Egyptian Journal of Medical Microbiology Volume 34 / No.2 / April 2025 217-224 Online ISSN: 2537-0979

ORIGINAL ARTICLE

# Impact of Matrix-Assisted Laser Desorption/Ionization Time-of-Flight Mass Spectrometry (MALDI-TOF MS) Coupled with Antimicrobial Stewardship Program on Pediatric ICU Patients in a Tertiary Care Pediatric Hospital

**[1]Hamsah A. Yousef, [1]Sahar M. Khairat, [1]Mona M. Abdelhalim, [2]Sally K.I. Ishak, [2]Elshimaa S. Ahmed, [1]Sherifa T. Salem***

[1]Department of Clinical and Chemical Pathology, Faculty of Medicine, Cairo University
[2]Department of Pediatrics, Faculty of Medicine, Cairo University

***Key words:***
***Antimicrobial resistance; Antimicrobial stewardship programs; Matrix-assisted laser desorption-ionization time of flight mass spectrometry; Cairo University Specialized Pediatric Hospital***

***Corresponding Author:***
Sherifa Tarek Salem
Department of Clinical and Chemical Pathology, Faculty of Medicine, Cairo University
ORCID: 0000-0003-2303-0619
cherifa_tarek@kasralainy.edu.eg

## ABSTRACT

***Background:*** *Antimicrobial resistance (AMR) poses a significant global threat to public health and safety. To address this challenge, antimicrobial stewardship programs (ASPs) play an important role in optimizing antimicrobial use, reducing adverse effects, and lowering healthcare costs. Integrating advanced diagnostics like MALDI-TOF MS enhances ASP effectiveness, potentially improving antimicrobial use, lowering AMR rates, and bettering patient outcomes.* ***Objective:*** *This study aimed to evaluate the clinical impact of implementing MALDI-TOF MS alongside ASP on the outcomes of PICU patients with various infections at Cairo University Specialized Pediatric Hospital (CUSPH).* ***Method:*** *A prospective cohort study was conducted in the PICUs at CUSPH. The 13-month study was divided into three phases: pre-implementation (baseline assessment), implementation (establishing guidelines and ASP orientation), and post-implementation. Key ASP indicators, such as length of stay, cure rate, mortality rate, length of therapy, and days of therapy, were measured.* ***Results:*** *In the post-implementation phase, both the average length of stay and mortality rate showed a notable decrease, with p-values of 0.059 and 0.06, respectively, suggesting a trend toward significance. The cure rate increased (p = 0.06). Additionally, the use of amphotericin significantly decreased (p = 0.03), while the use of cefepime (p = 0.002), clindamycin (p = 0.01), and linezolid (p = 0.03) increased. Klebsiella pneumoniae was the most isolated organism, accounting for 21% of cases.* ***Conclusion:*** *Integrating MALDI-TOF MS with ASP significantly reduce time to organism identification, improving time to optimal antibiotics therapy, with positive outcome measures including shortening hospital stays, increasing cure rate, and lowering mortality rates.*

## INTRODUCTION

Antimicrobial resistance (AMR) is one of the most pressing challenges in healthcare, The widespread and sometimes indiscriminate use of these drugs has accelerated the rise of resistant bacteria, making it increasingly difficult to treat even common infections. This growing resistance not only complicates treatment but also leads to longer hospital stays and higher healthcare costs[1].

In the fight against AMR, antimicrobial stewardship programs (ASPs) have become a vital weapon. ASPs are designed to ensure that antibiotics are used wisely and only when necessary, helping to prevent the overuse and misuse of antimicrobials. These programs also focus on minimizing the side effects of antimicrobial treatments, such as drug toxicity and harmful interactions, while aiming to reduce overall healthcare expenses. By adhering to evidence-based guidelines and encouraging thoughtful prescribing, ASPs are crucial in decreasing the spread of multidrug resistant organism (MDROs)[2].

Complementing ASPs, advanced diagnostic technology offers new possibilities for improving infection management. One of the most exciting developments is Matrix-assisted laser desorption-ionization time of flight mass spectrometry (MALDI-TOF MS). This technology allows for the rapid and precise identification of microorganisms at the species level, often within just 20 minutes. The swift and accurate results provided by MALDI-TOF MS are particularly critical in the management of urgent cases such as sepsis and pneumonia, where timely diagnosis is key to effective treatment. By quickly identifying pathogens, MALDI-TOF MS enables targeted therapy, which can significantly enhance patient outcomes and reduce the length of hospital stays[3].

