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**ORIGINAL ARTICLE**

# Frequency of Multi-Drug Resistant Bacteria in Pediatric and Neonatal Intensive Care Units at Zagazig University Hospital

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## ABSTRACT

**Background:** Multi-Drug Resistance (MDR) is defined as acquired resistance to at least one agent in three or more antimicrobial groups. The impact of multidrug-resistant (MDR) organisms in pediatrics are increasing globally. This study aimed to identify the frequency and clinical impact of Multidrug-resistant bacteria in pediatric and neonatal intensive care units at Zagazig University Hospital.

**Methods:** The present study was a cross-sectional study conducted in pediatric and neonatal intensive care units, pediatric department, Zagazig University children's hospital in the period between January 2019 to July 2019 on 150 cases (males and females) of critically ill infants, and children. Full history, clinical examination, and full laboratory tests were taken such as complete blood count (CBC), and C reactive protein (CRP). Microbiological techniques: cultures were done on samples from different sites that included: blood, urine, and tracheal aspirate. Statistical analysis was done for these data.

**Results:** The most common resistant organisms were Gram-negative bacteria like *Klebsiella* pneumoniae, its resistance rate was (24.3%), followed by Pseudomonas aeruginosa with a resistance rate of 19.5%. Staph epidermidis was the most prevalent Gram-positive bacteria, its rate was (11.3%), and most of these Staph epidermidis organisms were non-multi drug-resistant.

**Conclusions:** The risk factors for acquisition of MDR bacteria in this study were: Mechanical ventilation, prolonged hospital stay, CVC, and excessive use of antibiotics. MDR bacteria resulted in prolonged hospital stays and elevated mortality rates more than non-MDR bacteria.

**Keywords:** Multi-Drug Resistant Bacteria; Neonatal intensive care unit; pediatric intensive care unit.

## INTRODUCTION

Healthcare Associated Infection (HAI) is considered one of the greatest problems in various Pediatric Intensive Care Units (PICUs) around the world; because of increased mortality, morbidity, and costs of hospital admissions. Surveillance of HAI in pediatric and neonatal intensive care units is mandatory to determine the most prevalent pathogens and to setup strategies for proper antibiotic use. It is necessary to know that each unit has its own specific flora [1].Multi-Drug Resistance (MDR) is defined as acquired resistance to at least one agent in three or more antimicrobial groups. Extensive Drug-Resistance (XDR) is resistance to at least one agent in all antimicrobial groups, but bacteria remain sensitive to only one or two categories. Pan Drug-Resistance (PDR) is resistance to all agents in all antimicrobial groups [2].The emergence of antibiotic-resistant pathogenic bacteria possess a serious public health challenge worldwide. However; antibiotic resistance genes are not confined to the clinic, instead, they are widely prevalent in different bacterial populations in the environment. Therefore; to understand the development of antibiotic resistance in pathogens, we need to consider important reservoirs of resistance genes, which may include determinants that confer self-resistance in antibiotic-producing soil bacteria and genes encoding intrinsic resistance mechanisms

present in all or most non-producer environmental bacteria[3]. Resistance in bacteria is produced by one of two mechanisms: First, bacteria could accumulate multiple genes, and each gene is coding for resistance to a single drug in a single cell. Second, MDR may occur as a result of increased expression of genes coding for multidrug efflux pumps causing extrusion of a wide range of drugs [4]. Antibiotic resistance is one of the most common public health problems and challenges. In the U.S.A at least 2 million people acquire antibiotic-resistant infections and 23,000 people die each year. Managing this threat is a major health priority that needs collaborative global approach sectors [5]. MDR has proven to be highly prevalent in different clinical sectors in Egyptian patients, but the resistance mechanisms have been examined in a few studies [6]. Antimicrobial resistance is presented with high rates of mortality and elevated medical costs. MDR holds disease control by increasing the possibility of the spread of resistant pathogens. The cost of treatment is elevated, as the organisms become resistant to drugs that are commonly used leading to sensitivity diversion to more expensive therapies [7].This study aimed to identify the frequency and clinical impact of Multidrug-resistant bacteria in pediatric and neonatal intensive care units in Zagazig University Hospital.

