in early gastrointestinal adaptation, the association remains complex and is likely influenced by multiple maternal, neonatal, and perinatal factors²⁸. Therefore, the predominance of vaginal deliveries observed in our cohort should not be interpreted as evidence of a direct protective effect against neonatal jaundice.

A Canadian study by Blumovich *et al.*²⁹ (2020) reported that 4.2% of neonates delivered vaginally and 2.2% of those delivered by cesarean section were subsequently readmitted for phototherapy because of neonatal jaundice²⁹. Although the absolute rates differed according to delivery mode, these findings support the importance of postnatal surveillance irrespective of the mode of delivery. In clinical practice, early assessment of feeding adequacy, weight loss, and bilirubin levels remains essential, particularly during the first days of life when bilirubin concentrations may increase rapidly.

The World Health Organization (WHO) recommends further evaluation when jaundice persists beyond 14 days in term infants or 21 days in preterm infants, as prolonged jaundice may indicate an underlying pathological condition requiring specific investigation³⁰. In our cohort, jaundice persisting for more than 14 days was observed in 10.7% of neonates admitted with jaundice. This proportion was higher than the 3.14% reported by Berkoud (2017) but substantially lower than the rate reported by Wellé *et al.* (2022), who observed prolonged jaundice in nearly half of the infants studied^{31,32}. Such differences may be explained by variations in study populations, referral patterns, follow-up procedures, underlying etiologies, and, importantly, the operational definitions used to characterize prolonged or persistent jaundice. Nevertheless, the presence of prolonged jaundice in more than one in ten neonates in our cohort highlights the importance of systematic follow-up and appropriate diagnostic evaluation to distinguish prolonged physiological or breastfeeding-related jaundice from cholestatic, infectious, metabolic, or other pathological conditions.

We also evaluated the duration of hospitalization among neonates with jaundice, which ranged from 1 to more than 8 days, with a mean hospital stay of 2 days. This duration was shorter than that reported in comparable studies. Lehlmi *et al.*³³ (2020) and Ben Houmich³⁴ (2017) reported mean hospital stays of 4 and 6 days, respectively. Several factors may account for these differences, including variations in healthcare organization, admission and discharge criteria, availability of diagnostic and therapeutic resources, and differences in the clinical severity and etiological profile of the studied populations. The shorter hospitalization observed in our cohort may also reflect the predominance of physiological or clinically uncomplicated jaundice, allowing early discharge after adequate assessment and treatment. Conversely, longer hospital stays may be expected among neonates with severe hyperbilirubinemia, hemolytic disease, prematurity, associated infections, or other complications requiring prolonged monitoring and treatment. Thus, the duration of hospitalization should be interpreted in relation to the underlying cause and clinical severity of neonatal jaundice rather than considered as an isolated outcome.

Total, conjugated, and unconjugated bilirubin levels were measured in all 309 neonates included in

our study. The results confirmed elevated bilirubin concentrations consistent with neonatal jaundice. Among the affected neonates, 214 (69.26%) had total serum bilirubin levels below 180 $\mu\text{mol/L}$, 94 (30.42%) had levels between 180 and 340 $\mu\text{mol/L}$, and one neonate (0.32%) had a level exceeding 340 $\mu\text{mol/L}$. The overall mean total bilirubin concentration was $166.47 \pm 46.36 \mu\text{mol/L}$. Although physiological jaundice is generally benign, markedly elevated bilirubin concentrations are associated with an increased risk of bilirubin-induced neurological dysfunction (BIND), particularly when bilirubin levels are interpreted in relation to postnatal age, gestational age, and the presence of additional risk factors^{35,36}. Such cases require prompt clinical assessment and appropriate treatment according to established age- and gestation-specific thresholds.

The mean bilirubin concentration observed in our cohort was comparable to that reported by Lehlmi *et al.* (2020), who found a mean total bilirubin concentration of 172.7 $\mu\text{mol/L}$ ³³. Similarly, Chemsî *et al.*³⁷ (2020) reported a mean bilirubin concentration of 190.02 $\mu\text{mol/L}$ among neonates with jaundice. The relatively similar bilirubin concentrations across these studies may reflect comparable clinical characteristics of the studied populations and similar referral patterns. However, bilirubin concentrations should not be interpreted according to a single absolute threshold, as their clinical significance depends strongly on postnatal age in hours, gestational age, and the presence of neurotoxicity risk factors. Bilirubin levels normally increase during the first days of life and subsequently decline as hepatic bilirubin metabolism matures; therefore, age-specific assessment is essential for distinguishing physiological from potentially hazardous hyperbilirubinemia¹⁰.

