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Original article

The Burden of *Klebsiella* Infections in Neonates: Incidence, Risk Factors, and Outcomes from Zawia Medical Center

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Abstract
Klebsiella species are a major cause of late-onset sepsis and death in newborn intensive care units (NICUs), especially in resource-limited settings. The purpose of this study was to assess the prevalence, risk factors, and clinical outcomes of Klebsiella infections in a tertiary NICU in Libya. A retrospective cohort analysis was carried out, evaluating data of all neonatal patients admitted to the Neonatal/Pediatric ICU at Zawia Medical Center between January and December 2023. A positive culture verified the diagnosis from a sterile location. Data on demographics, clinical risk factors, and results were gathered and evaluated using acceptable statistical techniques. The incidence of Klebsiella infection was 15.4% (19/123). Mechanical ventilation was a significant risk factor, with 74% of infected neonates exposed compared to 24% in the uninfected group (OR: 8.85, 95% CI: 2.9–27.0, p<0.001). Crucially, the administration of blood products was strongly associated with infection: platelets (OR: 8.1, 95% CI: 2.8–23.7, p<0.001), fresh frozen plasma (OR: 5.6, 95% CI: 1.9–16.6, p<0.001), and red blood cells (OR: 4.0, 95% CI: 1.4–11.3, p=0.005). Preterm neonates were also at significantly higher risk (63% vs. 36.5%, p=0.003). All-cause in-hospital mortality was drastically higher in infected neonates (58% vs. 18%, p=0.001), with an attributable mortality of 42%. Kaplan-Meier analysis confirmed a significantly reduced median survival time in the infected group (7 vs. 22 days, log-rank p<0.02). Klebsiella infections are a common and fatal hazard in this context, and mechanical ventilation is an important modifiable risk factor. These findings underline the critical need for strict infection prevention strategies, particularly in ventilator care, as well as improved antibiotic stewardship to improve survival outcomes.
Keywords. *Klebsiella Infections, Neonates, Neonatal Intensive Care Unit, Healthcare-Associated Infections.*

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Introduction

The neonatal intensive care unit (NICU) is a key healthcare setting in which the most vulnerable patient population—newborns born preterm, with low birth weight, or with serious medical conditions—receives life-saving therapies [1]. While necessary, the use of intrusive equipment such as mechanical ventilators, central venous catheters, and long-term antibiotic courses dramatically increases the risk of healthcare-associated infections [2]. Gram-negative bacteria, particularly Klebsiella species, have emerged as a major source of illness and mortality in neonatal intensive care units (NICUs) [2,3].

Klebsiella infections are particularly alarming because of their proclivity for antibiotic resistance [4]. The organism's propensity to acquire extended-spectrum beta-lactamase (ESBL) and carbapenemase genes frequently leads to multidrug-resistant (MDR) strains, complicating treatment and raising the chance of fatality [5]. Infections produced by these organisms are linked to longer hospital stays, higher healthcare expenses, and a significant risk of consequences like septic shock and neurological damage [6].

In low- and middle-income nations, such as Libya, the problem is compounded by a lack of diagnostic capabilities, overcrowding, and difficulties implementing infection prevention practices [7]. Despite worldwide acknowledgment of this concern, there is a significant dearth of localized data describing the epidemiology, resistance trends, and clinical effects of Klebsiella infections in Libyan NICUs.

This study sought to fill this gap by evaluating the prevalence of Klebsiella infections in a tertiary-level NICU in Zawia, Libya. The precise goals were to quantify the prevalence of culture-confirmed Klebsiella infections, identify relevant risk factors (including clinical and therapeutic exposures), define antibiotic resistance profiles, and assess related outcomes, including death and duration of stay. The findings seek to give evidence-based insights that may be used to improve local antimicrobial stewardship, infection control methods, and, ultimately, neonatal survival and quality of care in this environment.

Methods

This retrospective single-site cohort research used medical data from neonates hospitalized in the mixed pediatric and neonatal critical care unit of Zawia Medical Center, Zawia, Libya. The study included all neonatal case admissions (infants aged ≤ 28 days) from January to December 2023.

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Infection control at our center is managed by a rigorous protocol overseen by a multidisciplinary committee comprising intensivists, infectious disease specialists, microbiologists, and environmental health technicians. Fundamental measures—including strict hand hygiene protocols, use of personal protective equipment (PPE), and disinfection of medical equipment—are mandatory.

