#### **ORIGINAL ARTICLE**

# Klebsiella pneumoniae in Neonatal Sepsis: A Growing Challenge of Multidrug Resistance in a Tertiary Care Setting

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### **ABSTRACT**

Key words: HCAI; LONS; hvKp; XDR; CRKP.

\*Corresponding Author: Aya Gaber Radwan Tanta 31512, Egypt Tel.: 01120690634, 01144838350 ayagaber11816@gmail.com aya.gaber@med.tanta.edu.eg **Background:** Neonatal sepsis, a potentially fatal medical condition marked by systemic infection in newborns, poses a substantial challenge for paediatricians and infection control professionals, particularly when attributed to Klebsiella pneumoniae (K. pneumoniae). Objectives: This research was designed to determine the predominant bacterial species causing late-onset neonatal sepsis (LONS) in the NICUs located at hospitals of Tanta University. The study specifically focused on evaluating the incidence of Klebsiella pneumoniae (K. pneumoniae) among these cases. Additionally, the research sought to conduct a comprehensive analysis of the phenotypes, antibiotic resistance profiles, antimicrobial resistance patterns, and of resistance mechanisms observed in K. pneumoniae isolates. Methodology: This study enrolled 100 neonates presenting with signs and symptoms of sepsis after 72 hours of birth. Standard microbiological techniques were employed for bacterial identification, with K. pneumoniae isolates confirmed through a series of biochemical reactions. The string test method was utilized to identify hypervirulent K. pneumoniae (hvKp) isolates. The determination of antibiotic susceptibility was carried out using the disc diffusion method and the colistin broth disk elution method. Results: Blood culture analysis revealed sepsis in 37% of the enrolled neonates. K. pneumoniae was identified as the predominant pathogen, responsible for 40.5% of these cases, with Staphylococcus aureus identified in 27%. Among the K. pneumoniae isolates, 33.3% were hvKp, and a significant proportion exhibited resistance: 53.3% were multidrug-resistant (MDR), 46.7% were extensively drugresistant (XDR), and 86.7% were carbapenem-resistant (CRKP). Colistin and tigecycline demonstrated the highest efficacy against these resistant isolates. Conclusion: The substantial prevalence of K. pneumoniae in LONS underscores the critical need for robust infection control measures

# **INTRODUCTION**

Healthcare-associated infections (HCAIs) pose a significant global public health challenge, jeopardizing the lives of hundreds of millions of patients annually. This health problem is particularly pronounced throughout the developing world, where the incidence of intensive care unit (ICU)-associated infections is demonstrably higher, two to three times greater than in developed countries <sup>1</sup>.

Neonatal sepsis is categorized as early-onset neonatal sepsis (EONS) or late-onset neonatal sepsis (LONS) based on its onset. EONS typically results from transplacental or ascending infections originating from the mother's genital tract, whereas LONS is associated with infections acquired postnatally, either in the hospital or the community. While the exact timeframe for distinguishing between them varies, most epidemiological studies utilize 72 hours as the standard reference point <sup>2</sup>.

The Global Burden of Disease estimates a staggering 1.3 million annual cases of neonatal sepsis worldwide, tragically resulting in 203,000 sepsis-attributable deaths. Blood culture is the definitive test for confirming neonatal sepsis. It offers good sensitivity, but it is time-consuming and prone to false negative results. Therefore, understanding the microbial characteristics of LONS and their antibiotic susceptibility is crucial for selecting appropriate empirical therapies and guiding effective infection control practices <sup>3</sup>.

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To date, current research has identified two primary pathotypes of *K. pneumoniae* in patient care settings: classical *K. pneumoniae* (cKP) and hvKp. While cKP strains often cause hospital-acquired infections, hvKp, a more recently emerged pathotype, has the capacity to cause a range of community-acquired, invasive, and fatal infections in immunocompetent individuals <sup>4</sup>.

Klebsiella pneumoniae stands out as a major contributor to HCAIs, accounting for a substantial proportion (18% to 31%) of all such infections. Within

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NICUs, bloodstream infections (BSIs) caused by K. *pneumoniae* are among the most frequently identified nosocomial infections, frequently leading to unfavourable clinical outcomes and extended hospital stays  $^5$ .

