_Original Article_

# Imipenem Resistance in Gram-Negative Bacteria in the Central Pediatric Teaching Hospital in Baghdad, Iraq

**Sahib Abdul-Mohammed, H[1] *, Kamal Mohammed, A[2], Mohsen Ahmed, Z[2]**

_1. Anatomy Department/Biology, College of Medicine, Baghdad University, Baghdad, Iraq_
_2. Central Pediatric Teaching Hospital, Baghdad, Iraq_

Corresponding Author: hudasahib_2015@Yahoo.com

**Abstract**

Antimicrobial resistance (AMR) is a serious challenge for infectious disease prevention and treatment, according to the World Health Organization. It is a worldwide problem caused primarily by inappropriate and insufficient therapy, misuse of antimicrobials without physician supervision, unnecessary hospital readmissions, and other factors. AMR has several consequences, including increased medical costs and mortality. The present study aimed to evaluate imipenem resistance in gram-negative bacteria in Central Pediatric Teaching Hospital in Baghdad, Iraq, and determine this bacteria resistance in different samples. Initially, a total of 100 different samples were collected from child patients from October 1, 2020, to August 31, 2021. Each isolate was identified using VITEK 2 automated microbiology system. The recorded data showed that the isolated organisms resistant to imipenem included _Klebsiella pneumonia_ (n=21), _Pseudomonas aeruginosa_ (n=19), and _Acinetobacter baumannii_ (n=16). In the current study, _Klebsiella pneumonia_ was the most common pathogen in males (n=57) compared to female (n=43), followed by _Pseudomonas aeruginosa_ and _Acinetobacter baumannii_, particularly in the age range of 1 day- 3 years. Depending on the sample type, _Klebsiella pneumonia_, the most imipenem-resistant bacteria, was found more in the urine of patients with urinary tract infections. _Pseudomonas aeruginosa_ was equally found in blood, urine, wound swab, and sputum samples. In comparison to other samples, _Acinetobacter baumannii_ was found in greater numbers in the blood and in an equal number in urine and cerebrospinal.

**Keywords:** Children, Different samples, Gram-negative bacteria, Imipenem antibiotic

## 1. Introduction

Antimicrobial resistance (AMR) is a serious challenge for infectious disease prevention and treatment, according to the World Health Organization. It is a worldwide problem caused primarily by inappropriate and insufficient therapy, as well as the misuse of antimicrobials without a supervision of a physician, unnecessary hospital readmissions, and other factors. AMR has several consequences, including increased medical costs and mortality (1). In recent years, a big number of resistant strains have emerged in many pathogenic microbes, and multidrug-resistant (MDR) bacteria and gram-negative pathogens are becoming more prevalent worldwide

(2). Clinical evidence suggests that infections caused by antimicrobial-resistant pathogenic organisms, particularly MDR bacteria, result in poorer outcomes, compared to infections caused by susceptible isolates (3, 4). Nonetheless, therapeutic medications have become increasingly ineffectual against bacterial infections in recent years, threatening the efficacy of conventional treatment (5). The most serious repercussions of this condition have been an increase in morbidity and mortality rate, health care cost, and treatment failure (6, 7). The indiscriminate use of these antibiotics, on the other hand, has resulted in the emergence and spread of drug-resistant bacteria pathogens, especially in