In our study, preterm neonates had higher mean bilirubin concentrations than term neonates ($167.43 \pm 45.29 \mu\text{mol/L}$ versus $138.81 \pm 67.78 \mu\text{mol/L}$). This finding is consistent with that reported by Bhutani *et al.*, who observed higher bilirubin concentrations among preterm infants than among term infants³⁶. The increased susceptibility of preterm neonates to hyperbilirubinemia can be explained by the immaturity of hepatic bilirubin conjugation, together with increased bilirubin production and enhanced enterohepatic circulation. In particular, the activity of uridine diphosphate-glucuronosyltransferase 1A1 (UGT1A1), the principal

enzyme responsible for bilirubin conjugation with glucuronic acid, is lower in preterm infants, resulting in reduced bilirubin clearance³⁸. The degree of hepatic immaturity is closely related to gestational age and may contribute to prolonged and more severe hyperbilirubinemia. These findings emphasize the importance of closer bilirubin surveillance in preterm infants, particularly when additional risk factors for bilirubin neurotoxicity are present.

White blood cells (WBCs), or leukocytes, play an essential role in neonatal host defense and inflammatory responses. In jaundiced neonates, WBC abnormalities may provide additional information when infection or inflammation is suspected³⁹. In our cohort, 94.8% of neonates ($n = 293$) had WBC counts within the reference range of 5–18 G/L, consistent with neonatal reference values reported by Lainey and Fenneteau (2018)⁴⁰. Leukocytosis was observed in 4.2% of neonates and may have reflected an underlying infectious or inflammatory process. However, WBC count alone is insufficient to establish an infectious diagnosis and should be interpreted together with clinical findings and, when appropriate, microbiological and inflammatory markers.

The mode of delivery may influence early neonatal microbial colonization, as vaginal birth exposes newborns to maternal vaginal and intestinal microorganisms during passage through the birth canal²¹. Nevertheless, in our cohort, no statistically significant association was observed between mode of delivery and infection among jaundiced neonates. This finding suggests that the mode of delivery alone may not be a major determinant of infection in this population and that neonatal infection is likely influenced by a combination of maternal, perinatal, and neonatal factors. Therefore, the absence of a significant association in our study should not be interpreted as evidence that vaginal delivery is intrinsically associated with either increased or decreased infection risk.

Our findings differ from those reported by Saizonou *et al.*⁴¹ (2014) and Bäckhed *et al.*⁴² (2015), who demonstrated that vaginal delivery is an important route of maternal microbial transmission and early neonatal gut colonization. Such microbial transmission is a normal component of neonatal adaptation and may have beneficial effects on immune and intestinal development, although its clinical consequences depend on maternal health, microbial composition, and the neonatal environment.

Thus, microbial exposure during vaginal delivery should be distinguished from the development of clinically significant neonatal infection.

Prematurity is an important determinant of neonatal morbidity and mortality, partly because of the immaturity of immune defenses and the increased susceptibility of preterm infants to infection^{43,44}. In our cohort, the 10 preterm neonates had a higher mean WBC count than term neonates ($14.29 \pm 8.48 \times 10^9/L$ versus $11.22 \pm 4.41 \times 10^9/L$). This difference may reflect developmental differences in hematological and immune responses; however, given the small number of preterm infants in our cohort, this finding should be interpreted cautiously and cannot by itself be considered evidence of subclinical infection. Previous studies by Gillard *et al.*⁴⁵ (2018) and Kemp⁴⁶ (2014) have emphasized the complex relationship between prematurity, immature immune responses, intrauterine inflammation, and neonatal infection.

The World Health Organization recognizes prematurity as an important risk factor for neonatal infection because of the immaturity of immune defenses and the greater vulnerability of preterm infants to bacterial, viral, and fungal pathogens⁴⁷. Accordingly, clinical management of preterm infants or neonates with suspected infection requires careful clinical surveillance and targeted laboratory and microbiological investigations when clinically indicated⁴⁸. Early recognition of infection is particularly important in jaundiced neonates because sepsis and systemic inflammation may contribute to worsening clinical status and may coexist with other causes of hyperbilirubinemia.

Finally, recent evidence from Choi *et al.*⁴⁹ (2025) suggests that neonatal characteristics and perinatal factors may influence the risk of readmission for hyperbilirubinemia following discharge. Although this finding provides useful context for post-discharge surveillance, it should be interpreted separately from the infection-related findings of our study, as our analysis did not specifically assess readmission risk after vaginal versus cesarean delivery.