## METHODS

The present study was a cross-sectional study conducted in pediatric and neonatal intensive care units, pediatric department, Zagazig University children hospital in the period between January 2019 to July 2019 on 150 patients who were diagnosed as critically ill infants, and children, a written informed consent was taken from all the patients or their parents before the start of the study. The thesis was accepted by the Faculty of Medicine's ethical review committee at Zagazig University. The work was carried out for human studies in accordance with the World Medical Association's Code of Ethics (Helsinki Declaration). Inclusion criteria included critically ill children and infants in PICU and NICU, whose ages ranged between 3 days to 16 years old and who had a community-acquired infection or hospital-acquired infection. Exclusion criteria: Immuno-deficient and immuno-suppressant patients. Age more than 16 years or less than 3 days. Methods: Each Patient is subjected to complete history taking including personal, hospital stays (date of admission, length of stay, clinical diagnosis, medication), empirical antibiotic administration: (type, duration), and history of blood or fluid culture. Risk factors e.g. mechanical ventilation, catheters, prolonged stay and insertion of the central line were evaluated. Clinical Examination: including weight, height, pulse, temperature, blood pressure, cyanosis, pallor, jaundice, rash, edema, fever or joint examination. Neurological examination was performed: level of consciousness, reflexes, tone, irritability or convulsions. Respiratory examination was performed: tachypnea, chest abnormalities, grunting or apnea.

Cardiovascular examination was performed: tachycardia, bradycardia, murmurs, hypertension, or hypotension. The gastrointestinal examination was performed: distension or organomegaly.

Blood samples were collected for C- reactive protein (CRP), Complete blood count (CBC), and blood cultures. Sputum (or deep tracheal aspirate), urine and Cerebrospinal fluid (CSF) samples were obtained from suspected cases. Samples collection occurred under complete aseptic conditions.

Samples from patients were cultured on a suitable media (e.g. blood agar, nutrient agar (oxoid), Macconkey, Muller-Hinton agar, and pseudo sel agar). Identification of Gram-positive and negative bacteria was done by morphology, Gram stain and biochemical reactions like coagulase, catalase, oxidase, urease, indole, and methyl rod tests.

Pediatric risk of mortality (PRISM III) score on admission was conducted.

The PRISM III score has 17 physiologic variables subdivided into 26 ranges. The variables most predictive of mortality were minimum systolic blood pressure, abnormal pupillary reflexes, and stupor/coma. Other risk factors, including two acute and two chronic diagnoses, and four additional risk factors, were used in the final predictors. The PRISM III score and the additional risk factors were applied to the first 12 hours of stay (PRISM III-12) and the first 24 hours of stay (PRISM III-24). Physiologic variables such as temperature, heart rate, systolic blood pressure, mental status, PH, total CO2, arterial Pa O2, glucose, potassium, creatinine, urea, white blood cells, platelets, PT or PTT were recorded [8].

***Microbiology work-up***

Identification of organisms by Matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF MS):

MALDI-TOF MS: is a diagnostic tool of microbial identification and characterization based on the detection of the mass of the molecules; it is an ionization technique in which a matrix absorbs energy from the ultraviolet laser to create ions from large molecules with minimal fragmentation. [9].

MALDI methodology is a three-step process. First, the sample is mixed with a suitable matrix material and applied to a metal plate. Second, a pulsed laser irradiates the sample, triggering ablation and desorption of the sample and matrix material. Finally, the analyte molecules are ionized by being

protonated or deprotonated in the hot plume of ablated gases, and then they can be accelerated into whichever mass spectrometer is used to analyze them. Detection of bacterial sensitivity by VITEK 2 compact: A sufficient bacterial inoculum size was used to prepare standard suspension fluids for antimicrobial susceptibility profiling with an automated system, e.g. the Vitek 2 system and MicroScan system. The turbidity of the bacterial suspension was adjusted with VITEK Densichek (bio Mérieux) to match the McFarland 0.5 standard in 0.45% sodium chloride. Card no (222, 204, 71) was used for Gram-negative bacilli, and card no (67) was used for Grpositive cocci (Biomerieux. Inc, Durham, USA).

