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"MOLECULAR CHARACTERIZATION OF OXA-23 GENE AND BLAIMP-1 GENE IN INVASIVE CARBAPENEM-RESISTANT *ACINETOBACTER BAUMANNII* IN ICU PATIENTS"

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ABSTRACT

INTRODUCTION: Carbapenem-resistant *Acinetobacter baumannii* (CRAB) poses a substantial health risk in the treatment of infectious diseases. Carbapenems were previously utilised as a last option for treating MDR Gram-negative bacteria infections. *A. baumannii* has lately exhibited an increase in carbapenem resistance. The bulk of carbapenem resistance mechanisms in *A. baumannii* are caused by enzyme breakdown by -lactamases.

AIM AND OBJECTIVES: To Study the Molecular characterization of OXA -23 gene and blaIMP gene in invasive carbapenem-resistant *Acinetobacter baumannii* in ICU patients

MATERIAL AND METHODS: The present study was a Cross-sectional study carried out in the Department of Microbiology for a period of 1 year i.e, May 2023 to May 2024 at a tertiary care centre. A total of 120 non-duplicate, consecutive, carbapenem-resistant isolates recovered from *Acinetobacter* species were included in this study. The isolates were obtained from the clinical samples. The isolates were identified by the standard biochemical tests and the Antimicrobial susceptibility testing was performed according to the CLSI guidelines 2023. The DNA was extracted using the Qiagen DNA extraction kit as per the manufactures guidelines and the gene Oxa -23 gene and blaIMP-1 was detected using the conventional PCR assay.

RESULTS: In the present study a total of 1034 clinical samples were collected out of which 120 Acinetobacter species were isolated. The maximum number of isolates were from the ETA samples with 91 (75.8%), 24 (20%) from blood and 5 (4.1%) from the tissue. The ratio of Males 75(62.5%) was more as compared to that of the Females 45 (37.5%) with the maximum age of 31-40 being affected the most followed by 41-50 and least in the age group above 61 years of age.

Antimicrobial susceptibility testing revealed that all the isolates were resistant to ceftazidime, cefepime, piperacillin/tazobactam, cefoperazone/sulbactam, aztreonam, imipenem, meropenem, amikacin, netilmycin, tetracycline, tobramycin, levofloxacin and co-trimoxazole. In the present study it was also observed that around 116 (96.6%) of the study isolates were susceptible to polymyxin B (colistin).

The Molecular characterization reveals that among the 120 isolates tested, there were no isolate observed positive for the blaIMP-1 gene (0%) and blaOXA-23 gene was present in all the 120 isolates (100%).

CONCLUSION: Further research is needed to track the spread of carbapenem-resistant OXA-type lactamase genes from A. baumannii in hospital settings, as they are becoming a major cause of carbapenem resistance. There should be effective infection control systems in place, as well as tight regulations governing antibiotic use.

KEYWORDS: CRAB**,** Carbapenem, CLSI, Molecular characterization, DNA, PCR, blaIMP-1, OXA-23

INTRODUCTION

Multidrug-resistant bacterial strains have emerged as the leading causes of nosocomial infections worldwide. Pandrug-resistant (PDR) bacterial strains are resistant to all antibacterial agents except polymyxins and tigecycline, while extensively drug-resistant (XDR) bacterial strains are resistant to all antibacterial agents. There is a significant risk of these "superbugs" spreading throughout the community and endangering public health [1].

A. baumannii is an important cause of nosocomial infections and a leading cause of mortality and morbidity among hospitalized patients and has been associated with a wide variety of diseases in hospitalized patients in the intensive care units (ICU) [2].

Nowadays, increasing drug resistant rate among *A. baumannii* strains is a major concern worldwide [3]. The most common mechanism of resistance is the production of *β*-lactamases, including enzymes of Ambler classes A, D, and B, with their genes being often associated with mobile genetic elements such as plasmids [4]. Carbapenem resistance caused by acquiring the MBLs is considered to be more serious than other resistance mechanisms because MBLs can almost hydrolyse all beta-lactam antibiotics except monobactams [3].

In *Acinetobacter* spp., β-lactamases are the most common contributors to resistance to extended-spectrum cephalosporins and carbapenems, including extended-spectrum β-lactamases (ESBL), metallo-β-lactamases (MBL), carbapenem-hydrolyzing class D β-lactamases (CHDL), and *Acinetobacter*-derived cephalosporinases (ADC) [2].

Carbapenem resistance in *A. baumannii* is mainly due to Class D and Class B carbapenemases belonging to Ambler's classification of β-lactamases. Although various mechanisms contribute to carbapenem resistance, the majority is due to class D carbapenemases such as $bla_{\text{OXA-23-like}}$, $bla_{\text{OXA-24-like}}$ and $bla_{\text{OXA-58-like}}$ $bla_{\text{OXA-23-like}}$ producing *A. baumannii* responsible for causing outbreaks have been reported from various regions of the world. Class D carbapenemase in transposons, have the ability to rapidly spread in successful clonal lineages of *A. baumannii* [5].