We employ an evidence-based strategy of active surveillance for infection with routine bacterial swabs from the nose, skin, and axilla of all patients for culture and sensitivity. Additionally, routine C-reactive protein (CRP) tests are done. Based on the CRP values, the patients are transferred to two separate suites (one for high CRP-positive and another for CRP-negative patients). Each suite has a designated team of nurses to prevent any potential transfer of microbes from one suite to another. Incubators are thoroughly sterilized and disinfected after each patient discharge. Environmental control is ensured through a mandated monthly lockdown of the entire unit for deep cleaning and sterilization.

Our antibiotic control protocol employs empirical initiation of antibiotics based on the CRP status of the patients. CRP-negative patients are treated with ampicillin and gentamycin as a first line. Once the patient's status becomes positive, they are switched to Claforan (Cefotaxime) as a second line. A combination of meropenem and ciprofloxacin is reserved as the third line for deteriorated cases.

To guarantee uniformity, data were collected using a standardized extraction form. Demographic and baseline characteristics, such as gestational age, birth weight, and Apgar scores; potential risk factors for infection, such as mechanical ventilation, central venous catheters, and prior antibiotic use; and specific details for any confirmed Klebsiella infection, such as the date of onset, source, and antibiotic susceptibility profile. Files with missing or incomplete data were automatically excluded from the analysis. The primary outcome assessed was all-cause in-hospital mortality, with secondary outcomes included comorbidities such as septic shock, duration of mechanical ventilation, and overall length of hospital stay.

For the purpose of this study, key terms were explicitly defined. Late-onset sepsis (LOS) was defined as a positive culture from a sterile site, such as blood or cerebrospinal fluid, obtained after the first 72 hours of life, accompanied by clinical signs of sepsis. A case of Klebsiella infection was confirmed only upon the isolation of Klebsiella pneumoniae or Klebsiella spp. from one of these sterile sites. The statistical analysis plan involved using software such as SPSS for all computations. Categorical variables were expressed as frequencies and percentages, while continuous variables were presented as means with standard deviations or medians with interquartile ranges based on their distribution. To identify risk factors, univariate analyses were conducted using appropriate tests (Chi-square, t-test, Mann-Whitney U), with variables showing a p-value <0.01 being entered into a multivariable logistic regression model to determine independent risk factors, reported as adjusted odds ratios with 95% confidence intervals. Ethical approval for this study was granted by the Institutional Review Board of the medical center, and due to its retrospective design, the requirement for informed consent was waived, with all patient data being anonymized to uphold confidentiality.

Results

A total of 123 neonates were admitted to the mixed neonatal/pediatric ICU during the one-year study period. Among these, 19 neonates developed a confirmed *Klebsiella* infection, yielding an incidence rate of 15.4%.

The baseline demographic and clinical characteristics of the infected and non-infected neonates are presented in (Table 1). The two groups were well-matched for gestational age, sex, and mode of delivery. However, a significantly higher proportion of neonates in the infected group were premature (63% vs. 36.5%, p=0.003) and had a lower mean birthweight (2.5 kg vs. 2.9 kg, p=0.062), though the latter did not reach conventional statistical significance.

Table 1 . Baseline and Clinical Characteristics of the Study Cohort

Characteristic	Infected (n=19)	Non-Infected (n=104)	p-value
Gestational Age (months)	34.8 (63.7)	34.9 (36)	0.92
Birthweight (Kg)	2.5 (0.79)	2.88 (0.62)	0.062*
Prematurity, n (%)	12 (63%)	38 (36.5%)	0.003
Sex (male), n (%)	11 (58%)	62 (60%)	0.88
Mode of delivery (C-section), n (%)	15 (79%)	66 (64%)	0.226

**Mann-Whitney test was performed*

The requirement for mechanical ventilation was a strong risk factor, with a significantly higher proportion of infected neonates having undergone the procedure compared to the non-infected group (74% vs. 24%) (OR: 8.85, CI = 95%: 2.9-27 p<0.001) (Table 2).

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Table 2. Analysis of Risk Factors for Klebsiella Infection

MV needed	Group		Total
	Infected	Not infected	
Yes	14	25	39
No	5	79	84
Total	19	104	123

There was no statistically significant association between gestational age (weeks) in the Klebsiella-infected vs. non-infected groups (p = 0.062). the mean age for the infected group was 34.8 weeks vs. 34.9 weeks for the non-infected group. However, when the gestational age was analyzed as a binary variable (i.e., full-term vs. pre-term), prematurity was significantly associated with Klebsiella infection (p = 0.035) (Table 3).