Identification of MDR and non MDR patients:

Patients with positive cultures were classified into two groups group (I), and group (II): Group (I) Patients who had MDR bacteria in PICU and NICU were assumed to (MDR). MDR bacteria is defined as an isolate that is resistant to at least one antibiotic in three or more antibiotic categories. Antibiotics used for checking antimicrobial sensitivity of Gram-positive cocci were:- amoxicillin, penicillin, tetracycline erythromycin, ciprofloxacin, amikacin, vancomycin and linezolid. Antibiotics used for checking antimicrobial sensitivity of Gram-negative bacilli were:-amikacin, ceftazidime, gentamycin, ciprofloxacin, imipenem and colistin [1].

Group (II) patients in PICU and NICU who lacked the diagnostic criteria of MDR bacteria were assumed as (Non MDR).

## STATISTICAL ANALYSIS

Data were checked, entered and analyzed using SPSS version 23 for data processing. Data were summarized using: The arithmetic mean and The standard deviation (SD). The comparison of data was done using: Chi- square test (X2), and Odds ratio (OR). Level of significance: the threshold of significance was fixed at 5% level (P-value). P value of < 0.05 indicates significant results.

## RESULTS

There was no statistically significant difference between patients with MDR and without MDR in studied groups as regard age, sex, need of mechanical ventilation and place of admission. While, there was statistically significant difference as regard infection (most of them were hospital acquired) and outcome (Table 1).

There was statistically significant difference between patients with MDR and without MDR as regard prolonged hospital stay, mechanical ventilation, (CVC) and excessive use of antibiotics. While regarding IV or umbilical catheter, (NGT), urinary catheter and previous operations there was no statistically significant difference (Table 2)

There was statistically significant difference between patients with MDR and without MDR as regard organisms present, where Klebsiella pneumoniae was the commonest organism (24.3%) in MDR patients followed by Pseudomonas aeruginosa (19.5%) then E. coli (14.6%), while Staph epidermidis was the commonest organism (34.5%) in non MDR patients (Table 3).

This study showed that Ninety-five and half percent (95.5%) of Klebsiella pneumoniae organisms were sensitive to colistin, about eighty-six percent (86.3%) were sensitive to tigecycline, fifty percent (50%) were sensitive to ciprofloxacin, and about forty-five percent (45.4%) were sensitive to amikacin (Table 4).

This study showed that One hundred percent (100%) of Staph epidermidis organisms were sensitive to linezolid, (94.1%) were sensitive to vancomycin, (77.8%) were sensitive to gentamycin, and (58.8%) were sensitive to ciprofloxacin and amikin. This study showed (100%) of Staph epidermidis organisms were resistant to ampicillin, penicillin and piperacillin, and (83.3%) were resistant to sulfa – trimethoprim (Table 5).

**Table 1:** Comparison between MDR and non-MDR of the studied group as regard patients characteristics.

| Variables | Non MDR No (68) % | MDR No (82) % | $\chi^2$ | p-value | Odds ratio (CI 95%) |
|---|---|---|---|---|---|
| **Age** | | | | | |
| **3 days-<30 days**<br>**1month-<1year**<br>**1 year- 16 years** | 46 67.6%<br>8 11.8%<br>14 20.6% | 47 57.3%<br>12 14.7%<br>23 28.0% | 1.7 | 0.4 | - |
| **Sex** | | | | | |
| **Male**<br>**Female** | 39 57.4%<br>29 42.9% | 40 48.8%<br>42 51.2% | 0.5 | 0.4 | - |
| **Need for ventilation** | | | | | |