This bacterium is considered an opportunistic pathogen that causes nosocomial infections, particularly in intensive care units [2]. *A. baumannii* is a common cause of bacteremia, nosocomial

pneumonia or ventilator-associated pneumonia, catheter-related infections, meningitis, peritonitis, skin and wound infections, urinary tract infections, and endocarditis [3].

A. baumannii is one of the ESKAPE pathogens, along with Enterococcus faecium, *Staphylococcus aureus*, *Klebsiella pneumoniae*, Pseudomonas *aeruginosa*, and Enterobacter spp., which are responsible for the majority of nosocomial infections and can "escape" the bactericidal activity of antimicrobial agents [4-5].

Furthermore, the MBL-encoding genes located on integrons can be disseminated easily from one bacterium to another. Many MBLs have been found in *A. baumannii*, including imipenemase (IMP), São Paulo metallo (SPM), Verona integron-encoded metallo-beta-lactamases (VIM), Seoul imipenemase (SIM) [6].

Carbapenems are considered the most effective treatment for *A. baumannii*. However, there have been numerous reports of growing carbapenem resistance. *A. baumannii* resistance might be carbapenemase or non-carbapenemase mediated. Carbapenemase-mediated resistance is primarily caused by class A (serine proteases), class B (metallo-beta-lactamases), and class D (oxacillinases) carbapenemases, whereas non-carbapenemase-mediated resistance is induced by efflux pump overexpression and/or loss of outer membrane porins [7].

The β-lactamases and resistance determinants were detected by PCR including Ambler class A ESBL genes (*bla*$_{TEM}$, *bla*$_{SHV}$, *bla*$_{CTX-M}$, *bla*$_{VEB}$, and *bla*$_{PER}$), Amber class B MBL genes (*bla*$_{IMP}$, *bla*$_{VIM}$, *bla*$_{GIM}$, *bla*$_{SPM}$, and *bla*$_{SIM}$), an Amber class C AmpC β-lactamase genes (*bla*$_{ADC}$), Amber class D carbapenemase genes (*bla*$_{OXA-23-like}$, *bla*$_{OXA24-like}$, *bla*$_{OXA-51-like}$, and *bla*$_{OXA-58-like}$), integrase genes (*intI1*, *intI2*, and *intI3*), IS elements (IS*Aba1*, IS*Aba2*, IS*Aba3*, and IS*18*), transposase genes, and a putative replicase gene, *repAci1* Resistance to carbapenem in *A. baumannii* is most frequently due to oxacillinases, which can be intrinsic or acquired [8,9].

IMP-type enzymes were first discovered in Japan in the late 1980s and have since been found in Enterobacteriaceae and Gram-negative nonfermenters (mostly in *P. aeruginosa* and Acinetobacter spp.). More than 20 different IMP allotypes have been identified, representing various sublineages [4]. The many IMP types frequently have a specific location on the globe; nevertheless, some (e.g., IMP-1, IMP-4, and IMP-7) were detected in diverse areas, indicating their potential for global dissemination [10].

Since the intrinsic blaOXA-51 gene is found on *A. baumannii's* chromosome, the organism is thought to be unique to it. In contrast to MBLs encoded by the blaIMP, blaVIM, blaNDM, and blaSIM genes, acquired OXA enzymes, which are produced by the blaOXA-23, blaOXA-40, and blaOXA-58 genes, are more prevalent in *A. baumannii* isolates [11-13].

A.baumannii can develop resistance to many classes of commonly used antimicrobial agents [9 ,10] where Carbapenems was considered as a last resort to treat infections caused by MDR, Gram-negative bacteria, but recently, carbapenem resistance has been increasingly common in *A. baumannii.* The Multi and extensively drug-resistant (MDR and XDR) *Acinetobacter baumannii* (*A. baumannii*) are two main causative agents of nosocomial infections leading to increased morbidity and mortality which have been progressively increasing globally over the last decade [11,14].

A. baumannii contains a number of carbapenem resistance mechanisms, including antimicrobial-inactivating enzymes, an efflux pump, deletion of the CarO outer membrane porin, and restricted target access [14, 15]. Oxacillinase (OXA), a class D β-lactamase, is a major cause of carbapenem resistance. This group of enzymes can break down oxacillin and third-generation cephalosporins, but they have low activity against carbapenems [16].

Carbapenems are very useful for the treatment of infections caused by Gram-negative bacilli that are resistant to other b-lactam antibiotics. However, carbapenem-resistant Gram-negative bacilli are increasingly being isolated from clinical samples. Since the early 1990s, *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, and a variety of Enterobacteriaceae species expressing IMP-type metallo-b-lactamases have been discovered in many Japanese hospitals, with identical or comparable enzymes later discovered abroad. The current study was conducted to investigate the molecular characterisation of invasive carbapenem-resistant *Acinetobacter baumannii* in ICU patients, with a focus on the blaIMP gene and OXA-23 gene.

