The Impact of Antimicrobial Stewardship in Treating Patients with *Escherichia coli* Bacteremia in a Small Single Center Community Hospital

Hardik H. Patel, PharmD, BCPS, MHA Candidate[1]; Betcy Benny, PharmD Candidate[2]; Prerna Nahar, PharmD Candidate[3]; Alex Landis, PharmD Candidate[3]
[1] Holy Redeemer Hospital, Meadowbrook, PA
[2] Saint Joseph's University Philadelphia College of Pharmacy
[3] Temple University School of Pharmacy

Abstract
Purpose: There are many challenges that pharmacist led antimicrobial stewardship programs can encounter including lack of resources, costs, and inaccurate antimicrobial susceptibility testing (AST) results. The COVID-19 pandemic has led to increased resistance especially with gram negative infections. At a small single center community hospital, gram negative infections, particularly *Escherichia coli* infections, predominately occur. Therefore, this study aims to address gram negative bacteremia burden and its impact on antimicrobial stewardship efforts for combatting *Escherichia coli* and ESBL organisms with such barriers during the pandemic.
Methods: In a retrospective cohort study, patients ≥ 18 years of age from a small community hospital were reviewed. Patients were excluded if their blood cultures were not positive for *Escherichia coli* and if antibiotics were not initiated during hospital stay. The primary endpoint was to determine the length of hospital stay. Critical secondary endpoints include antibiotic de-escalations, duration of antibiotics, time to definitive antibiotic therapy, serum procalcitonin levels, blood culture availabilities, MIC breakpoints, co-infection of COVID-19, and *Clostridioides difficile* occurrences.
Results: Out of 74 patients with gram negative bacteremia, 41 patients specifically had *Escherichia coli* bacteremia. The primary endpoint results showed that patients with *Escherichia coli* bacteremia that stayed in the ICU had a length of stay of 13.6 days. Patients with *Escherichia coli* bacteremia in the Non-ICU setting has a length of stay of 7.3 days, and patients with ESBL bacteremia in the Non-ICU setting had a length of stay of 6.8 days.
Conclusions: Despite the various challenges that antimicrobial stewardship programs (ASP) face in a single center small community hospital, the ASP at this small community hospital utilizes various policies and tools to increase appropriate antibiotic use and decrease hospital length of stay in patients with *Escherichia coli* bacteremia.

Key Words: Antimicrobial Stewardship Program; COVID-19; Escherichia coli; Bloodstream Infection; Procalcitonin

Introduction

Antimicrobial Stewardship Programs (ASP) are designed to prevent any unnecessary use of antibiotics and decrease antibiotic resistance. About 30% of all antibiotics prescribed in U.S acute care hospitals are either unnecessary or suboptimal. In 2014, Centers for Disease Control and Prevention (CDC) implemented Antibiotic Stewardship Program (Core Elements) in hospitals across the United States. The newest update to the Core Elements includes hospital leadership commitment, accountability, pharmacy expertise, action, tracking, reporting and education.[4] The percentage of hospitals implementing ASP increased from 48% in 2015 to 91% in 2020.[5] Antimicrobial Stewardship Programs became a necessity for healthcare system across the nation during year 2020-22 in addition to combating COVID-19. Such correlation between COVID-19 pandemic and its impact on rise in antimicrobial resistance required a closer look into local trends in community hospitals. Ultimately, the COVID-19 pandemic has led to the increase in antimicrobial use, difficulty following infection prevention actions, and an overall increase in healthcare-associated, antimicrobial-resistant infections. The pandemic has resulted in hospitals seeing sicker patients requiring a longer length of stay, consequently leading to more resistant infections. In particular, the rate of extended spectrum beta-lactamase (ESBL) producing enterobacterales in the hospital setting has increased by 32% from 2019-2020 alone.[1] Gram negative bloodstream infections are a major cause of morbidity and mortality and *Escherichia coli* accounts for majority of gram negative bacteria hospital infections.[2] The Infectious Disease Society of America (IDSA) addresses treatment of resistant gram negative infections, however we wanted to focus on the management of the most prevalent gram negative organism of *Escherichia coli* overarching guidelines that direct the management of gram negative bacteremia.[3] Currently, in a small single center community hospital, gram negative infections are increasing along with antibiotic resistance. Therefore, it is pivotal to assess gram negative bacteremia burden and its impact on antimicrobial stewardship efforts for combatting *Escherichia coli* and ESBL organisms during the COVID pandemic.