| Variables | Non MDR No (68) % | MDR No (82) % | $\chi^2$ | p-value | Odds ratio (CI 95%) |
|---|---|---|---|---|---|
| **Yes** | 39 57.4% | 57 69.5% | 0.8 | 0.3 | 0.5 (0.2-3.5) |
| **No** | 29 42.9% | 25 30.5% | | | |
| **Type of infection No(129)** | | | | | |
| ***Hospital-acquired*** | 31 (66.0%) | 68 (82.9%) | 4.8 | **0.02*** | 0.3 (1.3-2.7) |
| ***Community-acquired*** | 16 (34.0% | 14 (17.1%) | | | |
| **Place of admission** | | | | | |
| **PICU** | 21 (30.9%) | 35 (42.7%) | 2.2 | 0.1 | 1.6 (0.8-3.2) |
| **NICU** | 47 (69.1%) | 47 (57.3%) | | | |
| **Outcome** | | | | | |
| **Survival** | 58 (58.3%) | 51 (62.2%) | 9.9 | **0.002*** | 3.5 (1.6-3.9) |
| **death** | 10 (14.7%) | 31 (37.8%) | | | |

$\chi^2$: Chi-square test, **CI**: confidence interval. P value < 0.05 is significant.

**Table 3:** Type of organisms in the studied group.

| Variables | Non MDR (47) | | MDR (82) | | $\chi^2$ | p-value |
|---|---|---|---|---|---|---|
| | No | % | No | % | | |
| **Pseudomonas** | 3 | 6.3% | 16 | 19.5% | 59 | **0.001**** |
| **aeruginosa Klebsilla** | 2 | 4.9% | 20 | 24.3% | | |
| **Pneumoniae** | 2 | 4.9% | 12 | 14.6% | | |
| **E. coli** | 6 | 12.8% | 2 | 2.4% | | |
| **Staph haemolyticus** | 6 | 12.8% | 2 | 2.4% | | |
| **Staph hominis** | 16 | 34.5% | 1 | 1.2% | | |
| **Staph epidermidis** | 1 | 2.5% | 2 | 2.4% | | |
| **Staph saprophyticus** | 6 | 12.8% | 7 | 8.5% | | |
| **Staph aureus** | 5 | 10.3% | 2 | 2.4% | | |
| **Enterococcus faecalis** | 0.0 | 0.00% | 2 | 2.4% | | |
| **Strep pneumoniae** | 0.0 | 0.00% | 9 | 10.9% | | |
| **Acintobacter** | 0.0 | 0.00% | 3 | 3.6% | | |
| **Strep pyogenes** | 00 | 0.00% | 2 | 2.4 % | | |
| **Cambylobacter jejuni** | 00 | 0.00% | 2 | 2.4% | | |
| **Staph capitis** | | | | | | |

**Table 4:** The rate and percentage of sensitivity and resistance of the Klebsiella pneumoniae organism to the different antibiotics in the studied group.

| Antibiotics | Frequency of sensitive cases (total 22) | Percent of sensitive cases % | Frequency of resistant cases (total 22) | Percent of resistant cases % |
|---|---|---|---|---|
| **Amikacin** | 10 | 45.4% | 12 | 54.6% |
| **Ciprofloxacin** | 11 | 50.0% | 11 | 50% |
| **Colistin** | 21 | 95.5% | 1 | 4.5 |
| **Moxifloxacin** | 6 | 27.3% | 16 | 72.7 |
| **Tigecycline** | 19 | 86.4% | 3 | 13.6 |
| **Nitrofurantoin** | 3 | 13.6% | 19 | 86.4 |
| **Clindamycin** | 8 | 36.4% | 14 | 63.6 |
| **Tetracyclin** | 9 | 40.9% | 13 | 59.1 |

| Antibiotics | Frequency of sensitive cases (total 22) | Percent of sensitive cases % | Frequency of resistant cases (total 22) | Percent of resistant cases % |
|---|---|---|---|---|
| **Minocyclin** | 4 | 18.2% | 18 | 81.8 |
| **Ceftriaxone** | 4 | 18.2 | 18 | 81.8% |
| **Gentamycin** | 6 | 27.3 | 16 | 72.7% |
| **Imepenem** | 16 | 72.7 | 6 | 27.3% |
| **Nitrofurantoin** | 8 | 36.4 | 14 | 63.6 |
| **Piperacillin** | 0 | 0 | 22 | 100% |
| **Sulfa-Trimetroprim** | 0 | 0 | 22 | 100% |
| **Penicillin** | 0 | 0 | 22 | 100% |