developing countries (8). On various fronts, resistance has spread widely, and resistant genes are frequently carried on plasmids, which are easily transmitted across the gram-negative bacteria (GNB), particularly among the Enterobacteriaceae. Resistant gene exchange can occur in hosts (9) as well as in the ecosystem (10). The emergence of MDR jeopardizes the effective treatment of infections worldwide. The disease is defined as resistance to at least one agent in three or more of the specified antimicrobial categories used in treatment by the European Centre for Disease Prevention and Control (11). Resistance can also happen spontaneously through mutation (12). Even though resistant gram-positive infections have received much attention, the spread of resistant gram-negative infectious agents is now the most serious emerging issue in the field of bacterial resistance (13). Antimicrobial resistance in GNB can be explained by a number of biochemical processes. These mechanisms include the enzymatic breakdown of antibacterial drugs, as in the case of lactam resistance due to lactamases, and the alteration of the antimicrobial agent by modifying enzymes, as in the case of aminoglycosides (14). Therefore, after decades of excellence with antibiotics, the world is facing the serious threat of bacterial infections and antibiotic resistance in all countries, adding to the worldwide specter of the "post-antimicrobial era" (15). Imipenem in many centers has been pickings as the first choice for patients suffering from infections caused by various types of GPB and GNB since it keeps *in vitro* activities that are excellent to those of other antimicrobial (16).

## 2. Materials and Methods

A total of 100 different samples were collected from child patients in the Central Pediatric Teaching Hospital in Baghdad, Iraq. These samples were obtained from October 1, 2020, to August 31, 2021. Data were collected using a questionnaire form with items on the patient's age, sex, type of sample, diagnosis and Imipenem resistant.

### 2.1. Bacterial Identification and Antibiotic Susceptibility

The VITEK 2, an automated microbiology system was applied to identify each isolate. The reagent cards were automatically incubated. The VITEK 2 system was used following the manufacturer's guidelines. The integration of automated VITEK 2 technology with fully prepared VITEK 2 ID and susceptibility (AST) cards provided maintainable and accurate ID and AST results for important clinical Gram-negative cocci and Gram-negative bacilli. The samples were cultured on special media, such as MacConkey agar, blood agar, and chocolate agar for 18-24 h at 35-37 °C, depending on the sample type. The bacteria were suspended in a 2.5 mL sodium chloride solution (0.45%). The suspension in the VITEK2 system was adjusted to a 0.5 McFarland standard (bioMerieux, Marcy-l'Étoile, France).

### 2.2. Statistical Analysis

In this study, categorical variables were presented as absolute and relative frequencies. Moreover, continuous variables were presented as median and interquartile range or mean and standard deviation. Statistical analyses were carried out using SPSS software (Version 20.0; SPSS Inc., Chicago, USA) through Person's Chi-Square test.

The results were analyzed and evaluated using statistical tables with observed frequencies and percentages for descriptive statistics. Statistical hypotheses were used to show acceptance or rejection of the data (2). A $p$-value less than 0.05 was considered to be statistically significant. However, in two-sided tests, the $p$-value was considered significant at 0.025.

## 3. Results and Discussion

In this study, 100 isolated organisms from children were found to be gram-negative resistant to imipenem (Table 1). The most common organisms included *Klebsiella pneumonia* (21), *Pseudomonas aeruginosa* (19), and *Acinetobacter baumannii* (16).

**Table 1**. Distribution of Gram-negative isolates resistant to imipenem

| Organism | No. |
|---|---|
| *Klebsiella pneumonia* | 21 |
| *Pseudomonas aeruginosa* | 19 |
| *Acinetobacter baumannii* | 16 |
| *Proteus mirabilis* | 14 |
| *Burkholderia cepacia* | 14 |
| *Escherichia coli* | 10 |
| *Enterobacter cloacae* | 3 |
| *Enterobacter aeruginosa* | 2 |
| *Pseudomonas fluorescens* | 1 |
| Total | 100 |

