Impact of Rapid Identification (ID) and Antimicrobial Susceptibility Testing (AST) on Antibiotic Therapy and Outcomes for Patients with Bacteraemia/Candidaemia

Sahil Sheth[1,2], Michael Miller[2], Scott Baker[2]

[1]University of Maryland Eastern Shore – School of Pharmacy and Healthcare Professions, Maryland, USA;
[2]Peninsula Regional Medical Center – Department of Pharmacy, Maryland, USA

Sahil Sheth, PharmD
University of Maryland Eastern Shore
School of Pharmacy and Healthcare Professions
College Backbone Rd, Princess Anne, MD 21853
Office: Hazel Hall, Room 1041 (410-543-7306)

AMENDED ABSTRACT

Background: Bloodstream infections (BSI) are associated with increased morbidity and mortality, especially when caused by gram-negative or fungal pathogens. Studies have shown that rapid ID/AST improves patient outcomes such as shortened time to effective therapy and quicker antimicrobial de-escalation. The objective of this study was to assess the impact of rapid ID/AST with the Accelerate Pheno™ system (AXDX) from May 2018 to December 2018 on antibiotic therapy and patient outcomes.

Methods: This was an IRB-approved quasi-experimental study conducted at PRMC with a retrospective (pre-implementation group with VERIGENE® system testing for 100 patients) arm and a prospective (post-implementation of rapid ID/AST with AXDX for 100 patients) group. All patients with positive blood cultures from gram-negative rods or *Candida* species and hospital admission for greater than 24 hours were included. Data included patient demographics, Charlson comorbidity scores, source of infection, empiric and targeted antibiotic selection, time to escalation/de-escalation of antibiotics, antibiotic intensity score (at 96 hours), and hospital length of stay (LOS)

Results: Of 100 patients with gram-negative bacteraemia or candidaemia in each cohort, 84 met inclusion criteria in the pre-implementation group and 89 met criteria in the AXDX group for final analysis. There were no statistical differences between patient demographics, level of immunosuppression, diagnosis of septic shock, or Charlson comorbidity score in the two groups. Both groups had a comparable 14 day mortality (0% vs 3.6%, p = 0.11). AXDX group had a decreased time to first antibiotic intervention (26.3 vs 8.0 p=0.003), hours to most targeted therapy (14.4 vs 9, p=0.03), hospital LOS (6 vs 8, p=0.002), median days of broad-spectrum antibiotic therapy (3 vs 1, p<0.001), and average antibiotic intensity score at 96 hours (16 vs 12, p=0.002).

Conclusions: In this analysis of patients with gram-negative bacteraemia or candidaemia, rapid ID/AST implementation was associated with decreased hospital LOS, decreased use of broad-spectrum antibiotics, shortened time to targeted therapy, and an improved utilization of antibiotics within the first 96 hours of therapy.

INTRODUCTION

- Gram-negative rod bacteraemia is associated with significant morbidity and mortality in hospitalized patients[1]
- Early and effective antimicrobial administration is essential to improve patient outcomes and overall survival[2]
- Every hour of delay in initiating appropriate antimicrobial therapy in patients with sepsis has decreased survival by approximately 8%[2]
- Rapid ID and AST can optimize microbiology workflows, decrease time to result, and offer clinicians the potential to improve time to antibiotic tailoring[3]
- The Accelerate Pheno™ system is a fully-automated, rapid diagnostic system that is used directly on positive blood cultures. It performs gel electrofiltration and fluorescence *in situ* hybridization for ID and automated microscopy for observation of bacterial growth and extrapolation of MICs for AST
- The purpose of this study was to investigate and evaluate the impact of using rapid ID and AST via AXDX on antimicrobial stewardship and clinical patient outcomes

METHODS

Inclusion criteria

- Patients with positive blood cultures from gram-negative rods or *Candida* species
- Patients continuously hospitalized for the first 24 hours from blood draw

Exclusion criteria

- Patients with positive blood cultures within the past 7 days
- Patients deceased at time of positive blood culture
- Patients in comfort care or in hospice
- Patients designated for organ donation

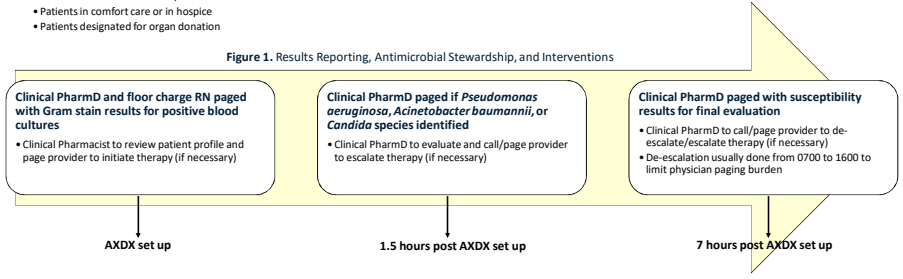
Primary Endpoints

- 14 day mortality
- Time to first antibiotic intervention
- Time to most targeted antibiotics

Secondary Endpoints

- Hospital and ICU LOS
- Antibiotic intensity score at 96 hrs
- 30-day readmission
- Days of mechanical ventilation