The increased use of ASP programs has resulted in reduced antimicrobial use and cost, and lower incidence of healthcare associated infections.[6] The small community hospital is governed by DNV which uses the Core Elements as a foundation

Corresponding Author: Hardik H. Patel, PharmD, BCPS, MHA Candidate
Redeemer Health - Holy Redeemer Hospital, Meadowbrook, PA
Email: hpatel@holyredeemer.com

DOI: https://doi.org/10.24926/iip.v14i4.5526

for antimicrobial stewardship accreditation standards.[7] The Antimicrobial Stewardship Committee (ASC) is a subcommittee of the Pharmacy and Therapeutics (P&T) committee; ASP efforts are analyzed and reported to Q&P on a quarterly basis as required by DNV. Pharmacist led Antimicrobial Stewardship Programs have shown significant improvements in healthcare. Previous studies have shown that pharmacist led antimicrobial stewardship programs can effectively improve health outcomes such as reducing hospital length of stay, mortality, inappropriate antimicrobial use, and costs.[8,9] Pharmacists are able to effectively focus on proper antimicrobial utilization while actively working in multidisciplinary groups within the healthcare system.[10] Overall, contributing to the appropriate use of antimicrobials leading to successful therapeutic outcomes. There are many challenges that an ASP at a small community hospital can face such as lack of resources and costs. This provides an opportunity to evaluate the antimicrobial stewardship program's current policies and tools that are utilized in a small community hospital specifically in managing gram negative bacteremia. This retrospective review aims to assess current antimicrobial stewardship practices expected at a local hospital level through current practices such as Infectious Diseases Pharmacist led interventions, policy driven measures, and the various tools utilized by the small community hospital's ASP.

Methods

Study Design and Setting:

A retrospective cohort analysis study was conducted to evaluate the impact of antimicrobial stewardship practices in treating *Escherichia coli* bacteremia in both non-ICU and ICU settings. This study was conducted at non-academic small single center community hospital with a 239-bed located in Pennsylvania, USA. All patients that were ≥18 years of age admitted in the hospital with positive blood cultures for *Escherichia coli* from July 2021 to July 2022 were analyzed. Patients were excluded if their blood cultures were not positive for *Escherichia coli* and if antibiotics were not initiated during hospital stay. Figure 1 represents flowchart of patient selection process for patients with gram negative bacteremia. During the study 74 patients with gram negative bacteremia were identified and 43 patients had *Escherichia coli* bacteremia. These patients were further categorized into E. Coli ESBL bacteremia (n=6), E. Coli bacteremia in Non-ICU setting (n=29), and E. Coli bacteremia in ICU setting (n=8). 41 patients were included in the analysis as 2 patients were excluded since antibiotics were not initiated.

The primary endpoint was to determine the length of hospital stay (Table 2). Critical secondary endpoints include antibiotic de-escalations (Table 3), duration of antibiotics, time to definitive antibiotic therapy, serum procalcitonin levels (Table 5), and blood culture availabilities (Table 6).

Antimicrobial Stewardship Practices/Policies:

At this small community hospital setting, Infectious Diseases Pharmacist-led Antimicrobial Stewardship Program (ASP) is driven by various interventions, policies, and tools specifically targeting gram negative infections/therapeutics listed in Table 1a. A detailed summary of antimicrobial stewardship interventions is also listed in Table 3 which assisted analyzing critical secondary endpoints.

As a means to assess prevalence and resistance patterns during time period from January 2021 to December 2022, ASP collaborated with a multidisciplinary team to develop yearly source specific cumulative antibiograms (urine and non-urine isolates) for 2021 and 2022 (Please refer to Figure 2). In addition, a segregated data analysis for the ESBL organisms was conducted to analyze patterns of resistance for urine and non-urine antibiogram during year 2021 and 2022 (Please refer to Figure 3).