The significant rise of multidrug-resistant (MDR) *K. pneumoniae* strains, exhibiting resistance to at least three distinct classes of antibiotic groups, has significantly compounded the global challenge of treating HCAIs. This challenge has been further exacerbated by the appearance of extensively drugresistant (XDR) strains, sensitive to a maximum of two antimicrobial categories, and pan-drug-resistant strains, resistant to all known antibiotics. Carbapenems have been considered a key treatment option for infections caused by bacteria producing extended-spectrum beta-lactamases (ESBLs) <sup>6</sup>.

The alarming surge in MDR-hv *Klebsiella* infections, coupled with the growing limitations of effective treatments, has classified these strains as "superbugs," posing significant challenges to public health. Therefore, the hypervirulence and metastatic capacity of these infections underscore the urgency of timely control, as they can inflict significant damage on vital organs <sup>7</sup>.

Given the limited data available on the incidence of *K. pneumoniae* in NICUs, this study was intended to identify the predominant bacterial causes of LONS. Specifically, the study sought to determine the incidence, phenotype, antibiotic sensitivity, resistance patterns, and mechanisms of antibiotic resistance of *K. pneumoniae* isolates.

# **METHODOLOGY**

### Study design:

This hospital-based, descriptive cross-sectional study with an analytical component enrolled 100 neonates exhibiting clinical signs of sepsis after the first

three days of life who were admitted to the NICUs of Tanta University Hospitals between September 2022 and December 2023. Prior to enrollment, informed consent was obtained from the parents of each neonate, and the study received ethical approval from the Institutional Ethics and Research Committee, Faculty of Medicine, Tanta University (approval code 35213/1/22). Comprehensive clinical histories of all neonates were reviewed, specifically collecting data on age, gender, weight at birth, and the presence of known sepsis risk factors including prematurity, chorioamnionitis, or the insertion of central venous catheters.

**Collection of samples:** Neonatal blood samples were collected under strict aseptic precautions via venepuncture of a peripheral vein. Blood cultures were drawn prior to the administration of the antimicrobial drugs. The collected bottles were clearly labelled with the patient's name, number, date, and time of collection<sup>3,8</sup>.

### Sample processing:

Blood culture bottles were incubated aerobically at 37°C promptly. Bottles were visually inspected daily for signs of microbial growth. Subcultures were done on blood agar, chocolate agar, and MacConkey agar after 24 hrs. When no visible bacterial growth was observed, subcultures were repeated on the fifth day. Bottles were discarded after seven days if no growth was observed <sup>8</sup>.

### Identification of the isolated bacteria:

Following after a 24-hour incubation period at 37°C, any bacterial growth was identified based on colony morphology, Gram staining, and biochemical reactions. Gram-positive bacteria were examined for catalase, coagulase, and sensitivity for optochin disk were conducted. For Gram-negative bacilli, oxidase, citrate utilization, urease, Triple Sugar Iron agar (TSI), motility indole ornithine (MIO) agar, and lysine decarboxylase were performed. The criteria outlined in table 1 were used to identify *K. pneumoniae* isolates.

**Table 1: Identification method for** *K. pneumoniae:* 

Test	Result	
Microscopic Examination	Gram-negative bacilli, non-specific arrangement, non-motile,	
	non-sporing and encapsulated	
Colony Morphology on MacConkey agar plate	Mucoid pink colonies due to lactose fermentation	
Biochemical Reaction:		
Catalase	Positive	
Oxidase	Negative	
Citrate utilization	Positive intense blue	
MIO	Negative indole	
	Negative motility	
	Negative ornithine decarboxylation	
Urease	Positive or late positive	
Lysine decarboxylase	Positive	
TSI	Acid butt acid slant with gas	

# Hypervirulent *K. pneumoniae* isolates were identified using the string test (screening test).

Briefly, an overnight broth culture was streaked onto MacConkey agar and incubated for 24 hours. Fresh colonies were then gently touched and stretched across the agar surface using a sterilized loop. The presence of a string longer than five mm was indicative of a positive result as illustrated in figure 3 <sup>10</sup>.