ABO and Rh incompatibility are important causes of hemolytic disease of the fetus and newborn (HDFN) and result from maternal–fetal blood group incompatibility. In our cohort, ABO incompatibility was identified in 6.1% of cases ($n = 19$), which was lower than the proportions reported by Lehlmi *et al.* (2020) and Nguendo-Yongsi (2021), who reported

rates of 20% and 11%, respectively^{33,48}. These differences may reflect variations in the distribution of maternal and neonatal blood groups, the prevalence of clinically significant alloimmunization, diagnostic criteria, screening practices, referral patterns, and sample size across study populations. In addition, the proportion of ABO incompatibility identified among jaundiced neonates may depend on whether laboratory confirmation of immune-mediated hemolysis was systematically performed.

Feto-maternal red blood cell alloimmunization occurs when a fetus inherits a paternal erythrocyte antigen that is absent in the mother, resulting in maternal sensitization and the production of specific IgG alloantibodies capable of crossing the placenta. The Rh(D) antigen remains one of the most clinically important targets, particularly when an Rh-negative mother carries an Rh-positive fetus⁵⁰. In our study, Rh incompatibility was identified in only 7 neonates (2.2%). The relatively low frequency observed in our cohort may reflect the effectiveness of antenatal screening and preventive strategies, particularly the use of anti-D immunoglobulin prophylaxis in Rh-negative mothers.

When maternal anti-D antibodies cross the placenta and bind to Rh(D)-positive fetal erythrocytes, immune-mediated hemolysis may occur and can lead to anemia and unconjugated hyperbilirubinemia. In severe cases, excessive bilirubin accumulation may result in acute bilirubin encephalopathy and kernicterus. Our findings are consistent with the continuing clinical importance of Rh alloimmunization highlighted by Tyndall *et al.*⁵¹ (2020), who emphasized the role of Rh antigens, including D, C, c, E, and e, in hemolytic disease of the fetus and newborn. Nevertheless, the introduction of systematic antenatal blood-group screening, antibody testing, and Rh immunoglobulin prophylaxis has substantially reduced the incidence and severity of Rh(D)-mediated disease in settings where these preventive measures are widely available. The persistence of Rh incompatibility in our cohort therefore highlights the importance of maintaining effective antenatal screening and prophylaxis programs, particularly in populations where access to preventive maternal care may be variable.

Phototherapy remains the cornerstone of treatment for neonatal hyperbilirubinemia and is widely used to prevent the progression of severe hyperbilirubinemia and bilirubin-induced neurological injury. In our

study, conventional phototherapy was the first-line treatment administered to all affected neonates, consistent with the findings reported by Berkoud (2017)⁵². In contrast, Ben Houmich⁵³ (2017) reported a greater use of intensive phototherapy modalities. These differences may be related to variations in the severity of hyperbilirubinemia at admission, gestational age, timing of treatment initiation, availability of phototherapy devices, and institutional treatment protocols. The choice between conventional and intensive phototherapy should therefore be guided by the total serum bilirubin concentration in relation to postnatal age and gestational age, as well as by the presence of risk factors for bilirubin neurotoxicity^{54,49}.

The effectiveness of phototherapy depends on several factors, including the irradiance and wavelength of the light source, the exposed body surface area, the duration of treatment, and the clinical characteristics of the neonate. In our cohort, the mean duration of hospitalization was approximately 2 days in both the conventional and intensive phototherapy groups. This duration was shorter than the 4-day mean reported by Cortey *et al.* (2014)⁵⁵. Differences in hospitalization duration may reflect variations in treatment protocols, discharge criteria, initial bilirubin concentrations, response to phototherapy, and post-discharge follow-up arrangements. The relatively short hospital stay observed in our cohort may indicate a favorable early response to treatment in most neonates; however, hospitalization duration should be interpreted cautiously because it is influenced not only by the effectiveness of phototherapy but also by institutional and organizational factors⁵⁶⁻⁵⁸.

The Kaplan–Meier analysis of hospitalization duration among neonates with jaundice showed a steep decline in the probability of continued hospitalization during the first three days, indicating that most neonates were discharged early. This observation is consistent with the descriptive findings presented in Table 2, which showed that the majority of hospital stays lasted between one and three days. Such a pattern is compatible with current clinical practice, in which early identification and timely initiation of appropriate treatment, particularly phototherapy when indicated, can result in rapid control of hyperbilirubinemia and allow discharge after adequate clinical assessment^{56,57}. The relatively short hospitalization observed in our cohort may also reflect the predominance of isolated or clinically

uncomplicated jaundice and the effectiveness of standardized management protocols.