We aimed in our study to evaluate the clinical impact of implementing MALDI-TOF MS and ASP, by creating clinical guidelines based on local epidemiology and antimicrobial susceptibility. We assessed the ASP's effect on optimizing antibiotic use, reducing expenditure, shortening therapy and hospital stays, and enhancing patient outcomes.

## METHODOLOGY

**Study Setting:**

This prospective cohort study was conducted in 3 Pediatric Intensive Care Units (PICUs) at Cairo University Specialized Pediatrics Hospital (CUSPH), a pediatric tertiary care teaching hospital.

**Inclusion Criteria:**

All patients admitted to the 3 PICUs of the CUSPH during the study period were included in this study.

**Study Design:**

The study was conducted on randomly selected 120 patients across the three PICUs from September 2022 to September 2023. The study was structured into three distinct phases: a pre-implementation phase from September 2022 to February 2023 (40 cases), an implementation phase from March 2023 to June 2023 (40 cases), and a post-implementation phase from July 2023 to September 2023 (40 cases).

**Phase 1: Pre-Implementation Phase**

**Objective:** To assess the baseline antimicrobial prescribing practices, resistance patterns, and clinical outcomes related to antimicrobial use.

**Activities:**

- Conducted a comprehensive evaluation of current antimicrobial prescribing practices.
- Examined clinical outcomes associated with antimicrobial therapy.

**Phase 2: Implementation Phase**

**Objective:** To establish and implement facility-specific antimicrobial stewardship guidelines based on our local disease epidemiology and antimicrobial susceptibility data.

**Activities:**

- Formed a multidisciplinary ASP team comprising infectious disease specialists, pharmacists, microbiologists, infection preventionists, and hospital administrators.
- Developed evidence-based antimicrobial guidelines tailored to our local epidemiology and susceptibility patterns.
- Provided education and training sessions for healthcare providers on antimicrobial resistance, appropriate antimicrobial use, and adherence to ASP guidelines.
- Implemented ASP core elements, including regular updates to guidelines and protocols.

**Phase 3: Post-Implementation Phase**

**Objective:** To evaluate the impact of the implemented ASP on clinical outcomes compared to the pre-implementation phase.

**Activities:**

- Measured ASP indicators such as length of hospital stay, mortality rates, cure rates, days of therapy, and length of therapy.
- Compared clinical outcomes between the pre-implementation and post-implementation phases to determine the effectiveness of the ASP.

**ASP design:**

ASP design was conducted by the clinical microbiology staff in collaboration with the departments of pediatrics and pharmacy. Antimicrobial stewardship strategic plans were approved by all ASP team members and disseminated to all PICU staff members in preparation for implementation.

During the implementation and post-implementation phases, the steps for antimicrobial prescription were as follows:

- Clinicians ensured culture specimens were taken before starting empiric antimicrobial therapy.
- ASP physician leader and clinical pharmacist revise and approve prior authorization request form for each targeted empiric antimicrobial agent, which was typically granted for 48 hours until culture and sensitivity results were available.
- If culture and sensitivity results were not yet verified, the physician contacted the ASP team to request re-evaluation and approval for continued use of the empiric antimicrobial therapy.

**Antimicrobial Prescription Guidelines:**

In our hospital, empirical therapy was initiated upon patient admission, guided by the diagnosis following Infectious Diseases Society of America guidelines (IDSA) and tailored based on our local epidemiology and antibiogram.

**Antimicrobial prescription was classified into 2 categories** according to the need for prior approval (authorization request form):

| **Antibiotics not requiring prior approval** | **Antibiotics must be according to cultures and need prior approval** |
|---|---|
| - Amoxycillin/flucloxacillin<br>- Amoxicillin/clavulanic acid<br>- Ampicillin/sulbactam<br>- Amikacin<br>- Gentamycin<br>- Acyclovir<br>- Azithromycin<br>- Cefobid<br>- Ceftazidime<br>- Ceftriaxone<br>- Cefotaxime<br>- Cefipime<br>- Ciprofloxacin | - Meropenem<br>- Imipenem<br>- Ertapenem<br>- Levofloxacin<br>- Tigecycline<br>- Colistin<br>- Vancomycin<br>- Tiecoplanin<br>- Linezolid<br>- Piperacillin Tazobactam<br>- All antifungals |

**Microbiology Workup:**

All pathogens retrieved from different patients' samples were identified using MALDI-TOF MS following manufacturer's instructions. Identified microorganisms were reported immediately along with their specific antibiograms, reducing the time to organism identification and allowing for the de-escalation of empirical antibiotic prescriptions based on our customized antimicrobial susceptibility patterns.