Table 3 Distribution of Prematurity by Klebsiella Infection

Group	Gestational Age		OR
	Full Term	Preterm	
Infected	7	12	2.97 (CI: 95% 1.1 - 8.2)
Not infected	66	38	

Blood product transfusions, including platelets, fresh frozen plasma (FFP), and red blood cells (RBCs), were all significantly associated with Klebsiella infection. Infection was observed in 37.1% (13/35) of patients who received platelet transfusions compared to 6.8% (6/88) of those who did not (p < 0.001; OR = 8.1, 95% CI: 2.8–23.7). Similarly, patients who received FFP transfusions had an infection rate of 40% (8/20) versus 10.7% (11/103) in those without FFP (p < 0.001; OR = 5.6, 95% CI: 1.9–16.6). RBC transfusion was also significantly associated with 32.1% (9/28) of transfused patients developing infection compared to 10.5% (10/95) of those without transfusion (p = 0.005; OR = 4.0, 95% CI: 1.4–11.3). Collectively, these findings indicate that receipt of any blood product was linked to a markedly increased risk of Klebsiella infection (Table 4).

Table 4 The Need for Blood Product Transfusion in the Infected vs. the Non-infected Group

Blood Product	Group		p-value	Odds Ratio (95% CI)
	Infected (%)	Not Infected (%)		
Platelets	13/35 (37.1%)	22/35 (62.9%)	<0.001	8.1 (2.8–23.7)
FFP	8/20 (40.0%)	12/20 (60.0%)	<0.001	5.6 (1.9–16.6)
RBCs	9/28 (32.1%)	19/28 (67.9%)	0.005	4.0 (1.4–11.3)

The method of transfer was not significantly associated with the risk of Klebsiella infection, with infection rates of 17.9% in transferred cases and 7% in newly presented cases (p = 0.167).
Clinical outcomes are summarized in Table 3. All-cause in-hospital mortality was significantly higher in neonates with *Klebsiella* infection (58% vs. 18%, p=0.001; CI = 95% 34%-80%). Among the 19 infected neonates, attributable mortality (defined as death that occurred during the acute phase of sepsis with clinical and laboratory signs of overwhelming infection, and no other more compelling cause of death) was 42% (8/19). The overall mortality for the entire cohort was 24% (30/123).

Table 5. Clinical Outcomes for Neonates with and Without Klebsiella Infection

Mortality, n (%)	Outcome		OR
	Infected (n=19)	Non-Infected (n=104)	
Died	11 (58%)	19 (18%)	**6.13 (2.2 – 17.4)**
Survived	8 (42%)	85 (82%)	

Survival analysis was performed using the Kaplan-Meier method and compared with the log-rank test. The median survival period for infected neonates was 7 days (IQR 4 – 25), while it was 22 days (IQR 14->30).

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(Figure 1), Neonates with a *Klebsiella* infection had a significantly lower probability of survival over time compared to non-infected neonates (log-rank p < 0.02).

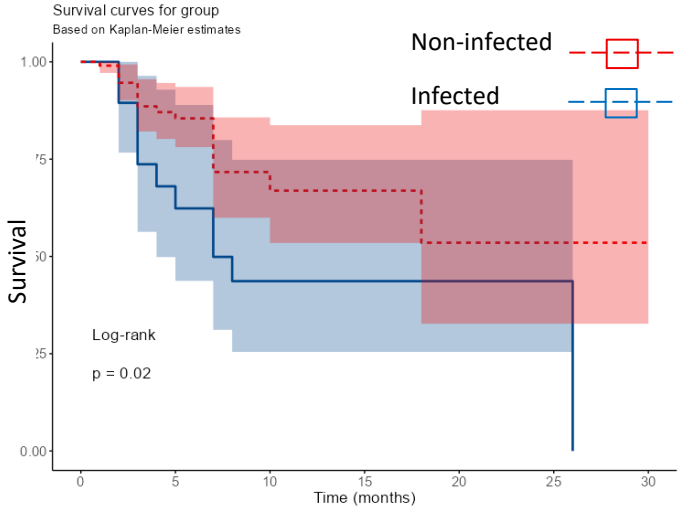

Figure 1. Kaplan-Meier survival curve comparing time to death for neonates with and without Klebsiella infection. The survival probability was significantly lower in the infected group (p < 0.02)

Discussion

This work provides crucial insights into the epidemiology of Klebsiella infections in a Libyan neonatal intensive care unit, with findings that both agree with and deviate from trends found in other contexts. The observed incidence rate of 15.4% far surpasses rates reported in other high-income nations, where recent studies have found Klebsiella infection rates of 2-5% in NICUs. Multicenter research in the United States, for example, revealed a 3.2% incidence, but data from Western European countries typically range between 2-4% [8]. However, it is crucial to understand this gap given Libya's unique sociopolitical circumstances following the 2011 conflict. The deterioration of the national healthcare infrastructure, persistent shortages of medical supplies, and difficulties in maintaining regular infection control methods are well-documented and give a more particular explanation than general "variances in resources." [9].

