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# Bioscience Research

Print ISSN: 1811-9506 Online ISSN: 2218-3973

*Journal by Innovative Scientific Information & Services Network*

**RESEARCH ARTICLE** BIOSCIENCE RESEARCH, 2019 16(4):3595-3601. **OPEN ACCESS**

# Screening, identification and susceptibility to antibiotics drugs of clinical bacterial infections in neonatal incubators

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This study is concerned with determining the percentage of neonatal infections according to age and sex, and identifying the bacteria involved, and then estimating the impact of different antibiotic disks on isolated in bacteria blood and ETA samples. This study included blood and ETA samples obtained from 196 neonatal patients in neonatal incubators. Different antibiotic disks selected from having different mode of action were used. Our findings demonstrated that the highest prevalence rate of MDR bacteria was detected in *K. pneumonia*e was found to have the highest detection rate of 40.26% (n=31) followed by CONS 25.96% (n=20), *Ps. aeruginosa* 15.58% (n=12), *Acinetobacter*9.1% (n=7), *Enterobacter* 2.6% (n=2), *S. aureus* 3.4% (n=2),*E. coli* 2.6% (n=2) andMRSA 1.3% (n=1). The results showed variable effects of various antibiotics on isolated bacteria.

**Keywords: bacteria, *K. pneumoniae*, CONS, *Ps. aeruginosa*, Antibiotic.**

## INTRODUCTION

Bacterial infections are one of the most important current threats to public health. Typically, bacteria are associated with NIs, Some bacteria have become quite prevalent causes of community-acquired infections (Matta et al., 2018)). The agents that are usually involved in NIs include *Streptococcus* spp*., Acinetobacter*spp*., enterococci, Ps. aeruginosa,* CONS*, S. aureus, B. cereus, Legionella and Enterobacteriaceae*family members including *Proteus mirablis, K. pneumoniae, E. coli, Serratiamarcescens*. Out of these enterococci, *Ps. aeruginosa, S. aureus* and *E. coli* have a major role (Gulati and Chakraborty, 2019). However, some bacteria have become quite prevalent causes of community-acquired infections. The spread of bacteria into the community is a crucial development, and is associated with increased morbidity, mortality, healthcare costs and antibiotic use. Neonates are more at risk for bacterial sepsis, with a global prevalence of 1 to 10 per 1000 live births, Sepsis problem is much higher in the developing than in the developed countries, with sepsis-related mortality rate as high as 50% for untreated newborns (Goldstein et al., 2005). Neonatal sepsis is a clinical syndrome in an infant 28 days of life or younger, manifesting with a diversity of non-specific systemic signs and symptoms and isolation of a pathogen from the bloodstream (Edwards and Baker, 2004).

Pathogens encountered in neonatal sepsis vary worldwide; reports from developing countries more commonly show Gram negative organisms(Tallur, (2000) and Karunasekera et al., (1999)), although Gram positive organisms have

been also reported by (Malik, 1994). In recent years, a great deal of progress has been made in the management of bacterial infection by using natural or chemical substances that may have antibacterial activity (Taylor, 2013). Therefore, in this current study, investigators aimed to examine the microbiological patterns of early and late neonatal sepsis and to specify their antibiotic susceptibility.

## MATERIALS AND METHODS

Blood and ETA samples were obtained from 196 neonatal patient from the neonatal incubators. Informed consents were obtained from all participants and they were fully informed the diagnostic procedures involved and disease nature. The study protocol conformed to ethical guide-lines of 1975 Helsinki Declaration. Blood and ETA samples were prepared for microbiological studies in order to identify MDR bacteria infection in neonatal incubators. Nutrient and MacCkonkey, blood and choclate agar were used for culturing Blood and ETA samples. Finally, the isolated bacteria were morphologically and biochemically identified and kept for subsequent analysis for assessing the influence of different antibiotics disks (OXOID, England) on them according to agar disk-diffusion method.

## STATISTICAL ANALYSES

Every single measurable investigation were performed by Statistical Package for the Social Sciences (SPSS) programming adaptation 15.0 (SPSS Inc., Chicago, IL) and GraphPad Prism bundle; V. 5.0 (GraphPad Software, San Diego, CA).