For critical samples like blood and body fluid cultures, antimicrobial susceptibility testing (AST) was performed using the VITEK®2 Compact system. For other cultures, AST was performed using disk diffusion method. All AST were interpreted according to the latest CLSI guidelines[4].

**Data collection & metrics:**

Data collection included name; age; sex; date of admission; date of discharge; clinical diagnosis; outcome of the patient; indication, and proof of infection at the start of antibiotic therapy; 48 hours and 5 days reviews of therapy; MALDI-TOF result; time to micro-organism identification and antimicrobial susceptibility testing (AST) results. Different metrics tools were assessed and compared in pre-implementation phase 1 versus post-implementation phase 3: Turnaround time to pathogen identification and total turnaround time (TAT); process measures (days of therapy "DOT" & length of therapy "LOT"); and outcome measures (mortality rate, cure rate & length of stay)[5].

**Statistical analysis**

Data analysis was conducted with SPSS version 24. Descriptive statistics, including mean and standard deviation, were used to summarize normal quantitative data, while median and interquartile range were applied for abnormal quantitative data. Frequencies were used to summarize qualitative data. Bivariate relationships were examined using cross-tabulations, with chi-square and Fisher's exact tests used for comparing proportions. The independent t-test was employed to compare normally distributed quantitative data, while the Mann-Whitney U test was used for skewed data. Statistical significance was determined with *p value* of less than 0.05.

## RESULTS

**Patient Demographics and Diagnosis:**

A total of 120 patients admitted to 3 PICUs at CUSPH were randomly selected during the pre-implementation, implementation, and post-implementation phases, with 40 patients in each phase; 63% (n=76) were males, and 37% (n=44) were females. The primary reason for antimicrobial prescriptions was pneumonia, accounting for 40% (n=48) of the cases, followed by sepsis 33% (n=39) and post-operative cases 17% (n=20).

**Isolated microorganisms:**

The majority of organisms isolated during the study were *Klebsiella pneumoniae*, accounting for 21% (n=25) followed by *Staphylococcus hominis* (18%, n=18), *Pseudomonas aeruginosa* (13%, n=15), and *Methicillin-resistant Staphylococcus aureus* (*MRSA)* (9%, n=11).

**Change of percent susceptibility of organisms:**

Change of percent susceptibility of the 4 most common isolated organisms (*Klebsiella pneumoniae, Pseudomonas aeruginosa, Staphylococcus hominis &* methicillin resistant *Staphylococcus aureus* "MRSA"*)* to different antibiotics are summarized in tables 1 & 2.

**Table 1: Change of percent susceptibility of gram-negative organisms**

| Antibiotic | *Klebsiella pneumoniae* | | | | *Pseudomonas aeruginosa* | | | |
|---|---|---|---|---|---|---|---|---|
| | **Phase 1** | **Phase 2** | **Phase 3** | **Change in %S*** | **Phase 1** | **Phase 2** | **Phase 3** | **Change in %S*** |
| Imipenem | 14% | 14% | 0% | Decreased | 0% | 67% | 0% | Decreased |
| Meropenem | 0% | 13% | 0% | Decreased | 17% | 50% | 0% | Decreased |
| Co-trimoxazole | **11%** | **0%** | **20%** | **Improved** | -- | -- | -- | -- |
| Amikacin | 33% | 17% | 0% | Decreased | -- | -- | -- | -- |
| Gentamicin | 14% | 14% | 0% | Decreased | -- | -- | -- | -- |
| Tigecycline | **29%** | **50%** | **67%** | **Improved** | -- | -- | -- | -- |
| Levofloxacin | 0% | 13% | 0% | Decreased | 60% | 67% | 20% | Decreased |
| Ciprofloxacin | **0%** | **0%** | **13%** | **Improved** | 50% | 50% | 20% | Decreased |
| Colistin | **-** | **13%** | **60%** | **Improved** | 100% | 100% | 100% | No change |
| Cefepime | **0%** | **0%** | **14%** | **Improved** | 0% | 67% | 0% | Decreased |
| Aztreonam | -- | -- | -- | -- | **20%** | **50%** | **80%** | **Improved** |