When examined geographically, our findings are similar to those of other Middle Eastern and North African nations. According to studies from Egypt and Tunisia, NICU Klebsiella infection rates were between 12 and 18%, indicating that the area has comparable issues [10]. Notably, a recent study from a tertiary hospital in Morocco found a comparable prevalence of 16.8%, with equally worrisome death consequences [11]. These comparable geographical trends point to common structural issues, such as high patient-to-nurse ratios, inadequate isolation capacities, and limits in adopting long-term infection control measures.

The mortality rate of 58% among infected newborns in our sample exceeds the 30-40% mortality rates commonly reported in international literature, although it is consistent with results observed in other resource-limited contexts [12]. A comprehensive assessment of newborn sepsis in low- and middle-income countries found that Gram-negative infections had an average death rate of 52%, with multidrug-resistant organisms causing particularly high case fatality rates (up to 60%) [13]. This shows that the high fatality rate found in our study may be due to limits in diagnostic ability, delays in adequate antibiotic therapy, and the presence of resistant bacteria.

The substantial link between mechanical ventilation and infection (74% vs. 24%) is consistent with international research. International studies have repeatedly shown mechanical ventilation as a key risk factor for healthcare-associated infections in NICUs, with reported odds ratios ranging from 3.5 to 5.0. Our findings reaffirm the universal value of ventilator-associated pneumonia prevention methods, while emphasizing the vital necessity for context-appropriate implementation in resource-constrained settings [14]. Notably, the prevalence of prematurity as a risk factor in our cohort (63% vs. 36.5%) follows global trends, but is more significant than in other high-income contexts [15]. This might be due to variances in the patient group, as our institution is a referral center for high-risk births, or to variability in survival rates among extremely preterm newborns across healthcare systems [16].

These findings illustrate both the general difficulty of avoiding Klebsiella infections in NICUs and the unique vulnerabilities encountered by hospitals with minimal resources. The convergence of high incidence rates and poor outcomes across multiple resource-limited settings suggests that structural factors such as staffing patterns, physical infrastructure, and access to laboratory support may be just as important in determining infection rates as specific clinical practices.

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One of the most worrying results is the much higher death rate among infected newborns (58% compared to 18% in uninfected babies). This substantial disparity in outcomes emphasizes the severity of Klebsiella infections in this fragile group, implying possible difficulties in prompt detection and adequate antibiotic therapy. The high attributable mortality rate of 42% further emphasizes the direct clinical impact of these infections on patient survival [17].

The high connection between mechanical ventilation and Klebsiella infection (74% versus 24%) is consistent with previous research indicating invasive devices as key risk factors for healthcare-associated infections [18]. This study emphasizes the need to implement and strictly adhere to ventilator-associated pneumonia prevention bundles, which include routine oral care with chlorhexidine, subglottic suctioning, and daily evaluations of readiness for extubation. The statistics indicate that minimizing needless ventilator days through better respiratory control practices might considerably reduce infection rates [19].