Imipenem-resistant bacteria are frequently resistant to other antimicrobial medications, and the prognosis in terms of death and morbidity is even worse (17). Drug resistance mechanisms are classified across several major categories, including drug destruction, drug binding site/target alteration, and changes in cell permeability and efflux pump expression, all of which result in lower intracellular drug deposition (18). AMR varies by country and region, depending on antimicrobial use policies and understanding of its occurrence (1). It was revealed that the distribution of pathogens differed between developing and developed countries as previously mentioned in a study conducted by Radji, Fauziah (19). In other studies, however, *Acinetobacter* was the most common pathogen, followed by *Klebsiella pneumonia* and *Pseudomonas aeruginosa*. Moreover, *Klebsiella pneumonia* was the most common pathogen in the current study (Table 1), followed by *Pseudomonas aeruginosa* and *Acinetobacter baumannii*. Out of 100 patients, 57 and 43 patients were male and female, respectively. All the patients were in the age range of 1 day to 3 years. These results were in line with those reported by Helmy and Kashef (11) and Tran, Ho-Le (15). The *p*-value was obtained at 0.006, which is less than 0.025 in 2- sided tests; therefore, the results presented in table 2 were significant (2). These results were in line with a previous study performed Parajuli, Acharya (20) in Nepal. Table 3 presents the distribution of gram-negative bacilli resistant to imipenem, according to the type of sample. It was revealed that *Klebsiella pneumonia* was the most imipenem resistant pathogen found in urine samples (n=13, 61.9 %) in urinary tract infection, blood infection (n=6, 28.6 %), and wound swab (n=2, 9.5 %) in wound infection. Moreover, *Pseudomonas aeruginosa* was found equally in the blood, urine, wound swab, and sputum samples (n=4, 21.1 %). While *Acinetobacter baumannii* represent 5 (31.2 %) in blood, 4 (25.0 %) Urine, 4 (25.0 %) in cerebrospinal fluid (CSF) and 2 (12.5 %) in wound swab (Table 3). These findings were in line with the results reported by Tran, Ho-Le (15). At least one of the tested B-lactam-resistance genes was found in 76% of MDR *Enterobacteriaceae*, even though B-lactamases have been commonly reported among *Enterobacteriaceae* (14). B-lactams are the most commonly prescribed class of antimicrobial agents worldwide due to their proven safety and efficacy (21). *Pseudomonas aeruginosa* was intrinsically resistant to several antibiotics despite the lower permeability of their outer membrane, the fundamental expression of various efflux pumps, and the production of antibiotics in enzymes activating (22). The overall prevalence of multidrug resistance in *Acinetobacter* spp. could be attributed to the bacteria's high likelihood of acquiring a resistance gene and their ability to remain and replicate in a hospital setting (23). Few studies, however, have looked into the fundamental mechanisms of antibiotic resistance (24). The problem of rising antimicrobial resistance becomes even more dangerous when one considers the small number of new antimicrobial agents in development (25).

**Table 2.** Distribution of Gram-negative bacilli resistant to imipenem, according to the relationship between age group and gender

| Age group | Gender | | Total | *P*-value |
|---|---|---|---|---|
| | **Male** N (%) | **Female** N (%) | | |
| 1 day - 3 Y | 31 (66.0) | 16 (34.0) | 47 (100.0) | |
| 4 Y - 6 Y | 5 (23.8) | 16 (76.2) | 21 (100.0) | |
| 7 Y – 9 Y | 10 (66.7) | 5 (33.3) | 15 (100.0) | |
| 10 Y – 12 Y | 8 (80.0) | 2 (20.0) | 10 (100.0) | 0.006 |
| 13 Y- 15 Y | 3 (42.9) | 4 (57.1) | 7 (100.0) | |
| Total | 57.0 | 43.0 | 100 | |