*%S = Percent sensitivity

**Table 2: Change of percent susceptibility of gram-positive organisms**

| Antibiotic | **MRSA** | | | | ***Staphylococcus hominis*** | | | |
|---|---|---|---|---|---|---|---|---|
| | **Phase 1** | **Phase 2** | **Phase 3** | **Change in %S*** | **Phase 1** | **Phase 2** | **Phase 3** | **Change in %S*** |
| Vancomycin | 100% | 100% | 100% | No change | 100% | 100% | 100% | No change |
| Linezolid | 100% | 100% | 100% | No change | 100% | 100% | 100% | No change |
| Teicoplanin | 100% | 100% | 100% | No change | 100% | 100% | 100% | No change |
| Doxycycline | **25%** | **67%** | **100%** | **Improved** | -- | -- | -- | -- |
| Erythromycin | **14%** | **33%** | **100%** | **Improved** | 0% | 40% | 0% | No change |
| Clindamycin | **14%** | **67%** | **100%** | **Improved** | **0%** | **60%** | **71%** | **Improved** |
| Co-trimoxazole | **29%** | **67%** | **100%** | **Improved** | 50% | 57% | 43% | Decreased |
| Ciprofloxacin | **0%** | **33%** | **100%** | **Improved** | **67%** | **71%** | **71%** | **Improved** |
| Levofloxacin | **29%** | **67%** | **100%** | **Improved** | 75% | 86% | 71% | Decreased |
| Gentamicin | 0% | 33% | 0% | Decreased | **50%** | **57%** | **71%** | **Improved** |

*%S = Percent sensitivity

**Turnaround time:**

MALDI-TOF MS led to a statistically significant decrease (*p-value* <0.001) in TAT for pathogen identification by 1 day (from 3 days to 2 days) (Figure 1).

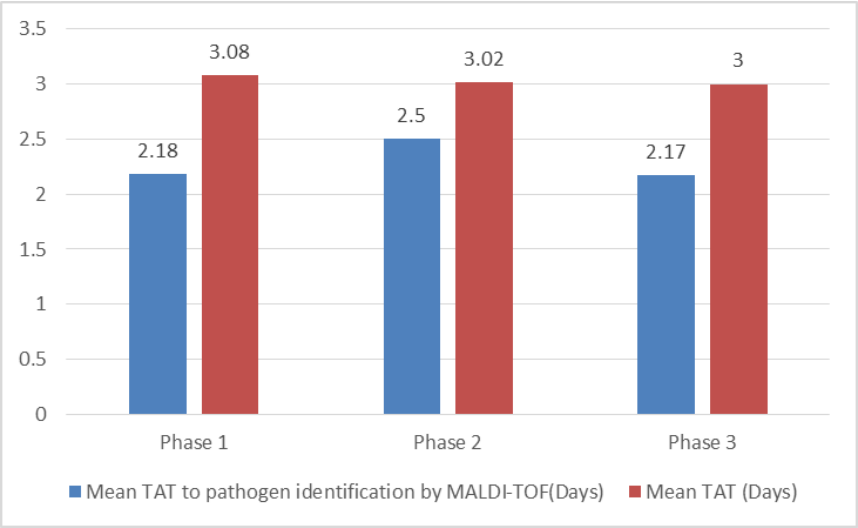


**Fig. 1:** The average turnaround time (TAT) to pathogen identification compared to average Total turnaround time in three phases

**Process Measures:**

**Days of therapy (DOT)**

The Days of Therapy per 1000 Patient Days increased from 1884 days/1000 PD in Phase 1 versus 2541 days/1000 PD in Phase 3, with no statistical significance (*P = 0.219*).

**Length of Therapy (LOT)**

The Length of Therapy per 1000 Patient days significantly increased from 896 days/1000 PD in Phase 1 versus 927 days/1000 PD in Phase 3 (*P = 0.01*).