Data Collection:

Data was obtained from a review of the electronic medical record (EMR) and recorded into a de-identified data collection form. Collected data consisted of demographic information such as age and gender, dates of admission, dates of discharge, dates of blood culture collection, dates of blood culture results posted, antibiotic treatments initiated, dates of antibiotics initiated, procalcitonin levels on admission, and IV to PO conversions.

Variables and Definitions:

- De-escalation- switching to an antibiotic with a narrower spectrum
- Surveillance- monitoring changes in populations of organisms to understand patterns of resistance
- Bug-Drug Mismatch Review- antibiotic patient is receiving does not provide accurate coverage for specific organism patient is currently infected with
- Appropriateness- utilizing antibiotics when necessary
- Length of hospital stay- time when patient was admitted into the hospital to when the patient was discharged

Statistical Analysis:

The descriptive statistics and key outcome measures identified are demographics (Table 1b), length of hospital stays (Table 2), broad therapy to de-escalating agents for E. coli bacteremia in non-ICU setting (Table 4), broad therapy to de-escalating agents for E. coli bacteremia in ICU setting (Table 4), agents utilized for ESBL-producing E. coli bacteremia in non-ICU setting, procalcitonin levels on admission (Table 5), presence of positive blood cultures (Table 6). Supporting tools involved comparison of antibiograms for year 2021 and 2022 as listed below.

Figure 2. Cumulative Antibiograms

- Year 2021
- Year 2022

DOI: https://doi.org/10.24926/iip.v14i4.5526

Figure 3. ESBL organisms URINE AND NON-URINE Antibiograms
- Year 2021
- Year 2022

Results

The primary endpoint was to determine the impact of antimicrobial stewardship pharmacist-led interventions on the length of hospital stay in patients with *Escherichia coli* bacteremia during COVID-19 pandemic in year 2021. The primary endpoint results showed that in patients with *Escherichia coli* bacteremia in the ICU setting the average length of stay was longer at 16.6 days, in patient with *Escherichia coli* bacteremia in the Non-ICU setting the average length of stay was 7.3 days, and in patients with ESBL E. coli bacteremia the length of stay was 6.8 days according to Table 2.

Critical secondary endpoints include antibiotic de-escalations, duration of antibiotics, time to definitive antibiotic therapy, serum procalcitonin levels, and blood culture availabilities.
The most common de-escalating agents are cephalosporins according to Table 4 in both the Non-ICU and ICU settings. De-escalation of agents occurred in 61% of patients through the ASP's interventions. A detailed summary of antimicrobial stewardship interventions is listed in Table 3. Out of 1061 antimicrobial stewardship interventions focused on targeted broad-spectrum antibiotics (Cefepime, Zosyn, Meropenem, Levofloxacin), highest number of interventions targeted carbapenem de-escalation (13.3%) highlighting increased efforts to one of the broadest spectrums of IV antibiotics to combat resistance.

Out of 27 patients in the E. coli bacteremia in Non-ICU setting, 18 de-escalations occurred and are shown in Table 4. De-escalations did not occur in 9 patients because therapy was broadened or only broad antibiotics was initiated. Average time to de-escalate was 3.3 days. In comparison, out of 8 patients in *Escherichia coli* bacteremia in ICU setting, 7 de-escalations occurred and are shown in table 4. De-escalations did not occur in 1 patient since therapy was broadened. Average time to de-escalate was 3.6 days.

Six patients had ESBL E. coli bacteremia and the antibiotics that were initiated and switched to are shown in Table 4. Three patients ended up on the appropriate antibiotics (carbapenems) and the other three patients ended up with inappropriate antibiotics.

Admission serum procalcitonin levels were available for 29 patients. One patient had a PCT level greater than a 100 and was not included in the PCT analysis. Blood cultures were collected in all patients included in analysis. Repeat blood cultures were only collected for 13 patients.