Antibiotic sensitivity testing of K. pneumoniae isolates was performed using the disc diffusion method (Kirby-Bauer method), adhering to the recommendations of the Clinical and Laboratory Standards Institute (CLSI)<sup>11</sup>, Susceptibility to Tigecycline (15 $\mu$ g) was evaluated based on EUCAST guidelines <sup>12</sup>.

The colistin minimal inhibitory concentration (MIC) for *K. pneumoniae* isolates was assessed in accordance with the colistin broth disk elution method. The MIC was defined as the lowest concentration of colistin that completely inhibits the multiplication of the test isolate, as per CLSI standard guidelines <sup>11</sup>:

MIC  $\leq$  2 µg /ml = intermediate strain MIC  $\geq$  4 µg/ml = resistant strain

### **Evaluation of ESBL producing strains:**

Isolates showed resistance of 3<sup>rd</sup> generation cephalosporins were considered suspected ESBLs producers. They were further confirmed using modified double disk synergy test. This test involved placing disks of piperacillin tazobactam, cefotaxime, ceftazidime, aztreonam and cefepime (30 μg each) at distances of 20mm from the center of amoxicillin clavulanic acid disc (20 and 10 μg, respectively).

#### **Interpretation:**

A clear-cut extension of the zone of inhibition around the extended-spectrum cephalosporin and aztreonam discs towards the amoxicillin clavulanic disc was interpreted as ESBL producer <sup>11</sup>.

### **Detection of ampC producing strains:**

Isolates exhibited resistance to cefoxitin. Or isolates showed resistance to cephalosporins with lacked synergy with clavulanic acid were considered suspected ampC producers. They were further confirmed using double disk synergy test. This test involved placing disks of cefotaxime, ceftazidime (30 µg each) at distances of 15 mm from a disc containing cloxacillin 300µg (ampC inhibitor) in the center.

# **Interpretation:**

Expansion of the zone of inhibition either one or both cefotaxime and ceftazidime towards cloxacillin disc confirmed a positive test <sup>11</sup>.

# Detection of carbapenemase producing strains:

Isolates exhibited resistance to discs of imipenem and meropenem were considered suspected carbapenem resistant. They were further confirmed using modified

carbapenem inactivation method (mCIM) according to  $^{11}$ .

### **Detection of Multidrug resistant (MDR) bacteria:**

According to the European Centre for Disease Control (ECDC), MDR bacteria are defined as those exhibiting resistance to at a minimum, one agent in three or more antimicrobial classes <sup>13</sup>.

# Detection of Extensively drug resistant (XDR) bacteria:

According to the ECDC, XDR bacteria are defined as those exhibiting resistance to at a minimum one agent in all but two or fewer antimicrobial categories. This means that XDR isolates are susceptible to only one or two antimicrobial classes <sup>13</sup>.

#### **Statistical analysis:**

Data analysis was performed using IBM SPSS Statistics for Windows, Version 25.0 (IBM Corp, 2017). Categorical data were expressed as the number and percentage of the total, while numerical data were expressed as the mean  $\pm$  standard deviation (SD). Intergroup differences were evaluated for categorical variables using Pearson's chi-square or Fisher's exact test and Student's t-test for continuous variables. Statistical significance was defined as a p-value less than or equal to 0.05.

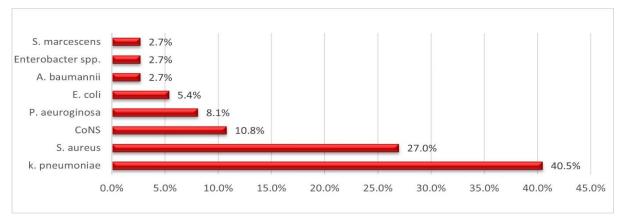
# **RESULTS**

This study included 100 neonates, with ages ranging from four to twenty-eight days (mean  $\pm$  standard deviation:  $12.07 \pm 5.74$  days). Males comprised 61% of the enrolled neonates. Of the 100 neonates, 60% born with birth weight ( $\geq 1500 \, \mathrm{gm}$ , <  $2500 \, \mathrm{gm}$ ), 15% had birth weight ( $\geq 1000 \, \mathrm{gm}$ , <  $1500 \, \mathrm{gm}$ ), and 75% were preterm (at or before 37 weeks). The most common risk factor for sepsis were surgical operations (47%), followed by insertion of central venous catheters (CVC) (34%), premature rupture of membranes (PROM) (11%) and chorioamnionitis (8%).