MATERIAL AND METHODS

This was a Cross-sectional study carried out in the Department of Microbiology for a period of 1 year i.e, May 2023 to May 2024. A total of 120 non-duplicate, consecutive, carbapenem-resistant isolates recovered from ICU patients of *Acinetobacter* species were included in this study. The

isolates were obtained from invasive clinical specimens including blood, endotracheal aspirates (ETAs) and the tissue. The isolates were identified up to the species level as *Acinetobacter baumannii* by standard biochemical tests and the Antimicrobial susceptibility testing was performed according to the CLSI guidelines 2023. The DNA was extracted using the Qiagen DNA extraction kit from the clinical samples where the confirmation of the gene blaIMP and OXA-23 was performed by the PCR [17].

The Antimicrobial Susceptibility Testing

The Susceptibility to different classes of antibiotics was determined by the Kirby Bauer disc diffusion method and interpreted according to the Clinical Laboratory Standard Institute guidelines. Antibiotics tested were ceftazidime (30 µg), cefepime (30 µg), piperacillin/tazobactam (100/10 µg), cefoperazone/Sulbactam (75/30 µg), amikacin (30 µg), netilmycin (30 µg), tobramycin (10 µg), aztreonam (30 µg), levofloxacin (5 µg), tetracycline (30 µg), co-trimoxazole (1.25/23.75 µg), imipenem (10 µg), meropenem (10 µg) and polymyxin B (10 µg) [17] were used as per the CLSI guidelines.

The Phenotypic Detection method

CarbAcineto NP test was used for carbapenemase phenotypic detection. All of the research isolates that needed to be evaluated were cultivated for 24 hours on a Mueller-Hinton agar plate, and the isolated colonies were then re-suspended in two 1.5 ml centrifuge tubes (A and B) containing 100 l NaCl (5 M). 100 l of solution A (phenol red solution with zinc sulphate) and 100 l of solution A with imipenem (6 mg/ml) were added to tubes A and B, respectively. Maximum 2 hours were allowed for the tubes to be incubated at 37 °C. The hydrolysis of imipenem caused a pH value reduction, which caused a colour shift in tube B, indicating the presence of carbapenemase [17,18]. BAA-1705 and BAA-1706 were simultaneously listed as positive and negative controls, respectively.

The Molecular Characterization of the Genes by phenotypic method

The DNA was isolated using the Qiamp DNA Blood Mini Kit (QIAGEN, Germany) as per the manufactures guidelines. The extracted DNA and the gene was confirmed by the PCR to detect the presence gene blaIMP-1 gene and OXA-23.

The DNA was eluted in 60 µl elution buffer and preserve at -20 °C till PCR analysis. For amplification of the target gene, PCR was carried out in a 50 µL reaction mixture with 30 no. of cycles. The primers were purchased from "**Saha gene'** and was reconstituted with sterile double distilled water based on the manufacturer's instruction.

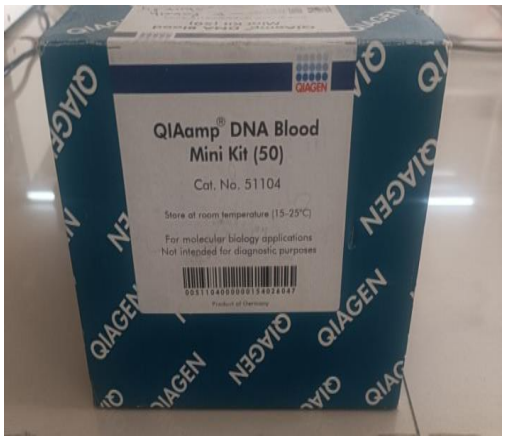


Figure No.1: The DNA Extraction kit

Fragment	**Gene**	**Primer sequence**	**Length (bp)**	**Reference**
A	OXA-23 FA OXA-23-RA	5'- ATTTCTGACCGCATTTCCAT-3' 5'- GGTTAGTTGGCCCCCTTAAA-3'	501 bp	19

Table No. 1 : Primers used to amplify OXA-23 gene fragments.

Fragment	Gene	Primer sequence	Length (bp)	Reference
A	blaIMP-1- FA blaIMP-1 -RA	’5′-GAAGGCGTTTATGTTCATAC-3′- 5′-GTAAGTTTCAAGAGTGATGC-3′	587 bp	20

Table No. 2 : Primers used to amplify blaIMP gene fragments.