Discussion

According to the segregated data analysis, the antibiogram for non-urine isolates accounting for gram negative organisms reported between January 2021 to December 2021 indicated that *Escherichia coli* remained the most prevalent organism (number of isolates identified 122) at our institution. The antibiogram analysis demonstrated that a total of 30 isolates which were ESBL producer in Non-Urine group. Of these, 20 isolates were identified as E. Coli – ESBL producer. In view of the high prevalence of *Escherichia coli*-ESBL producer in non-urine group, we focused on de-escalation efforts and therapeutics utilized for patients experiencing bacteremia with *Escherichia coli*, gram negative bacilli, since these organisms are a major threat in hospitalized patients. They have a mortality rate of 12-38% depending on appropriate antibiotic use.[2] Hence this study focused primarily on ASP led interventions, procalcitonin monitoring, and blood culture assays.

Reduction in hospital length of stay improves bed turnover, improving patient outcomes, decreasing mortality, and decreasing costs.[11] Antimicrobial stewardship programs have an impact on patient outcomes such as length of stay, re-admissions, and mortality. According to a Cochrane database systematic review on interventions to improve antibiotic prescribing practices for hospital in patients in 2017, lower use of antibiotics decreases mortality and reduces length of stay.[12] The CDC also emphasizes that ASPs can help improve clinical outcomes and minimize patient harms by improving antibiotic prescribing.[4] In our patient population the length of hospital stay for ICU patients were longer which is expected due to disease burden and complications. Data from CDC's National Hospital Discharge survey showed that patients hospitalized with sepsis have an average length of stay that was 43% higher than that of other patients.[13] However, the average length of stay for *Escherichia coli* bacteremia and ESBL *Escherichia coli* in the non-ICU setting is much shorter possibly due to the fact that these patients are not as sick and therefore require less antibiotic use overall. The average duration of any antibiotic that was ever given to a patient was 2.6 days. Typical duration of treatment for uncomplicated gram-negative bloodstream infections ranges from 7-14 days. Many retrospective studies and reviews have shown that there are no differences in clinical outcomes in patients treated for bloodstream infections with shorter courses of antibiotic therapy compared to prolonged courses especially in patients with urinary sources of infection.[14,15] Majority of the patients in our study had other sources of infection observed in the urine. Treatment duration was much shorter compared to a duration of 7 days and this is because the data does not account the duration of days in which a patient may have been sent home with on antibiotics as it only captures antibiotics given on an inpatient level. However, the ASP program has automatic 7 day stop dates for any antibiotics initiated in patients to avoid unnecessary prolonged antibiotic use. The automatic 7 day stop dates along with infectious disease stewardship interventions has led to an

DOI: https://doi.org/10.24926/iip.v14i4.5526

overall decrease in the antibiotic utilization and duration, thus overall decreasing selective pressure of antibiotics and resistance.

The most common de-escalating agents were cephalosporins according to Table 3 in both the Non-ICU and ICU settings. De-escalation of agents occurred in 61% of patients through the ASP's interventions. De-escalation of antibiotics did not occur in all patients since it depends on the severity of the infection and other comorbidities. The ASP assesses appropriateness of antibiotic use and de-escalates therapy as soon as blood culture panels and culture and susceptibility reports come back. The average time for culture and susceptibility reports to come back is 2.8 days, allowing ample time for the infectious disease stewardship team to de-escalate therapy for a narrower coverage in order to decrease resistance. The average time to de-escalate therapy was 3 days. Studies have shown that de-escalating antibiotic therapy leads to lower mortality and decreased resistance.[16,17] There is very limited data available on gram-negative bacteremia oral step-down therapy with cephalosporins. However, there are studies conducted stating that oral antibiotics with high bioavailability were effective treatments in hospitalized patients with gram negative bacteremia.[18] Out of all oral cephalosporins, cephalexin (Keflex) has the highest bioavailability of nearly 100%. De-escalating therapy from IV to PO is important to prevent cannula related infections and improve patient safety. Patients that transitioned from IV to oral antibiotics experienced similarly low rates of treatment failure than those who received only IV therapy.[19] Therefore, it's important to consider de-escalating patients from IV to oral antibiotics. Among 43 patients IV to PO oral step-down therapy occurred in 16 (37.2%) patients with cephalexin and oral fluoroquinolones being the most common oral-step down agents. Cephalexin and oral fluoroquinolones have high bioavailability's which are effective in treating hospitalized patients with gram-negative bacteremia due to their ability to reach adequate blood concentrations. Less than half of the patients ended up on oral antibiotic therapy, however that may be due the patients' clinical stability and bacteremia burden. The ASP has an IV to PO policy in place that allows the infectious disease stewardship team to safely switch hospitalized patients initially on intravenous antibiotics to an oral equivalent once the patient is clinically stable. The ASP's efforts are heavily focused on decreasing complications that may arise from IV antibiotic use and decreasing overall costs as well.