In the present study, 37% of the included neonates had confirmed LONS by positive results of blood culture. Among confirmed cases, Gram-negative bacteria represented many isolates (62.2%) with predominance of *K. pneumoniae* isolates (40.5%). While Gram-positive bacteria were isolated from 37.8% of which *S. aureus* was 27% as illustrated in table 2 and figure 1.

**Table 2: Results of neonatal blood culture:** 

THOSE IN THE SELECTION OF THE OTHER STOCKS CHILDREN		
Results of neonatal blood	No. of neonates	
culture	(n= 100)	
Culture-negative sepsis	63 (63%)	
Culture-positive sepsis	37(37%)	
Gram Negative	23(62.2%)	
Gram Positive	14(37.8%)	



**Fig. 1:** Bacterial outcome of LONS confirmed cases in the present study. *Klebsiella pneumoniae (K. pneumoniae)*, *Pseudomonas aeuroginosa (P. aeuroginosa)*, *Escherichia coli (E. coli)*, *Acinetobacter baumannii (A. baumannii)*, *Serratia marcescens (S. marcescens)*, *Staphylococcus aureus (S. aureus)*, Coagulase-negative *Staphylococci* (CoNS).

The current study revealed significant differences between the culture-positive sepsis group and the culture-negative sepsis group with regard to birth weight, gestational age, and sepsis risk factors. Additionally, a male predominance was observed in the culture-positive sepsis group, as shown in table 3.

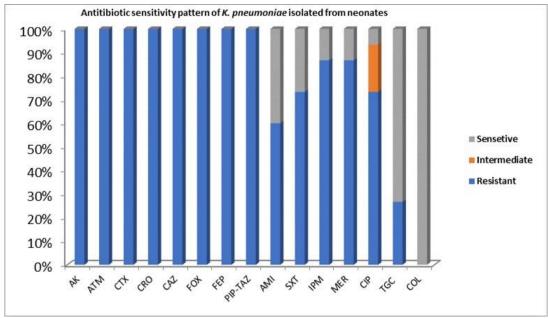
Table 3: Correlation between neonatal demographic characteristics and blood culture results:

Characteristics	Culture -negative sepsis N=63	Culture-positive sepsis N=37	P- Value
Gender			
Male	38 (60.3%)	23(62.2%)	0.855
Female	25(39.7%)	14(37.8%)	
Age (days)			0.282
Range	4–28	5–28	
Mean $\pm$ S. D	11.6±5.7	12.86±5.7	
Birth weight			0.032*
VLBW	5(7.9%)	10(27%)	
LBW	40(63.5%)	20(54.1%)	
Normal	18(28.6%)	7(18.9%)	
Gestational age			0.042*
Preterm	43(68.3%)	32(86.5%)	
Full term	20(31.7%)	5(13.5%)	
Risk factors for sepsis			0.035*
Post-surgical	23(36.5%)	24(64.9%)	
Chorioamnionitis	5(7.9%)	3(8.1%)	
Insertion of CVC	27(42.9%)	7(18.9%)	
PROM	8(12.7%)	3(8.1%)	

Standard deviation (SD), very low birth weight (VLBW), low birth weight (LBW), central venous catheter (CVC), premature rupture of membranes (PROM)

Regarding antibiotic susceptibility of neonatal *K. pneumoniae* isolates, resistance to beta-lactam drugs and beta-lactam/beta-lactam inhibitor combinations ranged from 60% to 100%. However, resistance to amikacin, ciprofloxacin, and co-trimoxazole was

observed in 100%, 73.3%, and 73.3% of isolates, respectively. Notably, colistin (0%) and tigecycline (26.5%) demonstrated the highest efficacy against these isolates, as illustrated in figure 2.