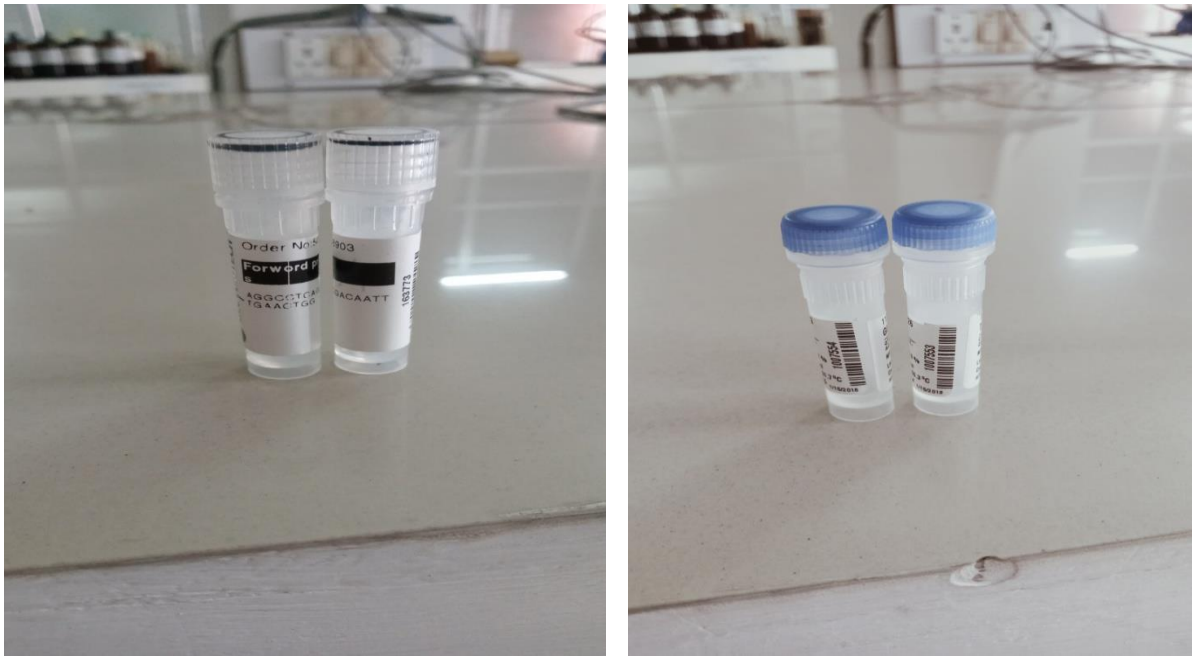


Figure No. 2: The blaIMP and OXA-23 primer from the Saha gene

Polymerase Chain Reaction (PCR)

For the PCR amplification, 2 µl of template DNA was added to 18 µl reaction containing 10 µl of Qiagen master mix, 2 µl of primer mix (1 µl each of the respective forward and reverse primers) and 6 µl of molecular-grade water.

The cyclic conditions for genes, initial denaturation at 95 °C for 15 min, 30 cycles of 94 °C for 30 s, 59 °C for 1 min 30 s and 72 °C for 1 min 30 s were followed by extension of 72 °C for 10 min.

The PCR cycling conditions

Step	**Program** **BlaIMP-1** **Time** **Temperature**	**Cycles**
Initial denaturation	15 min 95 ºC	
Denaturation	30 s 94 ºC	
Annealing	1 min30 s 59 ºC	30
Extension	1 min 30 s 72º C	
Final extension	10 min 72º C	

Table No. 3 : The PCR cycling conditions to amplify blaIMP-1 gene fragments.

The Agarose gel preparation and visualized by Gel Doc™ EZ Gel Documentation System

Step	**Program** **OXA-23** **Time** **Temperature**	**Cycles**
Initial denaturation	15 min 95 ºC	
Denaturation	30 s 94 ºC	
Annealing	1min 30 s 52 ºC	30
Extension	1 min 30 s 72º C	
Final extension	1 min 30 s 72º C	