Procalcitonin (PCT) is an essential biomarker utilized in the early detection of bacterial infections. Other biomarkers such as C-reactive protein (CRP) lack specificity in differentiating between bacterial or non-bacterial infections, whereas serum PCT levels are not elevated in viral infections which makes it an ideal biomarker in identifying bacterial infections. Serum levels greater than 0.25 ng/mL can indicate a bacterial infection. Early detection of bacterial infections with PCT can lead decrease in morbidity, mortality, and antibiotic overuse. High serum levels of PCT correlate to positive blood cultures and sepsis.[20] Therefore, PCT levels at baseline were evaluated in this study as well to address antimicrobial stewardship efforts in patients with *Escherichia coli* bacteremia in Non-ICU and ICU settings at a small community hospital. Admission serum procalcitonin levels were collected for 29 patients. 1 patient had a PCT level greater than a 100 and was not included in the PCT analysis. The average length of stay of patients in which PCT levels exceeded 2ng/mL was 9.6 days. This increase could be due other etiologies such as compromised renal function, cancer, or spinal cord injuries and this study did not excluded patients with other co-morbidities. Average PCT levels in the ICU were higher (23 ng/mL) compared to PCT levels in the Non-ICU setting (10 ng/mL). This is expected since patients in the ICU were more likely to be treated with sepsis or septic shock. The ASP policy regarding procalcitonin levels for systemic bacterial infections indicates that patients with PCT levels greater than 2.0 ng/mL have a high risk for sepsis and/or septic shock. The average time it took to de-escalate antibiotics when PCT levels in patients were above 2 ng/mL were 3 and 4 days in ICU and Non-ICU patients respectively. Studies have shown that using procalcitonin levels to guide de-escalation can decrease duration of antibiotics without complications.[21-23] The ASP implements the procalcitonin policy to further evaluate antibiotic use and its appropriateness.

Blood culture identification panels allow clinicians to easily interpret results of a positive blood culture within a short time frame. The BCID panel tests for bacterial pathogens along with their antimicrobial resistance genes such as the CTX-M gene for ESBL producing Enterobacterales. BCID panels are used to guide empiric selection of therapy.[24] According to the HNL Lab Medicine BCID panel's guidance for interpreting blood culture results, if *Escherichia coli* with no resistance markers is detected then ceftriaxone should be used as empiric therapy. If *Escherichia coli* with CTX-M is detected, then meropenem should be used as empiric therapy.[25] Our institution utilizes blood culture identification panels (BCID) to further assess optimal antibiotic use by ruling out resistant organisms. According to Table 6 the average time for BCID panels to get posted is 1.2 days, allowing the ASP sufficient time to de-escalate antibiotics. This is crucial as the rapid initiation of appropriate antibiotic therapy has led to reduction morbidity and mortality.[26] With a turnaround time of approximately 1 day, the antimicrobial stewardship team can promptly start appropriate antibiotics or even de-escalate antibiotics. This can help decrease any unwanted adverse drug events such as *Clostridioides difficile* infections as well. These rapid diagnostic tests improve patient care since they provide important and reliable pathogen-related information in a short time frame.[26]

Minimum inhibitory concentrations (MIC) provide clinicians information to select the most optimal antibiotic for their patients. CLSI defines MIC categories as Susceptible (S) meaning