**Fig. 2:** Antibiotic sensitivity pattern of *K. pneumoniae* isolated from neonates. Aztreonam (ATM), Amikacin (AK), Amoxicillin-clavulanic acid (AMC), Ceftazidime (CAZ), Ceftriaxone (CRO), Cefotaxime (CTX), Cefoxitin (FOX), Ciprofloxacin (CIP), Trimethoprim sulfamethoxazole (SXT), Piperacillin tazobactam (TZP), Cefepime (FEP), Imipenem (IPM), Meropenam (MER), Tigecycline (TGC), colistin (COL).

In this study, using the string test, five out of 15 (33.3%) isolated *K. pneumoniae* strains were identified as hypervirulent K. pneumoniae (hvKp). Regarding antibiotic resistance patterns, over half (53.3%) of the *K. pneumoniae* isolates exhibited multidrug resistance (MDR), while 46.7% were XDR indicating a significant challenge for treatment. Regarding resistance mechanisms, 86.7% were CRKP, and 13.3% were both ESBLs and ampC producers as demonstrated in table 4.

Table 4: Phenotypes, Resistance pattern and Resistance mechanism of isolated *K. pneumoniae* in the study:

Total=15	Phenotype		
	Non hvKp	hvKp	
Number	10	5	
Percentages %	66.7%	33.3%	
	Resistance pattern		
	MDR	XDR	
Number	8	7	
Percentages %	53.3%	46.7%	
	Resistance mechanism		
	ESBL+ampC	CRKP	
Number	2	13	
Percentages %	13.3%	86.7%	

Hypervirulent *K. pneumoniae* (hvKp), Multidrugresistant (MDR), Extensively drug-resistant (XDR), Carbapenems resistant *K. pneumoniae* (CRKP).



**Fig. 3:** Positive string test of a hypervirulent strain shows a viscous string greater than 5 mm in length.

# **DISCUSSION**

Neonates are particularly vulnerable to nosocomial infections, with neonatal sepsis posing a significant threat and ranking as the third leading cause of neonatal mortality globally. *K. pneumoniae*, a Gram-negative bacterium belonging to the *Enterobacteriaceae* family, is frequently implicated as a causative agent of neonatal septicaemia <sup>14</sup>.

This study, which included 100 neonates displaying clinical signs of LONS after three days of life, confirmed LONS in 37% of the participants through positive blood culture results. These findings are consistent with previous research, such as the study

performed by Mohsen *et al.* <sup>15</sup> at Cairo University Hospitals, which reported culture-positive sepsis incidences of 30.15%. However, our findings differ from those reported by El Sabbagh and Abd Elatty<sup>18</sup> who recorded higher rates of LONS (72%). Conversely, Gaballah *et al.* <sup>19</sup>, in a research performed in three main referral hospitals in northern Egypt, reported a lower rate of 19%.

The variation in culture positivity rates across studies is most likely caused by several factors, including high contamination rates in blood cultures drawn from infected neonates due to technical difficulties in sterile venepuncture in small infants. Further contributing to this variation is the ongoing debate surrounding the minimum day of onset for LONS and the lack of consensus on the inclusion of CoNS and fungi in reported results <sup>20</sup>.

While blood culture remains the gold standard for isolating causative pathogens in cases of neonatal sepsis, culture-negative sepsis cases are common. This can be explained by factors such as low bacterial load due to prior antibiotic use, inadequate sampling, suboptimal transport conditions, or the presence of slow-growing or fastidious bacteria. Additionally, some cases of sepsis may be caused by fungi or viruses <sup>15</sup>. Maternal antibiotic treatment before or during delivery can also mask the detection of bacteraemia in neonates <sup>18</sup>.

The present study highlighted the dominance of Gram-negative bacteria, particularly *K. pneumoniae* (40.5%), among confirmed LONS cases, followed by *P. aeruginosa*. These findings are in line with a previous study conducted by Awad *et al.*<sup>21</sup>, which reported that Gram-negative bacteria represented 47.4% of total isolates.

Consistent with our findings, Elkady *et al.*<sup>22</sup> reported *K. pneumoniae* as the most prevalent isolate from neonatal sepsis cases, with isolation rates of 32.6%. In contrast, Pataskar *et al.* <sup>23</sup> found that *E. coli* was the most prevalent pathogen (29%), followed by *K. pneumoniae* (19%) among septic neonates. The predominance of Gram-negative organisms as may be attributed to antibiotic misuse, inadequate hygiene practices during delivery, and new-born handling <sup>21</sup>.