Transfusions of platelets, fresh frozen plasma (FFP), and red blood cells (RBCs) all emerged as significant independent risk variables, and the analysis showed a particularly robust and dose-responsive association between the administration of blood products and the probability of Klebsiella infection. Getting any blood product is a strong indicator of infection, as evidenced by the much higher odds ratios, which are highest for platelet transfusions (OR = 8.1). Multiple studies demonstrate that blood product transfusions significantly increase infection risk in hospitalized patients [20]. A study found that red blood cell (RBC), platelet, and fresh frozen plasma (FFP) transfusions were independent risk factors for healthcare-associated infections, with platelets showing the highest odds ratio (OR = 8.903) [20]. Similarly, it is reported that all three blood products were associated with increased mortality and infection rates after cardiac surgery in a dose-dependent manner [21]. Péju et al. (2021) specifically examined septic shock patients and found that platelet transfusions (hazard ratio = 1.55) and FFP transfusions (hazard ratio = 1.38) independently increased ICU-acquired infection risk [22]. Sarani et al. (2008) focused on FFP transfusions in surgical ICU patients, demonstrating a significant association with various infections (relative risk = 2.99) and establishing a dose-response relationship [23]. These findings consistently support that blood product transfusions, particularly platelets, represent significant independent risk factors for nosocomial infections across different patient populations. Numerous mechanisms that are not mutually exclusive can account for this connection. First, the requirement for transfusion is a strong indicator of physiological instability and underlying clinical severity, both of which are inherent risk factors for nosocomial infection. Second, vascular access is required for every transfusion event, which increases the risk of catheter-related bloodstream infections by multiplying the opportunities for microbial introduction. Third, blood products are known to have immunomodulatory effects, which could increase susceptibility to opportunistic infections like Klebsiella and cause temporary immunosuppression in newborns who are already at risk. This is a serious therapeutic problem since the very treatments meant to stabilize severely unwell newborns can unintentionally put them at risk for potentially fatal infections. These results strongly support the adoption of two important strategies: strict adherence to maximal sterile barrier precautions during all procedures involving vascular access and blood product administration, and the adoption of conservative, evidence-based transfusion protocols to reduce needless exposure. The lack of substantial differences in most baseline characteristics between groups, except preterm and a trend toward lower birth weight, indicates that observed outcomes are mostly due to acquired risk factors rather than intrinsic patient features. This data highlights the potential for preventative actions to significantly reduce infection rates.

Antibiotic management of Klebsiella, as a very common nosocomial infection, is an important aspect of this topic. Our center employs an empirical protocol for antibiotic use based on CRP status. CRP-guided antibiotic treatments are supported by recent data, although the described strategy may need to be modified. According to meta-analyses, CRP-guided algorithms shorten the length of antibiotic treatment in hospitalized patients and neonates by 1.45–1.82 days without raising the risk of infection recurrence or death [24,25]. CRP-guided therapy duration was not inferior to set 14-day regimens in people with simple gram-negative bacteremia [26].

Even though CRP guidelines seem advantageous for treatment duration, the antibiotic selection method needs to be updated to reflect the latest data supporting monotherapy over aminoglycoside combinations. This highlights the set of challenges antibiotics stewardship (ABS) in low- and middle-income countries (LMICs) faces compared to high-income countries, requiring contextualized approaches rather than direct implementation of existing programs27. While LMICs bear a disproportionate burden of antimicrobial resistance, they also face resource constraints and infrastructure limitations [28]. Evidence on effective stewardship interventions in LMICs remains limited, though several initiatives across Latin America, Africa, and Asia have demonstrated feasibility when properly adapted to local contexts [27,28]. A systematic review found that hospital-based ABS interventions in LMICs successfully reduced antimicrobial consumption by 14.8%, decreased costs by 2.4%, and shortened hospital stays by 19.1% [29]. However, programs effective in high-income countries may not perform well in LMICs due to different healthcare needs, where decreased antibiotic access could be dangerous for patients lacking adequate treatment [30]. International

collaboration remains valuable for sharing educational materials and experiences while allowing for local adaptation.

Several restrictions should be addressed when interpreting these findings. The retrospective methodology increases the likelihood of documentation mistakes and missing data. The study's single-center design restricts generalizability, but the findings are likely to reflect issues experienced by similar institutions in resource-limited contexts. The absence of molecular characterization of isolates precludes extensive analyses of resistance mechanisms and transmission patterns, which would be useful for targeted treatments. Despite these limitations, this study presents compelling evidence for immediate action. Improving infection control methods, particularly for mechanical ventilation and other invasive operations, is an essential need. Furthermore, implementing antimicrobial stewardship programs and increasing laboratory capacity for quick diagnosis might assist in alleviating the high fatality rates found. Future research should concentrate on prospective, multi-center studies that use molecular typing to better understand transmission dynamics and resistance patterns. Economic assessments assessing the cost-effectiveness of various intervention options might potentially help guide resource allocation decisions in similar healthcare contexts.

Conclusion

Klebsiella infections are a leading cause of illness and mortality in the neonatal intensive care unit, with a 15.4% incidence and a worrying mortality rate of 58% among infected infants. The substantial link between mechanical ventilation and infection emphasizes the significance of strict infection prevention methods during invasive operations. These findings underline the crucial need for improved antimicrobial stewardship and strong infection control methods in comparable resource-constrained environments. Future efforts should concentrate on establishing preventative methods and expanding surveillance to lessen the impact of these illnesses.

Conflict of Interest

The author declares no conflict of interest.

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