**Table 5**: The rate and percentage of sensitivity and resistance of the Staph epidermidis organism to the different antibiotics in the studied group.

| Antibiotics | Frequency of sensitive cases (total 17) | Percent of sensitive cases % | Frequency of resistant cases (total 17) | Percent of resistant cases % |
|---|---|---|---|---|
| **Amikacin** | 10 | 58.8% | 7 | 41.2 |
| **Vancomycin** | 16 | 94.1% | 1 | 5.9 |
| **Ciprofloxacin** | 10 | 58.8% | 7 | 41.2 |
| **Gentamycin** | 7 | 41.2% | 10 | 58.8 |
| **Levofloxacin** | 10 | 55.6% | 7 | 44.4 |
| **Moxifloxacin** | 5 | 27.8% | 12 | 72.2 |
| **Tigecycline** | 6 | 33.3% | 11 | 66.7 |
| **Linezolid** | 17 | 100% | 0 | 0 |
| **Tetracycline** | 8 | 44.4% | 9 | 55.6 |
| **Sulfa-Trimetroprim** | 2 | 10.5% | 15 | 89.5 |
| **Erthromycin** | 5 | 27.8% | 12 | 72.2 |
| **Ampicillin** | 0 | 0 | 17 | 100 |
| **Penicilin** | 0 | 0 | 17 | 100 |
| **Colistin** | 3 | 22.2 | 14 | 77.8 |
| **Clarithromycin** | 7 | 41.2 | 10 | 58.8 |
| **Piperacillin** | 0 | 0 | 17 | 100 |
| **Meropenem** | 14 | 77.8 | 3 | 22.2 |
| **Ceftriaxone** | 7 | 41.2 | 10 | 58.8 |

## DISCUSSION

The present study was carried out in pediatric and neonatal intensive care units, faculty of medicine Zagazig University Children Hospital on 150 patients admitted to PICU and NICU in a trial to study this impact on our infants and children in our locality. The study showed high rate of MDR bacteria in PICU and NICU, 82 cases from the total 150 patients (54.6%) had acquired infection by multidrug resistant bacteria. The same high rate was found in a study done by Halim et al., [10] which showed that, MDR organisms was observed in 26 cases out of 39 (66.7%), while, non MDR organisms was observed in the remaining 13 cases (33.3%). Also, Gomila et al., [11] observed significant differences in MDR rate occurring between the different participating hospitals, ranging from <20% in some countries such as Hungary and Spain to almost 60% in other countries such as Bulgaria and Greece. The MDR rates by hospital varied in accordance with the country's trend of use of antibiotics.

In the present work we found increased frequency of Gram negative organisms with an increased

resistance rate. The most common organism being Klebsiella pneumoniae with resistance rate (24.3%) followed by Pseudomonas aeroginosa with resistance rate (19.5%) then, E. coli with resistance rate (14.6%).

This is in agreement with Halim et al., [10] who observed in their study on 66 patients that, Gram negative bacteria were the most prevalent pathogens representing 35/66 (53%) while Gram-positive organisms were only 25/66 (37.9%). Also, El-Nawawy et al., [12] revealed increased incidence of resistant organisms in PICUs, but more common was the appearance of MDR Gram negative bacteria. Their incidence were: Klebsiella pneumoniae (30.5%), Acinetobacter baumanii (22.22%), and Pseudomonas (16.67%).

In contrast, Vazhayil et at., [13] showed that, the predominant growth for MDR was from Gram positive organisms (51.92%), of which Staphylococcal aureus and Enterococcus (15.38%) were the commonest isolates followed by Corynebacterium (11.54%) and Streptococcus viridans (9.61%). The present study observed that the most frequent Gram positive organism causing infection in PICU and NICU was Staph epidermidis with rate of (11.3%) of all studied cases. It was more prevalent than staph aureus.