When the analysis was stratified according to gestational age (Figure B), preterm neonates appeared to have a slightly earlier discharge trend. However, this observation should be interpreted with caution because only a small number of preterm infants were included in our cohort. Previous studies have shown that preterm neonates may require longer hospitalization because of associated conditions such as respiratory distress, feeding difficulties, and other complications of prematurity, which may prolong the management of jaundice^{59,60}. Nevertheless, when jaundice occurs in the absence of significant comorbidities and is appropriately monitored and treated, preterm infants may also have relatively short hospital stays⁶⁰. Therefore, the duration of hospitalization in preterm infants is likely determined by the overall clinical condition rather than by gestational age alone.

When hospitalization duration was analyzed according to mode of delivery (Figure B), no statistically significant difference was observed between neonates delivered vaginally and those born by cesarean section. Both groups demonstrated similar hospitalization patterns, suggesting that delivery mode did not substantially influence the duration of hospital care in our cohort. This finding is consistent with the concept that the clinical course and resolution of neonatal hyperbilirubinemia are more strongly influenced by gestational maturity, feeding adequacy, bilirubin metabolism, and the underlying etiology than by the mode of delivery itself^{58,61}.

Nevertheless, this result should be interpreted cautiously because the number of neonates delivered by cesarean section was relatively small in our cohort. Some studies have suggested that cesarean delivery may be associated with delayed establishment of breastfeeding, which could contribute to increased bilirubin levels through reduced enteral intake and altered enterohepatic bilirubin circulation during the early postnatal period⁶²⁻⁶⁴. However, when adequate feeding is established and bilirubin levels are appropriately monitored and treated, this potential effect may not translate into a clinically meaningful prolongation of hospitalization, as observed in our study.

Overall, our findings indicate that hospitalization for neonatal jaundice was generally brief and was not significantly associated with the mode of delivery.

These results emphasize the potential benefits of early recognition, timely treatment, adequate feeding support, and standardized clinical monitoring in facilitating safe discharge while minimizing unnecessary hospitalization. However, hospitalization duration should be interpreted as a multifactorial outcome influenced not only by jaundice severity and treatment response but also by gestational age, associated neonatal conditions, feeding adequacy, and local discharge practices^{59,60,64}.

Conclusion

Neonatal jaundice remains a prevalent and clinically significant condition, particularly in resource-limited settings where early diagnosis and intervention may be constrained. This retrospective study reinforces the multifactorial etiology of hyperbilirubinemia, identifying ABO and Rh incompatibilities, prematurity, and perinatal infections as the most prominent contributing factors. Of particular note, ABO incompatibility especially among neonates with blood group B born to group O mothers was more frequent than anticipated, emphasizing the importance of routine immunohematological screening and vigilant postnatal monitoring.

Although vaginal delivery may theoretically confer microbial benefits through early exposure to maternal flora, our findings did not reveal a significant association between delivery mode and neonatal infection rates. However, premature infants demonstrated elevated leukocyte counts, consistent with their heightened susceptibility to systemic infections and inflammatory responses.

In terms of therapeutic intervention, conventional phototherapy remained the primary modality at our institution, even in the presence of more advanced technologies. This approach was associated with a relatively short duration of hospitalization, highlighting the effectiveness of standardized early treatment protocols.

Importantly, our Kaplan–Meier survival analyses provided additional insights into hospitalization dynamics. A marked decline in survival probability was observed within the first few days of admission, confirming that jaundice-related hospital stays are typically brief. When stratified by mode of delivery, the survival curves of neonates born vaginally and those delivered by cesarean section were largely comparable. However, a tendency toward longer

hospital stays among cesarean-delivered neonates was noted, which may reflect delayed breastfeeding initiation or increased postnatal observation. Additionally, leukocyte profiles demonstrated prognostic relevance: neonates with leukocytosis experienced significantly prolonged hospitalization, suggesting an underlying inflammatory burden that may complicate recovery. These findings underscore the utility of integrating immune and perinatal markers into risk stratification frameworks for jaundiced neonates.

In conclusion, incorporating survival analysis into the evaluation of neonatal jaundice adds prognostic depth to traditional clinical assessment. By identifying factors associated with prolonged hospitalization, such as leukocytosis and cesarean delivery, clinicians can better anticipate care needs and optimize early intervention strategies. Further prospective, multicenter studies are essential to validate these observations, improve individualized management, and elevate care standards for jaundiced neonates especially in low- and middle-income countries where resource optimization is critical.

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Conflict of interest

The authors declare that there are no conflicts of interest related to this article.

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