



## FREQUENCY OF ISOLATION ANTIBIOTIC SENSITIVITY AND RESISTANCE PATTERN OF PATHOGENIC MICROORGANISMS IN NEONATAL SEPSIS

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### ABSTRACT

**Background:** The leading cause of infant death and disability, particularly in nations with poor or medium incomes, is neonatal sepsis. The management of newborn sepsis relies on constant surveillance of infections and the development of drug resistance. The purpose of this research was to identify bacterial causes of newborn sepsis, trends in antibiotic resistance, risk factors, and outcomes for patients.

**Methods:** This cross-sectional study was conducted in different hospitals of Peshawar, Kuwait Teaching Hospital, Khyber Teaching Hospital (KTH), Hayatabad Medical Complex (HMC) Lady Reading Hospital (LRH). Total 118 neonates were presented in this study. Approximately 2 milliliters of blood were collected in an aseptic manner and then added to the patient's Tryptone Soya Broth while they rested. We used normal microbiological procedures to identify the bacteria. To find out how each bacterium was sensitive to antibiotics, we employed the disc diffusion technique. SPSS 22.0 was used to analyze all data.

**Results:** There were 67 (56.8%) males and 51 (43.2%) females among all neonates. Frequency of preterm births were 31 (26.3%). Mean weight of the neonates was  $3.11 \pm 5.13$  kg. Most common cause of neonatal sepsis was Klebsiella sp, E. coli and Coagulase negative Staphylococci. The drugs that worked best against both gram-negative and gram-positive bacteria were ciprofloxacin and amikacin. A staggering 82% of the bacterial isolates tested showed signs of multidrug resistance.

**Conclusion:** Among the microorganisms that were often identified in our investigation were Klebsiella spp. and E. coli. Quite a few of the patients showed signs of being resistant to more than one treatment. The need for ongoing assessment of antibiotic resistance rate is highlighted by the fact that the majority of the bacteria that were identified were resistant to ampicillin, ceftazidime, cefotaxime, and gentamycin.

**Keywords:** Neonatal Sepsis, Klebsiella spp., E. coli, ciprofloxacin, amikacin, multidrug resistance

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## **INTRODUCTION**

Newborns are susceptible to neonatal sepsis, a clinical condition that manifests as systemic symptoms of infection and the capacity to extract a pathogenic bacterium from the bloodstream, during the initial 28 days of life [1,2]. Neonatal sepsis can develop in either the early or late stages during the first 72 hours following birth [3]. Early onset infections can be caused by germs in the mother's genital canal that spread vertically after vaginal delivery or by contaminated amniotic fluid [4,5]. The bacteria that cause late-onset sepsis can be found in the clinical setting, in the community, or transmitted vertically from a newborn who contracted the illness during the first round of colonization [5]. Bacteria transmitted from the mother or the hospital during delivery are the primary cause of late-onset sepsis (LOS), which manifests itself after three days of life [6]. Bacterial infections contracted in the community or while hospitalised are common causes. Intravenous catheterization is one such example. In the majority of instances, these risk factors may be avoided with early detection and proper treatment [7]. The leading causes of this condition are often found in the human body and include *Staphylococcus aureus*, *Escherichia coli*, *Klebsiella pneumoniae*, and *CONS* [8]. Nevertheless, there are regional and national differences in the incidence of germs that cause infant sepsis [9]. It is estimated that between 400,000 and 700,000 babies die each year from neonatal sepsis, making it the leading cause of sickness and death in the first four weeks of life on a global scale. Nearly 42% of infant deaths occurred within the first week of life [10].