Table No. 4 : The PCR cycling conditions to amplify OXA-23 gene fragments

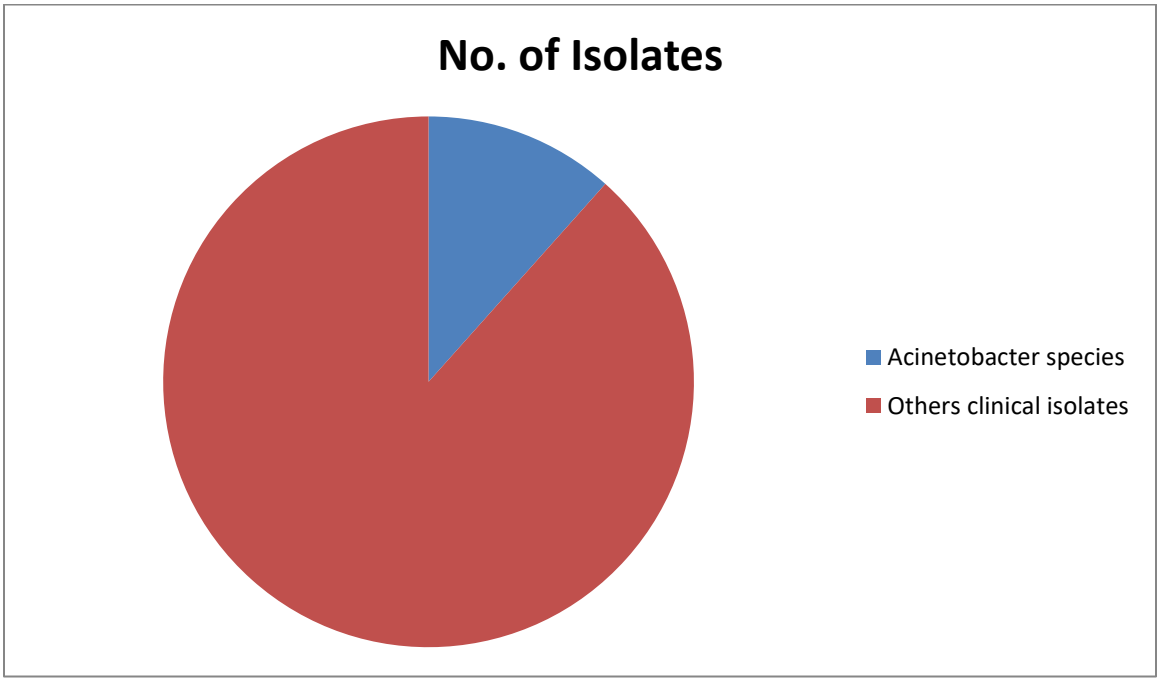
The Agarose Gel Electrophoresis was performed in order to identify the Purified PCR Product which was previously identified by its amplified DNA fragments. The resulting PCR product was subjected to 1 % agarose gel electrophoresis and visualized by Gel Doc™ EZ Gel Documentation System (Bio-Rad Laboratories Inc., Hercules, CA, USA). A 1 kb DNA Ladder (Thermo Fisher Scientific ™, Waltham, MA, USA) was used as the marker to evaluate the PCR product of the sample [21].

RESULTS

A total of 834 clinical samples were included out of which 120 invasive clinical isolates of Acinetobacter species were studied. The maximum number of isolates were from the ETA samples with 91 (75.8%), 24 (20%) from blood and 5 (4.1%) from the tissue [Table No. 6]. The ratio of Males 75(62.5%) was more as compared to that of the Females 45 (37.5%) with the maximum age of 31-40 being affected the most followed by 41-50 and least in the age group above 61 years of age [Table No. 7].

Type of Clinical Isolates	**Number of Isolates**	**Percentage**
Acinetobacter species	120	11.16%
Others clinical isolates	914	88.3%

Table No. 5: Total Number of clinical isolates



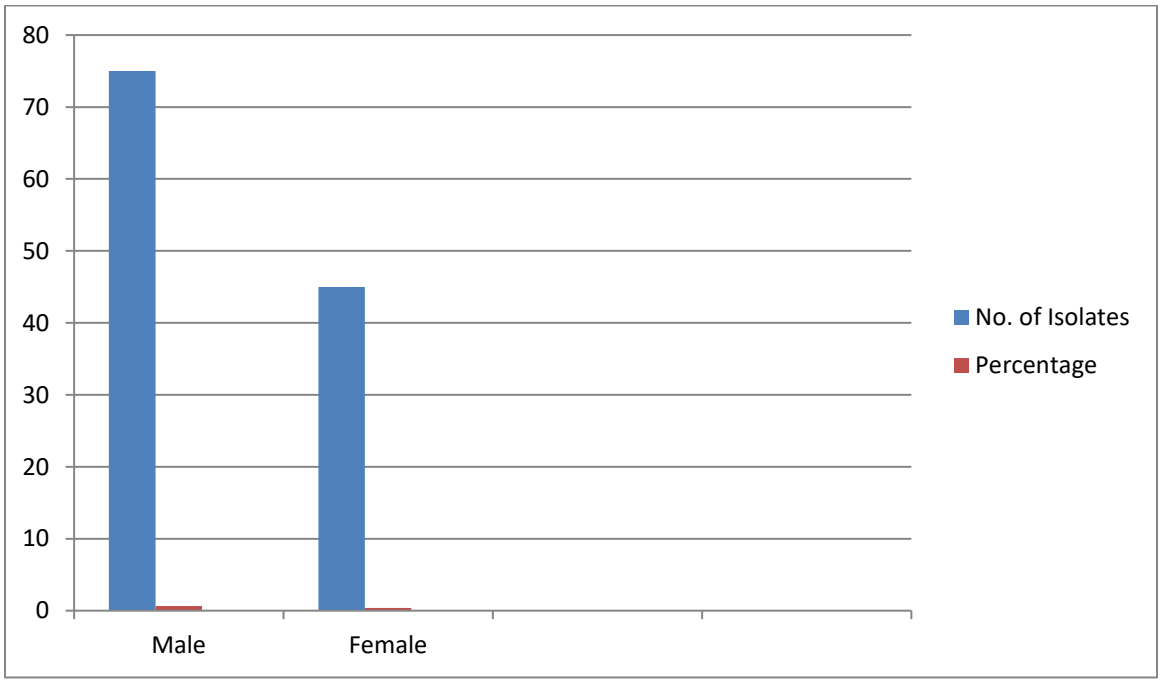
Graph No. 1: The graphical Respresentation of the Number of Isolates