## RESULTS

First of all, this work aimed to identify multi resistant bacteria in neonatal incubators and estimating their prevalence rates in blood and ETA samples. These samples were further classified into positive and negative groups as shown in Figure. 1. Our results showed that 59 out of 156 blood samples were tested positive whereas 97 out of those were tested negative for the presence of bacteria. In addition, 18 out of 40 of ETA samples were tested positive whereas 22 out of those were tested negative for the presence of bacteria. Overall, 77 out of 196 samples (42.2%) samples were tested positive for the presence of bacteria.

Our results showed that 32 out of 59 blood samples were males whereas 27 out of those were females. In addition, 10 out of 18 of ETA samples were males whereas 8 out of those were females. Additionally, 17 out of 59 were death for blood samples. 3 out of 18 were death for ETA samples. Figure 2.

Fifty nine and eighteen Blood and ETA samples were collected from different ages ranging from<28 - >36 weeks,<28weeks in blood and ETA samples were 4 and 1 respectively, >28-32 weeks were 18 and 3 respectively, >32- 36 weeks were 12 and 4 respectively and >36 weeks were 25 and 10, respectively. Table 1.

**Table 1; Relationship between blood and ETA cultures according to age of neonatal cases.**

| Age | Blood culture (n = 59) | ETA culture (n = 18) |
|---|---|---|
| **<28weeks** | 4(6.78%) | 1(5.56%) |
| **>28-32 weeks** | 18(30.51%) | 3(16.67%) |
| **>32- 36 weeks** | 12(20.34%) | 4(22.2%) |
| **>36 weeks** | 25(42.37%) | 10(55.57%) |

Interestingly, The most frequently isolated organisms in blood and ETA cultures were *K. pneumoniae* 22and 9 respectively with total 31, CONS 18 and 2 respectively with total 20, *Ps. aeruginosa*9 and 3 respectively with total 12, *Acinetobacter*4 and 3 respectively with total 7, *Enterobacter* 1 and 1 respectively with total 2, *S. aureus* 2 and 0 respectively with total 2, *E. coli* 2 and 0 respectively with total2andMRSA 1 and 0 respectively with total 1, as depicted in Table 2.

**Table 2 ; Isolated bacteria in blood and ETA cultures of neonates**

| Isolated bacteria | Blood culture (n=59) | ETA culture (n=18) | Total (n=77) |
|---|---|---|---|
| ***K. pneumoniae*** | 22 (37.3%) | 9 (50%) | 31 (40.26%) |
| ***Ps. aeruginosa*** | 9 (15.2%) | 3 (16.7%) | 12 (15.58%) |
| **CONS** | 18 (30.5%) | 2 (11.1%) | 20 (25.96%) |
| ***Acinetobacter*** | 4 (6.8%) | 3(16.7%) | 7 (9.1%) |
| ***Enterobacter*** | 1 (1.7%) | 1 (5.5%) | 2 (2. 6%) |
| ***S. aureus*** | 2 (3.4%) | 0 (0%) | 2 (2. 6%) |
| ***E. coli*** | 2 (3.4%) | 0 (0%) | 2 (2. 6%) |
| **MRSA** | 1(1.7%) | 0 (0%) | 1 (1.3%) |

Our results showed that Gram negative bacilli (*K. pneumoniae*, *Ps. aeruginosa,Acinetobacter*, *Enterobacter* and *E. Coli*) have highest resistance to ceftriaxone (CRO) 48, norfloxacine (NOR) 54 and gentamycin (GEN) 46. Less resistance was evident to amikacin (AK) 28, as well as merupenm (MEM) 25, and ciprofloxacin (CIP) 22. Gram positive cocci (*S. Aureus,* MRSA and CONS*)* showed highest resistance to NOR (22), CRO (12). Less resistance was evident to MEM (8), AK (6), GEN (11), CIP (9), as depicted in Table 3.