Figure 1. Results Reporting, Antimicrobial Stewardship, and Interventions



RESULTS

Figure 2. Flowchart of Study Participants

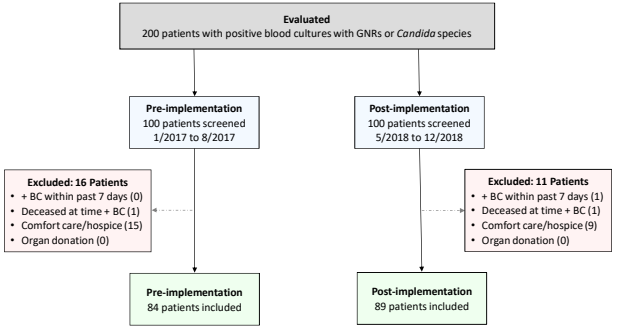


Figure 3. Distribution of Pathogens in Pre-implementation Group

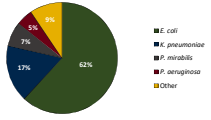


Figure 4. Distribution of Pathogens in Post-implementation Group

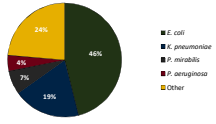
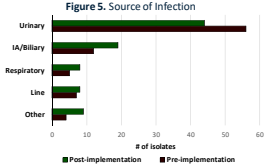


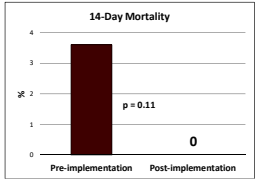
Table 1. Patient Demographics

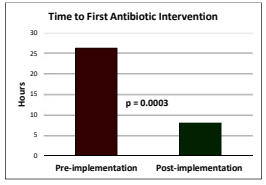
Variable	Pre-implementation	Post-implementation	P-value
Median age in years (IQR)	71 (60-79)	70 (60-79)	0.88
Female (%)	42 (50)	48 (53.9)	0.60
Immunosuppression (%)	13 (15.5)	19 (21.4)	0.32
Charlson Comorbidity Score (IQR)	5 (3.0-7.0)	5 (3.5-8.0)	0.29
Septic Shock Diagnosis (%)	13 (15.5)	7 (7.9)	0.12

Figure 5. Source of Infection



Primary Endpoints





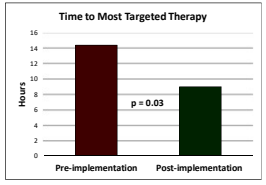


Table 2. Secondary and Pre-defined Endpoints

Endpoint Measured	Pre-implementation	Post-implementation	P-value
Hospital LOS (IQR)	8 (6-10.75)	6 (4.5-8.5)	0.002
Antibiotic Intensity Score (IQR)	16 (10.5-20)	12 (9-15.5)	0.0002
30 day readmission (%)	7 (8.6)	5 (5.6)	0.44
Hospital LOS post + BC (IQR)	6 (4-9)	5 (3-7)	0.01
Median days broad-spectrum antibiotics (IQR)	3 (2-3)	1 (0.5-2)	<0.0001

CONCLUSION

- Rapid ID/AST implementation via AXDX was associated with a statistically significant decrease in time to first antibiotic intervention, time to most targeted antibiotics, and antibiotic intensity score at 96 hours after positive blood culture which is essential in improving antimicrobial stewardship programs across hospital systems
- Hospital LOS for patients in the AXDX implementation group was significantly lower than pre-implementation group, which can have a substantial impact on decreasing hospital costs
- Clinical pharmacists can play a crucial role in reading AST results, identifying drug-bug mismatches, and contacting attending providers for possible escalation, de-escalation, or modification of therapy
- Multi-center prospective studies are required to fully evaluate the impact of rapid ID/AST implementation via AXDX and its effects on clinical outcomes and antimicrobial stewardship programs

Limitations

- Single center, retrospective data collection for pre-implementation patient group
- Low sample size in both groups
- More vigilant de-escalation during 0700 – 1600 during post-implementation group period
- Inherent provider and PharmD approach differences

Disclosures
Authors of this presentation have the following to disclose concerning financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation:
- **Sahil Sheth**: Grant investigator
- **Michael Miller**: Grant investigator
- **Scott Baker**: Nothing to disclose

Accelerate Diagnostics, Inc. provided financial support for this study but was not involved in the study design, data collection, or data interpretation

Acknowledgements
We thank the staff of **PRMC Microbiology Laboratory** for their collaborative efforts. We thank **Dennis Killian** and **John Jordan** for their administrative assistance. We thank **Accelerate Diagnostics, Inc.** for their provision of the Accelerate Pheno™ system. We thank **Shawn MacVane** from Accelerate Diagnostics, Inc. for his assistance with statistical analysis.

References

1. Suárez CJ, Lolans K, Villegas MV, Quinn JP. Mechanisms of resistance to beta-lactams in some common Gram-negative bacteria causing nosocomial infections. *Expert Rev Anti Infect Ther.* 2005;3(6):915-22.
2. Singer M, Deutschman CS, Seymour CW, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA.* 2016;315(8):801-10.
3. Maurer FP, Christner M, Hentschke M, Rohde H. Advances in Rapid Identification and Susceptibility Testing of Bacteria in the Clinical Microbiology Laboratory: Implications for Patient Care and Antimicrobial Stewardship Programs. *Infect Dis Rep.* 2017;9(1):6839.