Additionally, it ranks as the third leading cause of infant death [10]. Among underdeveloped nations, sepsis accounts for approximately half of all newborn fatalities; Sub-Saharan Africa has the highest neonatal mortality rate, at 27 per 1000 live births [8-10]. In order to improve the prognosis of newborns with sepsis, antibiotic therapy must be started as soon as possible. Hence, it is common practice to initiate therapy prior to receiving the findings of the blood culture [11,12]. Due to the limited sensitivity of the blood culture approach, the lengthy time it takes to receive results, and the difficulty in collecting enough blood samples for culture, many doctors also choose for empirical therapy for assumed newborn sepsis [13]. The World Health Organisation has published guidelines for the management of suspected

neonatal infections. The first line of treatment is empirical treatment with ampicillin combined with gentamicin. If the patient does not respond to this or if drug-susceptibility testing of bacterial isolates shows resistance to first-line therapy, the second line of therapy is a third-generation cephalosporin. Initial empirical treatment for early onset sepsis (EOS) should consist of ampicillin and gentamicin, according to some writers [14]. Various writers have offered conflicting advice about the empirical management of late onset sepsis (LOS).

For nosocomial LOS, there is ampicillin-gentamicin, and for EOS and LOS, there is piperacillin-tazobactam. Combining vancomycin with gentamicin is another possibility. However, there are times when empirical therapy isn't the way to go. For instance, drug-resistant bacteria and other germs are on the rise due to factors including patients' lengthy treatment durations and the usage of broad-spectrum antibiotics [14,15]. Neonatal sepsis's microbial aetiology and antibiotic susceptibility pattern are dynamic and geographically dependent. Neonatal sepsis pathogens are becoming more resistant to the empirical antimicrobial drugs that are regularly utilised.[9] Treatment may have become more challenging as a result of the prolonged and needless use of these antibiotics.[9] So, it's important to check the local causes of newborn sepsis and how each neonatal hospital reacts to antibiotics on a regular basis. This will help determine what empirical medicines to employ as a first line of defence before a definitive diagnosis is made.

## **MATERIALS AND METHODS**

This cross-sectional study was conducted in different hospitals of Peshawar, Kuwait Teaching Hospital,

Khyber Teaching Hospital (KTH), Hayatabad Medical Complex (HMC) Lady Reading Hospital (LRH) and comprised of 118 neonatal sepsis. Babies (those less than 28 days) hospitalised to the neonatal unit with signs of sepsis, such as difficulty breathing, fever, lethargy, and unwillingness to eat, were the subjects of this investigation. Babies born in or out of hospitals but showing severe sepsis symptoms were included in the research. This study did not include neonates whose antibiotic use occurred during the two weeks prior to data collection. The rationale behind this was to reduce the occurrence of false negative blood cultures,

which can occur when antibiotics are not effective in killing all bacteria but do reduce their population. We also did not interview any neonates whose parents or legal guardians were unable to do so. A peripheral vein was used to extract two millilitres of blood using the aseptic procedure. Written informed consent was obtained from the parents or legal guardians beforehand. A solution of 70 percent isopropyl alcohol & 2% tincture iodine was used to clean the region of the vein puncture prior to collection. After being left at room temperature for 5 to 10 minutes, the contaminated blood samples were promptly moved from the collecting location to the microbiological lab. Soy broth was prepared using Tryptone. The collection of blood samples was the first step in starting antibiotic treatment.

In accordance with the standards established by the Clinical and Laboratory Standards Institute, we assessed the antibiotic susceptibility of each bacterial isolate on Muller Hinton agar using the disc diffusion technique. We used descriptive statistics, including percentages and frequencies, to characterize the number of bacterial isolates and associated risk factors of newborn sepsis. SPSS 22.0 was employed for data analysis.