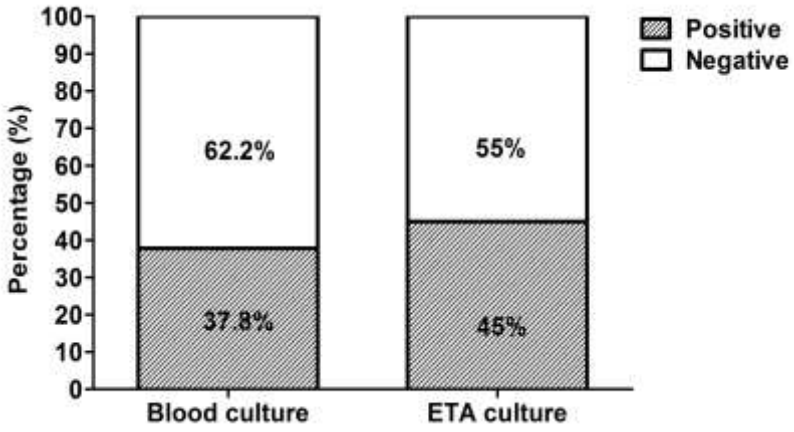


**Figure 1; Percentage of isolated bacteria.**

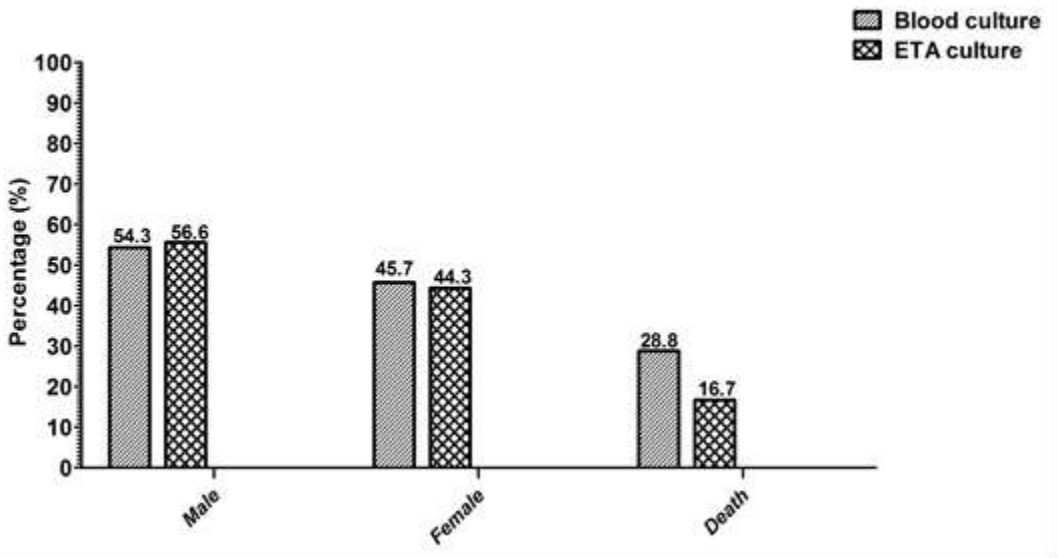


**Figure 2 ; Relationship between blood and ETA cultures according to sex of neonatal cases.**

| Organism (number) | MEM (10mg) | AK (30 mg) | PB (300mg) | CIP (5mg) | NOR (10mg) | GEN (10mg) | CRO (30mg) |
|---|---|---|---|---|---|---|---|
| ***K. pneumoniae*(n=31)** | 20(64%) | 23(74%) | 10 (32.2%) | 11 (35.5%) | 31(100%) | 31(100%) | 31(100%) |
| ***P. aeruginosa* (n=12)** | 5(41.6%) | 3(25%) | 4(33.3%) | 6(50%) | 12(100%) | 12(100%) | 12(100%) |
| ***Acinetobacter* (n=7)** | 0 | 2(28.5%) | 0 | 3(42.8%) | 7(100%) | 1(14.2%) | 2(28.5%) |
| ***Enterobacter* (n=2)** | 0 | 0 | 0 | 1(50%) | 2(100%) | 1(50%) | 1(50%) |
| ***E. coli* (n=2)** | 0 | 0 | 0 | 1(50%) | 2(100%) | 1(50%) | 2(100%) |
| **CONS (n=20)** | 8(40%) | 6(30%) | 7(100%) | 6(30%) | 19(95%) | 9(45%) | 10(50%) |
| ***S. aureus* (n=2)** | 0 | 0 | 1(50%) | 2(100%) | 2(100%) | 1(50%) | 1(50%) |
| **MRSA (n=1)** | 0 | 0 | 0 | 1(100%) | 1(100%) | 1(100%) | 1(100%) |

**Table 3 ; Resistance of isolated bacteria to various antimicrobials by disk diffusion method.**

## DISCUSSION

This study aimed to screening of bacterial infection of neonates admitted to the neonatal incubators and the effect of several antibiotics against them.