Type of isolates	**Number of Isolates**	**Percentage**
ETA	91	75.8%
Blood	24	20%
Tissue	5	4.1%
Total	**120**	**100%**

Table No. 6: Total Number of clinical isolates of Acinetobacter species

Gender	Total no. of Cases studies (N=120)	Percentage
Male	75	62.5%
Female	45	37.5%

Table No. 7 : Genderwise distribution of the *Candida albicans*



Graph No. 2: The graphical Respresentation of the Genderwise distribution

The ratio of Males 75 (62.5%) was more as compared to that of the Females 45(37.5%) [Table No. 7] with the maximum age of 31-40 being affected the most followed by 41-50 and least in the

age group above 61 years of age [Table No. 8]. There was no *Acinetobacter baumannii* isolated in the age group of 0-10 years of age.

S.No.	Age (in years)	No. of Cases	Percentage
1.	0- 10	-	-
2.	11-20	7	5.8 %
3.	21-30	16	13.3 %
4.	31-40	52	43.3%
5.	41-50	26	21.6%
6.	51-60	13	10.8%
7.	≥61	6	5 %

Table No.8 : Age wise distribution of *A.baumannii* patients from the study

Antimicrobial susceptibility testing revealed that all the isolates were resistant to ceftazidime, cefepime, piperacillin/tazobactam, cefoperazone/sulbactam, aztreonam, imipenem, meropenem, amikacin, netilmycin, tetracycline, tobramycin, levofloxacin and co-trimoxazole. In the present study it was also observed that around 116 (96.6%) of the study isolates were susceptible to polymyxin B (colistin.).

Among the 120 clinical isolates, the CarbAcineto NP test was positive in 112(93.3%) isolates and negative in 8 (6.6%)

The Molecular characterization for the detection of the genes in Acinetobacter was performed where the DNA was isolated using the Qiagen DNA extraction kit as per the manufacture's guidelines. The PCR was run for the detection of MBL Gene.