## RESULTS

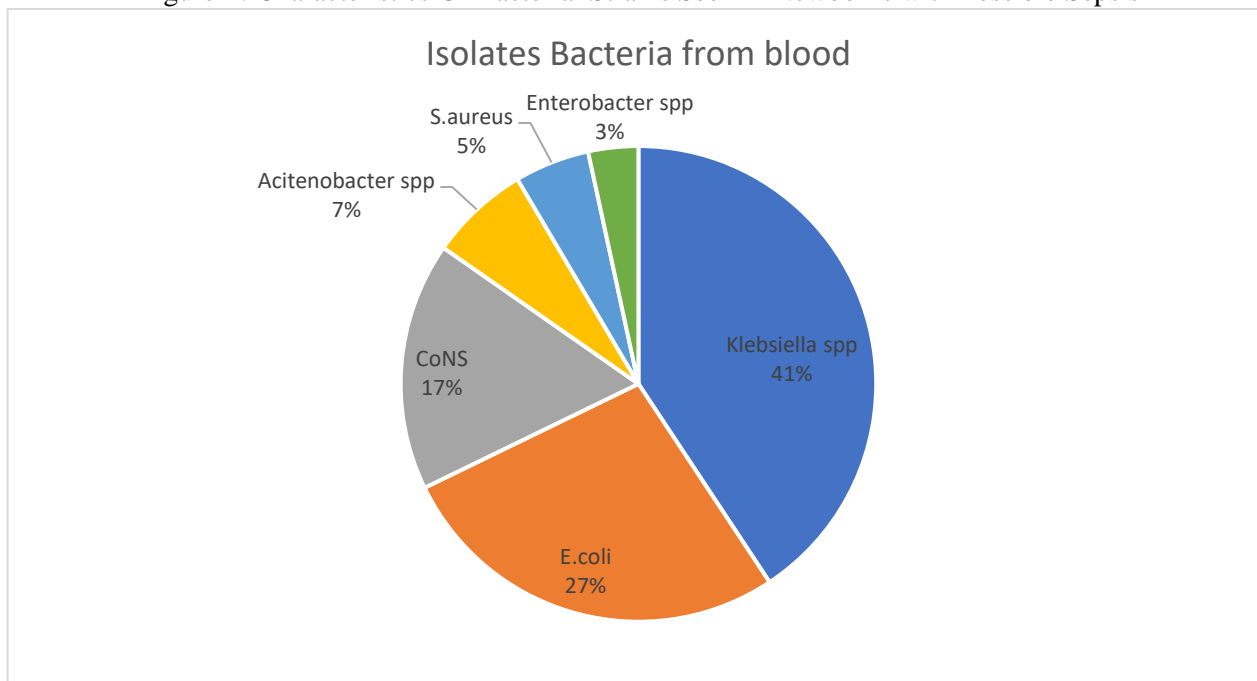
There were 67 (56.8%) males and 51 (43.2%) females among all neonates. Frequency of preterm births were 31 (26.3%). Mean weight of the neonates was  $3.11 \pm 5.13$  kg. Mean gestational age was  $36.4 \pm 8.25$  weeks. We found birth asphyxia in 10 (8.5%) cases. Vaginal delivery was the most common mode found in 95 (80.5%) cases. (table 1)

**Table-1: Baseline Details of The Included Neonates**

Variables	Frequency (118)	Percentage
<b>Neonates gender</b>		
Male	67	56.8
Female	51	43.2
<b>Preterm births</b>		
Yes	31	26.3
No	87	73.7
Weight (mean) kg	$3.11 \pm 5.13$	
Gestational age (mean) weeks	$36.4 \pm 8.25$	
<b>Asphyxia</b>		
Yes	10	8.5
No	108	91.5
<b>Delivery Mode</b>		
C-section	23	19.5
Vaginal	95	80.5

Most common cause of neonatal sepsis was Klebsiella sp, E. coli and Coagulase negative Staphylococci. (figure 1)

Figure-1: Characteristics Of Bacterial Strains Seen in Newborns with Possible Sepsis



The drugs that worked best against both gram-negative and gram-positive bacteria were ciprofloxacin and amikacin. (table 2)

Table-2: Patterns Of Antibiotic Resistance and Prevalence of Microorganisms in Infants Suspected of Having Sepsis

Antibiotics	Klebsiella spp (gram -)	E. coli (gram -)	Acinetobacter (gram -)	CoNS (gram +)
ciprofloxacin	26%	22%	23%	20%
Amikacin	22%	24%	23%	NA
Ampicillin	NA	64%	NA	86%
Gentamycin	15%	55%	56%	70%
SXT	40%	40%	100%	75%
Chloramphenicol	74%	51%	NA	44%
Ceftazidime	85%	99%	85%	60%
Cefotaxime	91%	67%	77%	NA
Cloxacillin	NA	NA	NA	100%