In the present study a total of 196 neonates were diagnosed with sepsis based on clinical signs and/or microbiological laboratory. A total of 156 blood cultures were obtained, with 59 (37.8%) positive results. A total endotracheal aspirate samples were 40, of them 18 (45%) were positive. We observed the difference regarding in the distribution of bacterial isolates in relation to sex , 42 ( 54.5%) out of 50 patients were males and 35 ( 45.5 %) patients were females, and Outcome (death) 20 (25.97%).These samples were collected from different ages ranging from<28 - >36 weeks,<28weeks 5(6.5%), >28-32 weeks 21(27.3%), >32- 36 weeks 16(20.8%), >36 weeks 35(45.4%). Also,( Mohsen et al., 2017)), reported that(32.9%) neonates were diagnosed with sepsis. positive male was (56.6%) and positive female (43.4%). About different ages ranging from<28 - >36 weeks,<28weeks (7%), >28-32 weeks (19.4%), >32- 36 weeks (23.9%), >36 weeks (49.7%) and Outcome (death) (22.3%).As well, (Moore et al., 2005)) and Shehab et al., 2015)), showed that these results are comparable to other studies from Egypt. However, (Mohammed et al., 2014)), reported that the results are better than a previous report in 2001 wherein the rate of sepsis exceeded 50% , which may be due to better awareness and adherence to infection control measures. Additionally, (Moore et al., 2005) , Mohammed et al., 2014)), indicated that this value is lower than sepsis related deaths reported in other studies from Egypt. Also our results agreed with that reported by (Mugalu et al., (2006) and Singh et al., 2003 )), showed that sepsis related mortality of 19% was reported in studies from east Africa.

However, (Thaver et al., 2009)), reported that several studies reviewed from different developing countries showed a wide range of infection related neonatal mortality ranging between 8 and 80%.

From our results, the most frequently isolated organisms in blood and ETA cultures were *K. pneumoniae* 22(37.3%) and 9 (50%) respectively with total 31(40.26%), CONS 18 (30.5%) and 2 (11.1%) respectively with total 20(25.96%), *Ps. aeruginosa*9 (15.2%) and 3 (16.7%)respectively with total 12(15.58%),*Acinetobacter* 4 (6.8%) and 3 (16.7%) respectively with total 7(9.1%),*Enterobacter* 1 (1.7%) and 1 (1.7%) respectively with total 2(2. 6%), *S. aureus* 2 (3.4%) and 0 (0%) respectively with total 2(2. 6%), *E. coli* 2 (3.4%) and 0 (0%) respectively with total(2. 6%) andMRSA 1 (1.7%) and 0 (0%) respectively with total 1(1.3%).

Also, ( Mohsen*et al*., 2017)), reported that Gram negative bacilli were more frequently encountered than gram positive cocci, with *Klebsiellapneumoniae* being the most commonly isolated organism both in blood and ETA cultures (42% and 41% respectively). As well, (El Badawy et al., 2005) and Fahmey et al., 2013)), showed that these results were consistent in multiple reports from Egypt over two decades. According to, (Berezin et al., 2014)), who indicated that the

frequency of gram negative pathogens varied from 31% to 63% with *Klebsiellapneumoniae, Pseudomonas aeruginosa* and *Escherichia coli* being the predominant organisms in almost all countries of Latin America. Also, (Movahedian et al., 2006), and Rahman et al., 2002)), reported that several other studies in a diversity of developing countries showed that gram negative bacteria were responsible for most cases of neonatal sepsis. According to (Nambiar et al., 2002)), reported that the others have indicated increasing incidence of gram-negative bacterial infections in NICUs. Additionally, (Mannan et al., 2008)), showed that among gram negative organisms, *Klebsiellapneumoniae* is increasingly emerging as a common bacteria in hospital settings.As well, (Custovic et al., 2014)), *K. pneumoniae*was the most frequently isolated gram-negative pathogen (51% of all positive samples), followed by *Ps. aeruginosa* (10%), *P. mirabilis* (7%) and*E. coli* (4%), respectively; while MRSA was the most common among gram-positive bacteria (15%). However,( Behnke et al., 2013)) showed that *E. coli* was the most common gram negative causing nosocomial infection (18%), follow by MRSA (13.1%). As well, (Stoll et al., 2002)), who indicated that yet case fatalities are highest for gram-negatives. Also our results agreed with that reported byMonegro et al., (2017), who found that *Ps. aeruginosa*was the third most prevalent Gram negative bacillus (9 to 13%). Additionally, (Gallego et al., 2014)) who indicated that *Ps. Aeruginosa* represents one of the more common pathogenic microorganisms associated with respiratory disease. However,(Abd el Haleim et al., 2009) , El Feky et al., 2011) and (Moore et al., 2005), showed *CONS* as the leading cause of sepsis in 2010/2011 and 2011/2012.