**Days of Therapy for Each Antimicrobial:**

All through the 3 phases, there was a statistically significant decrease in the use of amphotericin B (*P = 0.03*). Conversely, there was a statistically significant increase in the use of cefepime (*P = 0.002*), clindamycin (*P = 0.01*), and linezolid (*P = 0.03*) (Table 3).

**Table 3:** Days of Therapy/1000 patient Days for Each Antimicrobial in the 3 Phases

| Antimicrobial | Phase 1 (PD* 1301) | Phase 2 (PD* 923) | Phase 3 (PD* 490) | *P value* |
|---|---|---|---|---|
| Vancomycin | 109 | 238 | 273 | 0.48 |
| Meropenem | 530 | 616 | 482 | 0.54 |
| Imipenem | 27 | 0 | 55 | 0.35 |
| Ampicillin sulbactam | 40 | 23 | 0 | 1.0 |
| Piperacillin tazobactam | 23 | 12 | 104 | 0.9 |
| Cefepime | 100 | 176 | 231 | 0.002 |
| Ceftriaxone | 19 | 7 | 0 | 0.56 |
| Ceftazidime | 3 | 9 | 8 | 0.26 |
| Amikacin | 52 | 34 | 37 | 0.6 |
| Gentamicin | 2 | 18 | 14 | 0.2 |
| Tigecycline | 17 | 79 | 80 | 0.94 |
| Ciprofloxacin | 38 | 31 | 65 | 0.79 |
| Levofloxacin | 58 | 100 | 55 | 0.42 |
| Colistin | 331 | 352 | 245 | 0.26 |
| Clindamycin | 21 | 46 | 127 | 0.01 |
| Azithromycin | 0 | 4 | 0 | - |
| Ceftazidime avibactam | 85 | 78 | 84 | 0.34 |
| Linezolid | 179 | 94 | 247 | 0.03 |
| Teicoplanin | 9 | 0 | 33 | 0.12 |
| Ertapenem | 24 | 34 | 0 | 0.32 |

*PD = Patient days

**Outcome Measures**

**Length of stay**

The average length of stay decreased from 32.5 days in Phase 1 to 12.25 days in Phase 3 (*P = 0.059*), indicating an improvement though not statistically significant.

**Mortality rate and cure rate**

The mortality rate decreased from 33% in Phase 1 to 23% in Phase 3, while the cure rate increased from 68% in Phase 1 to 78% in Phase 3 (*P = 0.06* for both).

## DISCUSSION

Several studies have shown that combining MALDI TOF MS identification with antimicrobial stewardship intervention improves patient outcomes compared to standard organism identification approaches. However, this combination is only available at a few institutions, indicating that more research was required[6].

The distribution of the isolated organisms in our study showed that, *Klebsiella pneumoniae* was the most prevalent organism (21%), followed by *Staphylococcus hominis* (18%), *Pseudomonas aeruginosa* (13%), and *MRSA* (9%), which aligns with some previous research, such as Campos et al.[7], who also noted the predominance of *Klebsiella pneumoniae* and *Acinetobacter baumannii* in their study and with *Kamath*[8] who reported that *Klebsiella pneumoniae* as the commonest pathogen (38.7%).

However, our study disagreed with Cavalieri et al.[9], where *E. coli* (30%) was reported as the most common isolate followed by *methicillin-sensitive S. aureus (MSSA)* (9%), *Streptococcus pneumoniae* (8%), and *Pseudomonas aeruginosa* (7%) However, these

discrepancies could be due to epidemiological variations.

In our study, MALDI-TOF MS resulted in a significant reduction in the average time to organism identification across the 3 phases when compared to the total TAT (from 3 days to 2 days, *p<0.01*) leading to a quicker and much more accurate identification process across the three phases of the study allowing for faster and potentially more targeted empiric treatment.

Our findings were similar to Uzuriaga et al.[10], who observed a statistically significant decrease in the microbiological identification time by MALDI-TOF MS in the intervention group when compared to the control group where microbiological identification was done using conventional method (11.44 h CG vs. 4.48 h IG (*p <0.01*) allowing for rapid communication of microbiological identification to clinicians and early optimization of antibiotic prescription.