The variations in types of MDR bacteria may be due to differences in location, population demographics, and office police towards pharmaceutical representatives and sampling.

We found that coagulase negative Staphylococci (CONS) were a major cause of laboratory confirmed nosocomial blood stream infection, also it was implicated in device related infections, pneumonia and surgical wound infections. Staph epidermidis that was isolated from several blood (14 cases) and urine culture (3 cases) was the most prevalent CONS in critically ill children and infants. This in agreement with Becker et al., [14] who reviewed that *Staph epidermidis* was the most frequently recovered Staphylococcal species in their study. This bacterium colonizes the body surface, where it is particularly prevalent on moist areas, such as the axillae, inguinal and perineal areas, anterior nares, conjunctiva, and toe webs. On the contrary, Hassan et al., [15] observed that the most frequent Gram positive organism associated with health care infection was staphylococcus aureus with rate of (37%) from all Gram-positive organisms. Results of the present study showed that risk factors of MDR bacteria were significantly: prolonged hospital stay, excessive antibiotic usage, CVC and mechanical ventilation. This goes with Hassan et al., [15] who stated that, risk factors which were significantly associated with HAI in their study were; mechanical ventilation, invasive device utilization, neonatal age, neutropenia, ICU residence and hospital stay more than 7 days. Also multiple antibiotics usage, beta lactam usage, and ICU residence. Also, Cornejo et al., [16] reported that the risk of infection with MDR bacteria has been related to a number of factors, including previous antimicrobial therapy, cross-transmission, and length of hospital stay.

In contrast, Tfifha et al., [17] stated that, risk factors such as invasive procedure, antibiotics intake, length of hospital stay did not show any significant correlation with carriage of MDR.

In comparison between MDR bacteria and non MDR in the present study there was no statistically significant difference between patients with MDR and those without MDR as regard age, sex, place of admission and need for ventilation.

This is in agreement with Choudhuri et al., [18] in whose study there was no difference between the MDR and non-MDR groups with respect to age, sex, clinical diagnosis, cause of ICU admission, need for mechanical ventilation and/or invasive monitoring, and the length of ICU stay.

Another study done by Giuffrè et al., [19] showed that results of analysis of the variables associated with being colonized, simultaneously or subsequently by multiple genera/species of MDR Gram negative bacteria were: Low birth weight/gestational age, exposure to some invasive procedures and antibiotic therapy. Days of breast- and formula feeding proved also to be significantly associated with multiple colonization. The only independent risk factor by the logistic regression was the number of days of formula feeding. Thirty-three out of 42 (78.6%) of multi-colonized infants yielded *Enterobacter* species versus 146 out of 332 (44.0%) who were mon-colonized. In the present study there was statistically significant difference between patients with MDR and those without MDR in type of acquired infection where most of MDR infections were hospital acquired.

This is in parallel with Murni et al., [20] who reviewed that one hundred and seventy-four microbiological isolates in the PICU and pediatric wards were cultured from blood samples of 170 patients with clinical features of nosocomial bloodstream infection. Bacteria were identified in 168 cases. Patients with nosocomial blood stream infections were resistant to selected antibiotics.

The enhanced complexity of the patient, with a consequent increase in the duration of the hospital stay and greater need for intravascular devices, has increased the risks for HAIs [21].

On the other hand, Ben Ayed et al., [22] concluded that the problem of MDR is no longer limited to hospital-acquired or health care–associated infections, since MDR strains have been reported as important and increasing strains that can spread

the resistance among different populations of bacteria. The present study found that the most common Gram negative organism (Klebsiella. pneumoniae) was mostly resistant to penicillin, piperacillin and sulfa-trimethoprim with resistance rate (100%) and cefotriaxone with resistance rate (81.8%). This is in agreement with Khaertynov et al., [23] who observed that, all *Klebsiella pneumoniae* isolates were resistant to ampicillin, and six of them being resistant to all amino-penicillins (including protected ones), gentamycin and third-generation cephalosporins.