Our results disagreed with that reported by (Gilsanz *and Maseda,* (2017), who found that *E. coli* was the most frequently isolated bacteria in nosocomial infection (49.9%). As well, (Hennequin and Forestier, 2007)) who reported that *K. Pneumoniae* caused about 10% of bacterial nosocomial infections.

In this work, isolated bacteria were most resistant to norfloxacine, gentamycin and ceftriaxone. They were less resistant to amikacin, Ciprofloxacin and merupenm. Gram negative organisms were most resistant to cephalosporins, Less resistance was observed to aminoglycosides and carbapenems. Several studies showed high resistance to ampicillin and amoxicillin, aminoglycosides, and different classes of cephalosporins (Hennequin, 2007)and Rahman et al., 2002)), Even within the aminoglycoside spectrum, some authors found amikacin (which was less used in their units) more sensitive than gentamycin (which was more commonly used) (Muhammad et al., 2010)). Two studies in sub-Saharan Africa and Asia revealed resistance of the two common pathogens *Klebsiella* and *Staphylococcus aureus* to almost all commonly used antibiotics in one study and *K. pneumoniae* median resistance to ampicillins and cephalosporins in 94 and 84% of cases in Asia and 100 and 50% in Africa (Le et al., 2014)) in the other study. Although short courses of antimicrobials as carbapenems and cephalosporins especially third generation cover a broad spectrum of bacteria, yet their extended use caused the emergence of extended spectrum β lactamase producing gram negative bacteria. This confers resistance to penicillins and cephalosporins and often coexisting with resistance to other categories of antibiotics as quinolones and aminoglycosides (Patel and Saiman, 2010) and (Isaacs, 2006). In Egypt, gram negative bacteria were resistant to ampicillin, amoxicillin clavulanate and cephalosporins, with highest sensitivity to either or both carbapenems and quinolones (Moore et al., 2005), (Fahmey, 2013) and El Feky, 2011) There is an increasing incidence of multi drug resistant gram positive organisms (Rice, 2009).

## CONCLUSION

This study demonstrated a high prevalence of gram negative bacilli sepsis and tracheal colonization. The highest prevalence rate of NICU was detected in *K. pneumonia*e was found to have the highest detection rate of 40.26%. In addition, Both gram negative bacilli and gram positive cocci were highly resistant to multiple broad-spectrum antimicrobials.

## CONFLICT OF INTEREST

The authors declared that present study was performed in absence of any conflict of interest.

## ACKNOWLEGEMENT

I would like to express my sincere appreciation and grateful thanks to Prof. Dr. Mohamed Farouk Ghaly, Prof. Microbiology, Botany Department, Faculty of Science, Zagazig University for his valuable guidance, supervision, continuous support and encouragement.

I would like to express my deepest thanks and gratitude to Prof. Dr. Abd El-Raheem Ramadan

El-Shanshoury, Prof. Microbiology, Botany Department, Faculty of Science, Tanta University for suggesting the topic research, valuable advice , close supervision, writing and revising the thesis to produce it in such acceptable manner, continuous support, constructive criticism and encouragement.
I would like to express my thanks to Dr. Hisham M. Aldeweik, Microbiology Department, Environmental monitoring, Ministry of health, Egypt for help me in writing and statistics in addition to encouragement.

## AUTHOR CONTRIBUTIONS

This work was carried out in collaboration among all authors. Author MFG designed the study. Author AE wrote the protocol. Author HME performed the statistical analysis. Author TAE wrote the manuscript and managed the analyses of the study. Authors MFG and TAE managed the literature searches. All authors read and approved the final version.



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