Notably, implementing our intervention was associated with a marginally significant reduction in the average length of hospital stays, from a mean of 32.5 days in the pre-implementation phase to 12.2 days in the post-implementation phase (*P=0.059*). This improvement in efficiency and the reduced length of hospital stays can contribute to better capacity for providing medical services, especially in an overcrowded tertiary hospital.

Our findings were similar to Wassef et al.[11], who observed a significant decline in the mean length of hospital stays from a mean of 10.66 days to 9.16 days post-implementation, and *Campos et al.* [7], who reported significantly lower length of stays in the intervention period (44 days vs. 39 days; *p = 0.005*). Additionally, *Renk et al.*[12], reported a decrease in the mean PICU length of stay from pre-implementation (6 days) to post-implementation (5 days) supporting the idea that interventions or changes in procedures can impact on the duration of hospitalization, where reducing the length of hospital stays can have various positive implications, including better resource utilization, improved patient flow, and potentially lower healthcare costs.

The reduction in mortality rate was observed in our study from 33% in Phase 1 to 23% in Phase 3 (*P = 0.06*), as well as the increase in the cure rate from 68% in Phase 1 to 78% (*P = 0.06*), in Phase 3, suggests a positive impact of the intervention on patient outcomes, our findings align with *Wassef et al.* [11], who also reported a decrease in overall mortality from 31.1% to 24.8%.

It's interesting to note the discrepancy with *Chorafa et al.*[13], where no increase or, in some cases, a reduction in mortality rate was reported after the intervention in eight out of eleven studies. Similarly, Aiesh et al.[14], reported that the mortality mean was 2.34 ± 0.57 in the pre-ASP period, while the mean was 2.88 ± 0.95 in the post-ASP period. However, these discrepancies highlight the complexity of antimicrobial stewardship programs and their impact on mortality rates.

In our study, we observed that the total days of therapy (DOT) per 1000 patient days did not decrease and actually showed a slight, insignificant increase in Phase 3 (2,541 days/1000 PD) compared to Phase 1 (1,884 days/1000 PD) (P value=0.219). This is likely due to the high rate of multidrug-resistant organisms (MDRO) in the study population, leading physicians to prescribe double or even triple antibiotics to combat this resistance. Additionally, this can be explained by the short period of this study. It may need to be conducted on a larger scale and over a longer duration period to be able to reduce antibiotic resistance efficiently which needs a longer period of strict implementation of properly monitored ASP.

This finding was similar to the results reported by Kazzaz et al.[15], who noted a rising trend in total antibiotic consumption over time. We suggest that this increase might be attributed to the prevalence of multidrug-resistant (MDR) organisms and the challenges associated with their treatment.

Our finding contrasts with Renk et al.[12], where a significant reduction in total DOT/1000 PD of the PICU stays from 1226 to 1000 (*p = 0.005*) was reported in the post-implementation period. Alfraij et al.[16], 2023, also reported an overall reduction in DOT after implementing Tele-ASP from 922 to 485 DOT/1000 PD (*p < 0.05*).

The discrepancies in findings could stem from various factors, including differences in patient populations, interventions implemented, and the nature of the antimicrobial resistance landscape in each study setting.

In our study, the length of therapy/1000 patient days significantly increased from 896 PD/1000 PD in Phase 1 to 927 PD/1000 PD in Phase 3 (*P<0.01)*, This increase could be attributed to the same causes mentioned earlier.

This contrasts with Renk et al.[12], where LOT/1000 PD was reduced insignificantly by 83 days (*p = 0.09*). Also, Wassef et al.[11] and Chorafa et al.[13], observed a significant reduction in the length of therapy from 1502 days to 1318 days (*p = 0.001*) and from 8.8 ± 7.8 days in 2017 to 6.7±3.8 days in 2018, (*P=0.036*) respectively.

Our study showed positive effect of the ASP in optimizing some antimicrobial DOT in phase 3 compared to phase 1 including meropenem (from 530 to 482/1000 PD, *p=0.054*), levofloxacin (58 to 55/1000 PD, *p=0.42*), colistin (331 to 245/1000 PD, *p=0.26*) and ceftazidime avibactam (85 to 84/1000 PD, *p=0.34*). This agreed with Renk et al., who stated that Mean carbapenem utilization decreased by 44%, particularly for meropenem by 49%, which was marginally significant (*p = 0.07*) [12]. Wassef et al.[11] reported a significant decrease in DOT regarding ceftazidime,

ceftriaxone, amikacin, cephalosporins, aminopenicillins with beta-lactamase, piperacillin-tazobactam, meropenem, ciprofloxacin, all aminoglycosides, trimethoprim-sulfamethoxazole, vancomycin, and metronidazole in the post-implementation phase, and Chiotos et al.[17] who stated that overall vancomycin DOT per 1000 patient days in the PICU decreased from a baseline mean of 182 DOT per 1000 patient days to 109 DOT per 1000 patient days (a 40% reduction).