While our findings aligned with previous studies in identifying *K. pneumoniae* as a significant pathogen in neonatal sepsis, the prevalence of Gram-positive bacteria in our study (37.8%) deviates from that reported by G/eyesus *et al.* <sup>24</sup> which reported a rates of 67.5%. Similarly, *S. aureus*, which accounted for 27% of our isolates, was reported as the most common isolate in a study done by Zhou *et al.* <sup>25</sup> (64.1%). In contrast, CoNS was the predominant isolate in study conducted by Herbozo *et al.* <sup>26</sup>.

The high prevalence of *K. pneumoniae* suggests a potential common source of infection, possibly within the hospital setting. It's important to know that the

causative organisms in neonatal sepsis can vary significantly across geographical locations and even within the same hospital over time <sup>27</sup>. This emphasizes the need for careful consideration when extrapolating data to other settings. The specific pattern of causative organisms can be influenced by the patient's underlying condition, infection site, hospital antimicrobial protocols, and resistance patterns <sup>28</sup>.

Our study revealed a male predominance (62.2%) among culture-positive septic neonates, a finding consistent with a study conducted by Mohsen *et al.* <sup>15</sup>. However, Gaballah *et al.* <sup>19</sup> reported a higher proportion of females (61.5%) in their LONS cases. This difference in findings may be explained by the potential influence of sex-linked factors, such as the regulation of gamma globulin synthesis, which is believed to be located on the X chromosome, leading to a weaker immune response in males <sup>17</sup>.

In this work, the mean body weight was lower in neonates with culture-positive sepsis, with 54.1% exhibiting LBW and 27% exhibiting VLBW. These results aligned with previous studies concluded that LBW is a significant risk factor for neonatal sepsis <sup>27,30</sup>. However, Mezgebu *et al.* <sup>29</sup> revealed that 73.6% of septic neonates had normal birth weights. This variation may be attributed to factors such as an immature and fragile cutaneous barrier in preterm infants, as well as prolonged hospital stays, which increase exposure to the NICU environment, including invasive devices and procedure <sup>30.</sup>

Regarding gestational age, our study showed that 86.5 % of culture-positive septic neonates were preterm, consistent with a study done by Stylianou-Riga *et al.* <sup>30</sup>. On the contrary, Mezgebu *et al.* <sup>29</sup> found that sepsis was common in full-term babies. The increased susceptibility of preterm infants to sepsis can be attributed to compromised innate immunity, including impaired cytokine production, reduced expression of adhesion molecules, and decreased response to chemotactic factors. Additionally, transplacental passage of antibodies reaches its peak during the third trimester, resulting in significantly reduced humoral responses in most preterm infants <sup>31</sup>.

In the present study, 48.7% of the recruited neonates had a history of surgical operations. This percentage was lower than the 73.75% reported by Shwetal Bhatt *et al.* <sup>32</sup> but higher than the 6.9% reported by Kessler *et al.* <sup>33</sup>. The discrepancies in these findings may be explained by the presence of well-developed surgical setups in the previous study, leading to a lower sepsis rate. Nonetheless, precise and well-organized strategies are crucial for preventing postoperative sepsis <sup>34</sup>.

Four cases (10.8%) with a history of PROM were identified among culture-positive septic neonates in our study. However, El Sabbagh and Abd Elatty <sup>18</sup> reported higher incidences of PROM (45%). The higher incidence in their studies could be attributed to factors

such as low socioeconomic status and limited access to antenatal care

In the current study and according to string test, five strains out of 15 isolated *K. pneumoniae* (33.3%) were hvKp. These results were consistent with that of Mukherjee *et al.*<sup>4</sup> who reported hvKp strain proportions of 26%. However, other study by Ghonaim *et al.* <sup>16</sup> reported higher rates of hvKp strains. Conversely, Cubero *et al.* <sup>35</sup> reported lower proportions of hvKp strain, at 5.4%. The variation in hvKp strains prevalence may be attributed to geographical, demographic, and methodological differences in defining hvKp strains <sup>4</sup>.