A staggering 82% of the bacterial isolates tested showed signs of multidrug resistance. (table 3)

Table-3: Pattern Of Multidrug Resistance in Bacteria Isolated from Newborns Suspected of Having Sepsis

Isolates Bacteria	Multi Drug Resistance (MDR)
Klebsiella spp	93.4%
Acinetobacter spp	100%
E. coli	78.1%
CoNS	70%

## DISCUSSION

This research aimed to identify the causes of neonatal sepsis and the patterns of antibiotic resistance in newborns admitted to a Pakistani hospital. Pathogens causing newborn sepsis are primarily Gram-positive bacteria, according to the study. Researchers also found that gram-negative

and gram-positive bacteria with multidrug resistance were responsible for a disproportionately high number of cases of newborn sepsis, suggesting serious problems with antibiotic resistance. Among the Gram-positive bacteria that were found to cause newborn sepsis, *S. agalactiae* and CoNS were the most common, accounting for nearly eight out of

ten infections. In addition, several Tanzanian research found that, in cases of newborn sepsis, Gram-positive bacteria were more commonly identified than Gram-negative ones, with *Staphylococcus aureus* being the most frequently isolated pathogen [16]. On the other hand, other research has shown that Gram-negative bacteria, such as *Klebsiella*, *E. coli*, *Pseudomonas*, and *Salmonella*, are the most prevalent culprits in cases of newborn sepsis [17,18]. Our investigation revealed a combination of infections, including those passed down from mothers after birth [19] and those picked up in healthcare settings or the community [6]. These results could be an indication of how poorly obstetric and neonatal care is done.

The most common bacteria found were *Klebsiella* spp. (41%), followed by *E. coli* (27%). However, prior research pointed to *S. aureus* and CoNS as the main culprits responsible for neonatal sepsis [20]. One possible explanation for the greater incidence of *Klebsiella* spp in our study might be that these bacteria are common in hospitals and can cause infections during birth or hospital stays [21,22]. Additionally, contaminated medical equipment and inadequate personal hygiene practices among family members or carers might play a role [23]. Based on our findings, EOS was most commonly caused by *Klebsiella* spp. and *E. coli*, whereas LOS was more commonly caused by CoNS and *S. aureus*. On the other hand, data from Africa suggested that EOS was more commonly caused by *S. aureus* and CoNS [24]. The etiological agents of EOS and LOS might alter over time and across different locations, which could explain these contradictory results [25]. Possible additional causes include vertical transfer from a mother's infected vaginal tract or early horizontal transmission during childbirth [26].

The initial line of defence against newborn sepsis, according to several sources [27,28], should be ampicillin and gentamicin. The vast majority of the bacteria we tested were resistant to ampicillin (68–85%) and gentamicin (75–100%), according to our results. This jibes with earlier research in Ethiopia that found 90–100% bacterial resistance to ampicillin and gentamicin [29]. The same was true in India [30] and Egypt [29], where practically all bacterial isolates were ampicillin-resistant. The overuse of these antibiotics can be contributing to the high resistance rate.

The efficacy of ciprofloxacin and amikacin against *Klebsiella* spp. and *E. coli* was consistent with that of earlier research [31]. This suggests that these two antibiotics may one day be considered as an empirical option for treating newborn sepsis. Compared to a previous research that also examined this setting and showed an 88% rate of MDR [32], our 86% prevalence is somewhat lower. Mothers' nutritional condition, age, or sex did not correlate with infant sepsis in a statistically meaningful way.

## CONCLUSION

Among the microorganisms that were often identified in our investigation were *Klebsiella* spp. and *E. coli*. Quite a few of the patients showed signs of being resistant to more than one treatment. The need for ongoing assessment of antibiotic resistance rate is highlighted by the fact that the majority of the bacteria that were identified were resistant to ampicillin, ceftazidime, cefotaxime, and gentamycin.

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