An improvement was observed in the susceptibility of *Pseudomonas aeruginosa* to Aztreonam and decreased susceptibility to amikacin, meropenem, ciprofloxacin, levofloxacin, piperacillin/tazobactam and gentamicin in Phase 3 compared to Phase 1. This disagreed with the findings of Aiesh et al.[14], who reported a statistically significant increase in the susceptibility of *Pseudomonas aeruginosa* to amikacin, gentamicin, tobramycin, ciprofloxacin, meropenem, piperacillin, and piperacillin/tazobactam.

Additionally, Sid Ahmed et al.[18] reported a decrease in the resistance patterns of multidrug-resistant *Pseudomonas aeruginosa* to piperacillin/tazobactam, meropenem, ciprofloxacin, and amikacin.

In our study, we observed improved susceptibility to Co-Trimoxazole, Tigecycline, Colistin, Cefepime, and Ciprofloxacin while decreased susceptibility for meropenem and imipenem in *Klebsiella pneumoniae* in Phase 3 compared to Phase 1. This contrasts with the findings of Elsawah et al.[19], who reported a decrease in the incidence of carbapenem-resistant *Klebsiella* from 85.25% of total *Klebsiella* isolates to 48.6%.

## CONCLUSION

The synergy between ASPs and MALDI-TOF MS represents a groundbreaking approach to tackling AMR. Combining the strategic oversight of antimicrobial use with the advanced diagnostic capabilities of MALDI-TOF MS offers a powerful dual strategy. This integration not only sharpens diagnostic accuracy but also fine-tunes antimicrobial stewardship, leading to improved patient care and a stronger defense against AMR.

## LIMITATIONS

- Relatively small sample size and short observation period.
- Lack of financial resources and an effective IT electronic system linking multidisciplinary departments, which may have impacted data collection and analysis.
- Highly prevalent multidrug-resistant organisms (MDROs) resulted in prescription of multiple antimicrobial agents to overcome this resistance.

**Declarations:**

**Ethical Approval:**

The study was approved by the Research Ethical Committee of the faculty of medicine, Cairo University on 04/08/2022 (MD-175-2022).

**Data availability:**

All data generated during this study are included in this published article.

**Competing interests:**

The authors declare that they have no competing interest. The authors have no relevant financial or non-financial interests to disclose.

**Funding:** No funds, grants, or other support was received.

## REFERENCES

1. Akinkugbe O, Cooke FJ, Pathan N. Healthcare-associated bacterial infections in the paediatric ICU. JAC Antimicrob Resist. 2020;2(3). https://doi.org/10.1093/jacamr/dlaa066.
2. Fresán-Ruiz E, Izurieta-Pacheco AC, Girona-Alarcón M, et al. Antimicrobial stewardship improvement in pediatric intensive care units in Spain—What have we learned? Children (Basel). 2022;9(6):902. https://doi.org/10.3390/children9060902.
3. Żukowska M. Advanced methods of bacteriological identification in a clinical microbiology laboratory. J Pre Clin Clin Res. 2021;15(2):68-72. https://doi.org/10.26444/jpccr/134646.
4. Clinical Laboratory Standards Institute (CLSI). Performance standards for antimicrobial susceptibility testing. 32nd Informational Supplement (M100-S32), Wayne, PA, USA. 2022
5. Benić MS, Milanič R, Monnier AA, et al. Metrics for quantifying antibiotic use in the hospital setting: Results from a systematic review and international multidisciplinary consensus procedure. J Antimicrob Chemother. 2018;73(vi50-vi58). https://doi.org/10.1093/jac/dky118.
6. Niwa T, Yonetamari J, Hayama N, et al. Clinical impact of matrix-assisted laser desorption ionization-time of flight mass spectrometry combined with antimicrobial stewardship interventions in patients with bloodstream infections in a Japanese tertiary hospital. Int J Clin Pract. 2019;73(5). https://doi.org/10.1111/ijcp.13332.
7. Campos AF, Arantes T, Cambiais AMVB, et al. Impact of an Antimicrobial Stewardship Program intervention associated with the rapid identification of microorganisms by MALDI-TOF and detection of resistance genes in ICU patients with Gram-negative bacteremia. Antibiotics. 2022;11(9):1226. https://doi.org/10.3390/antibiotics11091226.