Concerning antibiotic susceptibility of *K. pneumoniae* isolated from neonatal samples. Resistance to beta lactam drugs and beta lactam/beta lactam inhibitor combinations ranged from 60% to 100%. Resistance to amikacin, ciprofloxacin and cotrimoxazole were detected in 100%, 73.3% and 73.3% of isolates respectively. Colistin and tigecycline demonstrated the highest efficacy. These results aligned with previous studies conducted in Egyptian University Hospitals by Ghonaim *et al.* <sup>16</sup>, Salama *et al.* <sup>17</sup>, Elkady *et al.* <sup>22</sup>, and Attia *et al.* <sup>28</sup>. Globally, high levels of antibiotic resistance have been reported by Pataskar *et al.* <sup>23</sup> in similar study conducted on septic neonates in NICUs.

These high levels of resistance are primarily linked to antibiotics commonly used in empirical treatment and life-threatening conditions. Resistance can even be encountered during the initial stages of treatment <sup>17</sup>. The emergence of resistance is often attributed to antibiotic overuse, driven by factors such as readily available pharmaceuticals, increased self-prescription, and frequent empirical prescriptions by healthcare professionals <sup>36</sup>.

In this study, no resistance to colistin was detected among *K. pneumoniae* isolates. This contradicts the findings of Shawky *et al.* <sup>37</sup> who reported that 13.8% of their *K. pneumoniae* isolates were resistant to colistin.

On the contrary, other studies done by G/eyesus *et al.* <sup>24</sup>; Pokhrel *et al.* <sup>27</sup> reported low levels of resistance among neonatal sepsis isolates.

It is noteworthy that despite the general recommendation against using some antimicrobials, such as ciprofloxacin, colistin, and tigecycline, in the treatment of children and neonates, they were included in this study. This inclusion is justified by certain guidelines that advocate for the empiric use of these antimicrobials in treating severe neonatal conditions caused by MDR bacteria based on culture results <sup>28</sup>.

More than half (53.3%) of *K. pneumoniae* isolates were MDR while 46.7% were XDR. These results matched with those stated by Bhatta and his colleagues<sup>38</sup>, who reported MDR rates of approximately 52.4% among isolated *Klebsiella* species. In addition, more or less similar results obtained by Attia *et al.* <sup>28</sup> who found that 47.8% of *K. pneumoniae* isolates were

XDR, 41.3% were MDR and the remaining 10.9% were sensitive.

On the contrary, Awad *et al.* <sup>21</sup> at Al Azhar University reported higher incidences of MDR *K. pneumoniae*, at 77%. Globally, a study conducted by Pokhrel *et al.* <sup>27</sup> reported that MDR *K. pneumoniae* isolates constituted 69% of neonatal sepsis episodes. In contrast, Gaballah *et al.* <sup>19</sup> reported a lower XDR isolate rate of 5%.

Regarding resistance mechanism, 86.7% were CRKP, 13.3% were ESBL+ampC producers. These results aligned with those reported by Hassuna *et al.* <sup>6</sup> and Kindu *et al.* <sup>38</sup> reported higher rates of CRKP (70.5% and 95% respectively) among their sepsisdiagnosed neonates. However, Pataskar *et al.* <sup>23</sup> reported higher levels of ESBL producers (74.4%) among *K. pneumoniae* isolates from septic neonates. However, Odoyo *et al.* <sup>39</sup> found that only 22.7% of their isolates were resistant to meropenem.

# CONCLUSION

Our findings emphasize the critical need for a comprehensive approach to combatting *K. pneumoniae* infections in NICUs. This includes robust infection control measures, strict adherence to antimicrobial stewardship guidelines, and judicious use of antibiotics to mitigate the growing threat of antibiotic resistance and hypervirulence.

## **Declarations:**

Consent for publication: Not applicable

Availability of data and material: Data are available upon request.

**Competing interests:** The author(s) declare no potential conflicts of interest with respect to the research, authorship and/or publication of this article. This manuscript has not been previously published and is not under consideration in another journal.

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