Also, Ben Ayed et al., [22] reviewed similar antibiotic sensitivity, MDR Gram negative isolates showed high resistance to ampicillin-sulbactam (98.8%), cefotaxime (94.2%), amoxicillin-clavulanic (93%) and piperacillin-tazobactam (90.7%) in their study.The increased resistance among Gram negative bacteria is frequently related to the high selective pressure of antimicrobials that are commonly used in hospitals. The inclusion of gentamycin in many protocols of postoperative antibioprophylaxis (especially in digestive, urological, and gynecological surgery), as well as its frequent use in antibiotherapy, has led to increased selective pressure and incidence of aminoglycoside-resistant strains [24]. Results of the present study proved high sensitivity of most common organism (Klebsiella pneumoniae) to colistin (95.5%) and tigecyclin (86.3%). This is in agreement with Azzab et al., [25] who concluded that the most common Gram negative bacilli were Klebsiella pneumoniae, of which 100% were sensitive to colistin and 94.6% were sensitive to tigecycline, but 94.6% of isolates were resistant to cefotaxime, 70.2% to imipenem, and 64.9% to ertapenem. Also, Ibrahim et al.,[26] observed that the best sensitivity for MDR gram negative bacteria has occured with polymxin (79.1%), colistin (75.6%) and impipenem (68.6%). *In contrast*, Khaertynov et al., [23] *found that Klebsiella pneumoniae* isolates were sensitive to meropenem, amikacin, and ciprofloxacin in their study. The difference of bacterial sensitivity to antibiotics may be due to bacterial status that is one of the determinants for antimicrobial activity. The bacterial phenotypes are different under antibiotic exposure, such as susceptibility, resistance, tolerance, and persistence [27]. In the present study, Gram positive bacteria were sensitive mostly to vancomycin (94.4%) and linezolid (100%), and all were resistant to piperacillin, ampicillin and penicillin (100%).

This is very near to Ibrahim et al., [26] who reviewed the same result of Gram positive bacteria resistance against ampicillin and penicillin (.100%) and, piperacillin (94.4%), but sensitivity to linezolid (100%) and vancomycin (93%).

In contrast, Kulkarni et al., [28] stated that there have been reports from different parts of India isolating MRSA strains with additional resistance to linezolid (Linezolid-resistant MRSA, LR-MRSA) and to multiple antibiotics such as vancomycin, linezolid, and tigecycline (multidrug resistant Staph aureus, MDRSA). The emergence of MDR among Staphylococcus aureus isolates may be significant, though the exact prevalence and clinical implications remain to be unknown.

Resistance levels could be explained by the practices of self-medication and the purchase of antibiotics over-the-counter common in these settings. Policies and regulations promoting rational antibiotic use are also minimal or non-existent. Additionally, limitations in managing nosocomial infections, sub-optimal infection control measures, unsafe water, poor hygienic conditions, lack of knowledge, and inadequately trained personnel might also be associated with the prevailing resistance in these regions [29].

## CONCLUSION

In conclusion, the most common MDR bacteria was Klebsiella pneumoniae. The risk factors for the acquisition of MDR bacteria in this study were; mechanical ventilation, prolonged hospital stay, CVC, and excessive use of antibiotics. MDR bacteria resulted in prolonged hospital stay and elevated mortality rates more than non-MDR bacteria. The present study has some limitations including a small number of patients, the lack of antibiotic stewardship programs in hospitals and this study was based on cross-sectional analysis, so large-scale prospective studies would be needed.

Based on these results, we can have some recommendations. This study showed a high prevalence of MDR organisms in pediatric and neonatal intensive care units and this needs preventive policies and effective measurements to face this emergence. Frequent national surveillance should be adopted in all intensive care units. The antibiotic strategy should be directed toward the limitation of antibiotic misuse to decrease the emergence of the MDR organisms, also, infection control programs must be followed to limit the spread of infection. We should focus on detecting risk factors of MDR bacteria aiming to manage this problem properly, so, frequent studies should be done to detect these risk factors in PICU and NICU to help decrease hospital stay and mortality rate among this group. The antibiotic rotation policy should be introduced in all neonatal and pediatric intensive care units.

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