8. Kamath SR. Multidrug resistance: The growing menace in PICU. Indian J Crit Care Med. 2023;27(1):6-7. https://doi.org/10.5005/jp-journals-10071-24394.
9. Cavalieri SJ, Kwon S, Vivekanandan R, et al. Effect of antimicrobial stewardship with rapid MALDI-TOF identification and Vitek 2 antimicrobial susceptibility testing on hospitalization outcome. Diagn Microbiol Infect Dis. 2019;95(2):208-211.https://doi.org/10.1016/j.diagmicrobio.2019.05.020.
10. Uzuriaga M, Leiva J, Guillén-Grima F, Rua M, Yuste JR. Clinical Impact of Rapid Bacterial Microbiological Identification with the MALDI-TOF MS. Antibiotics. 2023; 12(12). https://doi.org/10.3390/antibiotics12121660.
11. Wassef MAA, Sayed AM, Aziz HSA, Meligy B, Halim MMA. Implementation and evaluation of antimicrobial stewardship program in medical ICU in Cairo University Specialized Pediatric Hospital. Open Access Maced J Med Sci. 2020;8(B):716-722. https://doi.org/10.3889/oamjms.2020.4553.
12. Renk H, Sarmisak E, Spott C, et al. Antibiotic stewardship in the PICU: Impact of ward rounds led by paediatric infectious diseases specialists on antibiotic consumption. Sci Rep. 2020;10(1):65671. https://doi.org/10.1038/s41598-020-65671-0.
13. Chorafa E, Komatsiouli V, Iosifidis E, et al. Antimicrobial stewardship programs in PICU settings: A systematic review. Pediatr Crit Care Med. 2023;24(1). https://doi.org/10.1097/PCC.0000000000003069.
14. Aiesh BM, Nazzal MA, Abdelhaq AI, et al. Impact of an antibiotic stewardship program on antibiotic utilization, bacterial susceptibilities, and cost of antibiotics. Sci Rep. 2023;13(1). https://doi.org/10.1038/s41598-023-32329-6.
15. Kazzaz YM, AlTurki H, Aleisa L, et al. Evaluating antimicrobial appropriateness in a tertiary care pediatric ICU in Saudi Arabia: a retrospective cohort study. Antimicrob Resist Infect Control. 2020;9(1):42. https://doi.org/10.1186/s13756-020-00842-2.
16. Alfraij A, Abdelmoniem A, Elseadawy M, et al. The effect of Telehealth Antimicrobial Stewardship Program (Tele-ASP) on antimicrobial use in a pediatric intensive care unit: Pre- and post-implementation single center study. J Infect Public Health. 2023;16(9):1361-1367.https://doi.org/10.1016/j.jiph.2023.06.010.
17. Chiotos K, Fitzgerald JC, Hayes M, et al. Improving Vancomycin stewardship in critically ill children. Pediatrics. 2022;149(4). https://doi.org/10.1542/peds.2021-052165.
18. Sid Ahmed, M. A., Abdel Hadi, H., Abu Jarir, S., Al Khal, A. L., Al-Maslamani, M. A., Jass, J., Ibrahim, E. B., & Ziglam, H. (2020). Impact of an antimicrobial stewardship programme on antimicrobial utilization and the prevalence of MDR Pseudomonas aeruginosa in an acute care hospital in Qatar. JAC-Antimicrobial Resistance. 2020;2(3). https://doi.org/10.1093/jacamr/dlaa050
19. Elsawah H, Samir A, Elrazzaz M, Ramadan A, Elnaggar A, Taema K. Carbapenems consumption and Klebsiella resistance in intensive care units in Egypt: A study to evaluate the effect of an antimicrobial stewardship program. J Infect Prev. 2022 Jul;23(4):142-148. doi: 10.1177/17571774211060436.