P-value <0.025 in two-sided test

**Table 3.** Distribution of Gram-negative bacilli resistant to imipenem, according to the type of Sample

| Organism | Total N (%) | Type of sample | | | | | | | | | | | P-value |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Blood N (%) | Urine N (%) | Wound Swab No % | Sputum N (%) | CSF N (%) | Tracheal tube No % | Peritoneal N (%) | Oral lesion N (%) | Pus swab N (%) | Throat Swab No. % | Pleural fluid | |
| *Klebsiella pneumonia* | 21(100.0) | 6(28.6) | 13(61.9) | 2(9.5) | 0 (0.0) | 0(0.0) | 0(0.0) | 0(0.0) | 0(0.0) | 0(0.0) | 0(0.0) | 0(0.0) | |
| *Pseudomonas aeruginosa* | 19(100.0) | 4(21.1) | 4(21.1) | 4(21.1) | 4(21.1) | 0(0.0) | 1(5.2) | 0(0.0) | 1(5.2) | 0(0.0) | 1(5.2) | 0(0.0) | |
| *Acinetobacter baumannii* | 16(100.0) | 5(31.2) | 4(25.0) | 2(12.5) | 0(0.0) | 4(25.0) | 0(0.0) | 0(0.0) | 0(0.0) | 1(6.3) | 0(0.0) | 0(0.0) | |
| *Proteus mirabilis* | 14(100.0) | 2(14.3) | 10(71.4) | 2(14.3) | 0(0.0) | 0(0.0) | 0(0.0) | 0(0.0) | 0(0.0) | 0(0.0) | 0(0.0) | 0(0.0) | |
| *Burkholderia cepacia* | 14(100.0) | 5(35.7) | 5(35.7) | 1(7.2) | 1(7.2) | 0(0.0) | 2(14.2) | 0(0.0) | 0(0.0) | 0(0.0) | 0(0.0) | 0(0.0) | 0.000 |
| *Escherichia coli* | 10(100.0) | 0(0.0) | 6(60.0) | 1(10.0) | 1(10.0) | 0(0.0) | 0(0.0) | 0(0.0) | 0(0.0) | 1(10.0) | 0(0.0) | 1(10.0) | |
| *Enterobacter cloacae* | 3(100.0) | 1(33.4) | 1(33.3) | 0(0.0) | 0(0.0) | 0(0.0) | 0(0.0) | 1(33.3) | 0(0.0) | 0(0.0) | 0(0.0) | 0(0.0) | |
| *Enterobacter aeruginosa* | 2(100.0) | 0(0.0) | 0(0.0) | 2(100.0) | 0(0.0) | 0(0.0) | 0(0.0) | 0(0.0) | 0(0.0) | 0(0.0) | 0(0.0) | 0(0.0) | |
| *Pseudomonas fluorescens* | 1(100.0) | 0(0.0) | 0(0.0) | 0(0.0) | 0(0.0) | 0(0.0) | 0(0.0) | 0(0.0) | 0(0.0) | 0(0.0) | 0(0.0) | 1(100.0) | |
| Total | 100(100.0) | 23(23.0) | 43(43.0) | 14(14.0) | 6(6.0) | 4(4.0) | 3(3.0) | 1(1.0) | 1(1.0) | 2(2.0) | 1(1.0) | 2(2.0) | |

*P*-value <0.025 in 2-sided

## 4. Conclusion

Based on the obtained results in the current study, *Klebsiella pneumonia* was the most common pathogen in males, followed by *Pseudomonas aeruginosa* and *Acinetobacter baumannii*, particularly in the age group of 1day-3 years. Depending on the type of sample, *Klebsiella pneumonia*, the most imipenem resistant, was found more in urine with urinary tract infection. Moreover, *Pseudomonas aeruginosa* was found equally in all four blood, urine, wound swab, and sputum samples. In comparison to other samples, *Acinetobacter baumannii* was found in greater numbers in the blood and in an equal number in urine and CSF.

## Authors' Contribution

Study concept and design: A. K. M.
Acquisition of data: H. S. A.
Analysis and interpretation of data: H. S. A.
Drafting of the manuscript: Z. M. A.
Critical revision of the manuscript for important intellectual content: H. S. A., A. K. M. and Z. M. A.

Statistical analysis: A. K. M.
Administrative, technical, and material support: H. S. A., A. K. M. and Z. M. A.

## Ethics

All the procedures in this study, were performed according to the guidelines instructed by the Human Ethics Committee of the Baghdad University, Baghdad, Iraq (No: 4578784-78).

## Conflict of Interest

The authors declare that they have no conflict of interest.

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