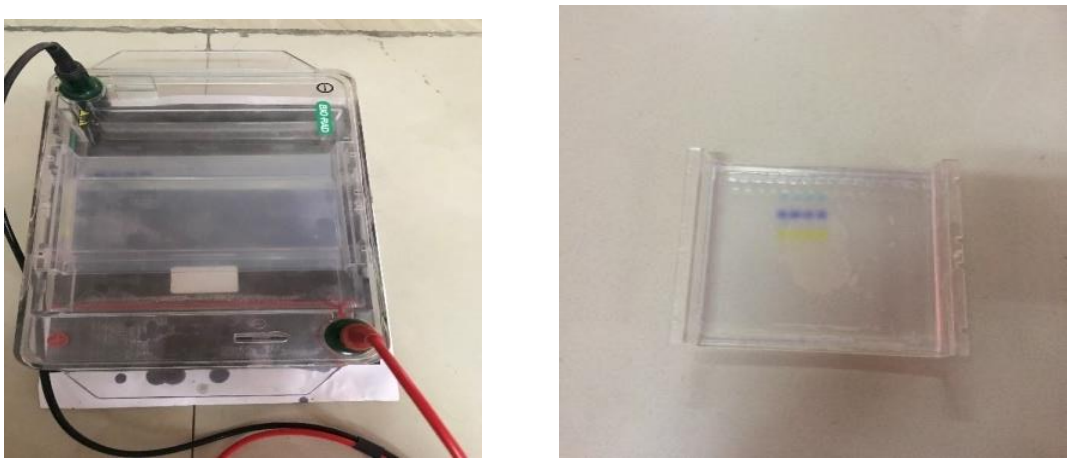


Figure No. 3: Electrophoresis unit under Run of Amplified product

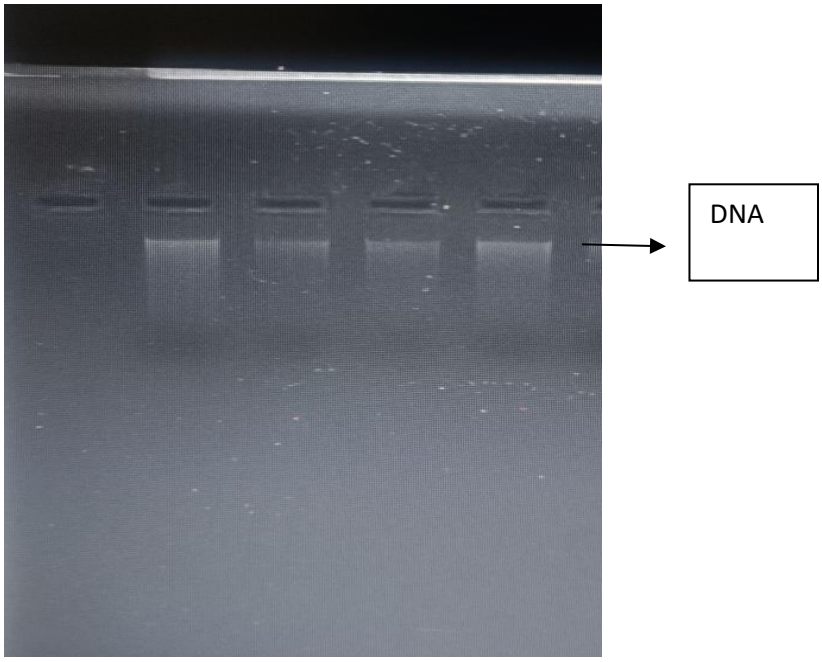


Figure No.4: The DNA Extraction

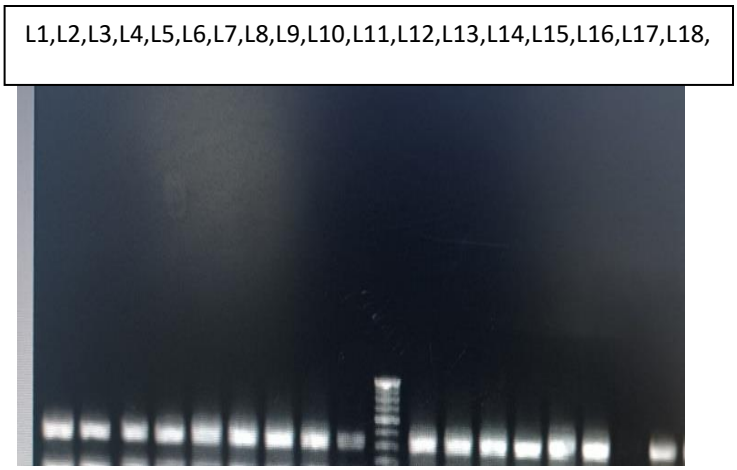


Figure No.5 : The Amplified DNA with PCR for OXA-23 gene of *A. baumannii* . Lane -1-9 are positive for OXA-23 gene; Lane 10 is the DNA Ladder; Lane 11-16 are OXA-23 gene positive; Lane 17 is the Negative control for OXA-23 gene; Lane 18 is the positive control for OXA-23 gene

The acquired OXA carbapenemase, blaOXA-23 gene was present in all the 120 isolates (100%). The molecular detection of the blaoxa-23-like gene revealed a 501 bp band in all clinical isolates, which preliminarily confirmed the identification of the clinical isolates as being *A. baumannii*. It was also noted that there was no blaIMP gene observed in the present study.

DISCUSSION

A. baumannii infections linked to healthcare are becoming more often reported cases of multidrug resistance worldwide. Therefore, the recommended antibiotic for treating severe MDR *A. baumannii* infections is carbapenems. Global *A. baumannii* carbapenem resistance evolution is greatly influenced by a number of new resistance mechanisms, such as class D, class B metallo-b-lactamases, and OXA carbapenemases [16].

A. baumannii is responsible for hospital-acquired infections and has recently become one of the most important healthcare-associated infections in hospitals. Infection caused by this bacterium often leads to significant mortality and morbidity

Due to therapeutic challenges, hospital-acquired infections (HAIs) caused by *Acinetobacter baumannii* (HA-AB), particularly carbapenem-resistant strains (HA-CRAB) pose a serious health threat to patients worldwide. *Acinetobacter baumannii* is an opportunistic pathogen of emerging

importance in the clinical settings and responsible for up to 20% of infections in ICUs around the globe [15]. The majority of reported clinical cases involved ventilator-associated pneumonia/pulmonary infections, bloodstream infections, skin and soft tissue infections, including burn and surgical wound infections, endocarditis, meningitis, and urinary tract infections. Furthermore, Acinetobacter infections are not limited to hospital settings; reports have surfaced of instances involving apparently healthy individuals of all ages, occurring in community settings, after natural catastrophes, and during wars [22,23]. Treatment of infections caused by this organism is becoming a substantial clinical concern, because *A. baumannii* has widespread resistance to several of the commonly used antibiotics including cephalosporins, aminoglycosides, quinolones, and carbapenems. *Acinetobacter baumannii* is of particular concern due to its predilection to acquire antibiotic resistance determinants [24].

In the present study a total of 1034 clinical samples were included out of which 120 clinical isolates of Acinetobacter species were studied. The maximum number of isolates were from the ETA samples with 91 (75.8%), 24 (20%) from blood and 5 (4.1%) from the tissue. This study was similar to the study performed by other author Sharma RK et al. where the percentage of Acinetobacter isolates was found to be (6.42%) [19, 25] .There were other studies which were also parallel to our study stating the rate of Acinetobacter to be similar studies by Fayyaz et al [26] (10.9%) and Goossens [27] (4.9%) but in contrast with the study by Sabir et al, where the percentage of positive culture was found to be 87.17%, which was much higher than the present study [28].

The ratio of Males 75(62.5%) was more as compared to that of the Females 45 (37.5%) with the maximum age of 31-40 being affected the most followed by 41-50 and least in the age group above 61 years of age. There was no *Acinetobacter baumannii* isolated in the age group of 0-10 years of age. This study was in support with the study performed by the other authors, where the rate of male was more (75.36%) as compared to the female (24.28%) [25]. Another study was also found to be similar in the study by Fayyaz et al [26] but in contrast with the studies by Tahseen and Talib and Saleem et al. [29, 30].

In the present study antimicrobial susceptibility testing revealed that all the isolates were resistant to ceftazidime, cefepime, piperacillin/tazobactam, cefoperazone/sulbactam, aztreonam, imipenem, meropenem, amikacin, netilmycin, tetracycline, tobramycin, levofloxacin and co-trimoxazole. In

the present study it was also observed that around 116 (96.6%) of the study isolates were susceptible to polymyxin B. This study was similar to the study by the author authors where polymyxin B was observed to be susceptible [25] [19]. It was also noted that around 118 (98.1%) of the study isolates were susceptible to polymyxin B and colistin, which was parallel to the study performed by the other author [20].

Among the 120 clinical isolates, the CarbAcineto NP test was positive in 112 (93.3%) isolates and negative in 8 (6.6%). This study was similar to the study by other author Vijaykumar S et al in 2016 [20].

In the current study it was observed that the Molecular characterization reveals among the 120 isolates tested, there were no isolate observed positive for the blaIMP-1 gene (0%) and blaOXA-23 gene was present in all the 120 isolates (100%). This study was similar to the study performed by other research investigators Saranathan et al. and Amudhan et al. showed IMP-like and blaVIM-like as the prevalent rate of MBL genes to be similar [31]. There was another study which was in accordance to the current from East India showed the OXA-23 genes as the prevalent type of oxacillinase contributing to carbapenem resistance [32].

In the current study it was found that there was no blaIMP-1 gene found. This study was in support to the study by Fallah F et al where there were only 3 isolates observed positive for blaIMP gene [20] . There was another study performed by Khalid H et al in 2024 where the PCR assays of the isolates identified bla-VIM-1, bla-VIM-2, bla-IMP-1 and bla-IMP-2 genes at the rates of 17%, 40.1%, 29.9% and 4.2%, respectively [33]. There was another study where bla-IMP-1 gene expression was not found [34].

In addition, Shahcheraghi et al. examined 100 A. baumannii strains from more than one hospital in Tehran, Iran, and did not detect any bla-VIMor bla-IMPgenes MBL-encoding genes [35] Resistance to beta-lactams is related to various enzymes that are produced, including extended spectrum beta-lactamases (ESBLs) and metallo-beta-lactamases (MBLs) which belong to Ambler A and B divisions [36].

Studies have reported that carbapenem resistance in *A. baumannii* is mainly due to carbapenemase mediated. However, non-carbapenemase-mediated resistance mechanisms such as reduced

membrane permeability due to porin changes and overexpression of efflux pumps make a trivial contribution toward carbapenem resistance in *A. baumannii*.

Carbapenems are currently the primary medications used for the treatment of infections caused by multidrug-resistant *A. baumannii*. Nonetheless, there is growing concern as carbapenem resistance among A. baumannii isolates may become more widespread [6]. Resistance of *A. baumannii* to carbapenems could be caused by a variety of factors, such as the development of beta-lactamases, changes in proteins that bind to penicillin and outer membrane proteins, and an excess of efflux pumps [7].

Nowadays, the growing drug resistance rate among *A. baumannii* strains is a serious global issue . Resistance mechanisms often involve the development of β-lactamases, such as those found in Ambler classes A, D, and B. These enzymes are commonly linked to mobile genetic elements like plasmids Carbapenem resistance produced by MBL acquisition is thought to be more significant than other resistance mechanisms since MBLs can virtually completely hydrolyze all beta-lactam antibiotics except monobactams [37].

Further research is needed to monitor the dissemination of carbapenem-resistant OXA-type _-lactamase genes from *A. baumannii* in hospital settings, as they are becoming a substantial source of carbapenem resistance.

CONCLUSION

Patients' excessive use of antimicrobial medications led in the destruction of normal flora and the substitution of MDR isolates. This study found that β-lactamase-producing *A. baumannii* strains are a growing danger in ICUs. Proper diagnosis and isolation strategies can lower severe outcomes and patient mortality rates.

Declarations:

Conflicts of interest: There is no any conflict of interest associated with this study

Consent to participate: We have consent to participate.

Consent for publication: We have consent for the publication of this paper.

Authors' contributions: All the authors equally contributed the work.

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