DOI: https://doi.org/10.24926/iip.v14i4.5526

isolates of the organism are inhibited by the normal achievable concentrations of the antibiotic when the recommended dose is used. Susceptible dose dependent (SDD) is when isolates of the organism are inhibited depending on the dose of the antibiotic. Intermediate (I) is defined as isolates of the organism with response rates that may be lower than the susceptible isolates. This category shows clinical efficacy in sites of the body where the antibiotic is concentrated in or when a higher than normal dose of a drug is used. Resistant (R) is defined as when isolates of the organism are not inhibited by the normal achievable concentrations of the antibiotic when the recommended dose is used.[27] Among all the de-escalating agents, cephalosporins were the most common agent utilized as seen in Table 3. Ceftriaxone and cefazolin were the most common cephalosporin de-escalating agents. Clinical MIC breakpoints are currently set and published by two organizations, the European EUCAST (European Committee on Antimicrobial Susceptibility Testing) and the American CLSI (Clinical and Laboratory Standards Institute). Cefazolin is recognized as a surrogate test agent for oral cephalosporins. The CLSI standards on AST reports an MIC breakpoint of cefazolin for treating uncomplicated urinary tract infections as ≤16 µg/ml when a dose of 1g q8h is given. Co-infections with *Escherichia coli* in the urine were observed in 19 patients. Even though some patients also had urine infections, we focused on bloodstream infections considering that CLSI guidelines for MIC breakpoints were updated to include infections other than urinary tract infections. According CLSI standards regarding AST, the MIC breakpoint based on the dose of 2g q8h for cefazolin when treating infections other than uncomplicated urinary tract infections (UTIs) due to *Escherichia coli* was ≤ 2 µg/ml.[27] The HNL lab does susceptibility testing for the small community hospital setting and the MIC of cefazolin with systemic infections due to *Escherichia coli* was reported as ≤ 4 µg/ml in 29 patients. Our local lab reports a higher MIC value than the recommendation by CLSI. This is because there are many barriers when implementing new MIC breakpoints in labs that use FDA or commercial MIC susceptibility testing systems. It could take several years before new MIC breakpoints are implemented as the manufacturers of these systems cannot ship the equipment needed to assess these breakpoints, since it will take time for the FDA to clear the susceptibility testing systems that include the revised CLSI breakpoints.[28] Despite this barrier, ID specialists and pharmacists play an important role in assessing the impact of CLSI revised breakpoints on patient management. Through working with our local HNL lab, the infectious disease stewardship team implements ways to increase infection control measures and optimize antibiotic use to overall help decrease hospital length of stay.

Conclusion

Despite the various challenges that antimicrobial stewardship programs (ASP) face in a single center small community hospital, the ASP at this small community hospital utilizes various policies and tools to increase appropriate antibiotic use and decrease hospital length of stay in patients with *Escherichia coli* bacteremia. Pharmacists have a great impact in the ASP, as they play pivotal roles in utilizing various strategies to improve health outcomes. Limitations of the study include the small population size, retrospective study design, and different primary diagnoses can be confounding factors. These limitations may make it difficult to predict whether the results can be extrapolated to other facilities. Future research can focus on a more rigorous study design with a multicenter approach on a larger population sample. Despite its limitations, this study has shown the various pharmacist led interventions a small community hospital utilizes to improve patients' healthcare.

Conflict of Interest Statement: No potential conflicts of interests were noted by the authors of this paper.

Ethics Approval Statement: The research was approved by the Holy Redeemer Hospital's Institutional Review Board.

Disclaimer: The statements, opinions, and data contained in all publications are those of the authors.

References

1. Covid-19 & Antibiotic resistance [Internet]. Centers for Disease Control and Prevention. Centers for Disease Control and Prevention; 2022 [cited 2022 Aug 14]. Available from: https://www.cdc.gov/drugresistance/covid19.html
2. Moehring R, Anderson D. Gram-negative bacillary bacteremia in adults [Internet]. UpToDate. Wolters Kluwer; 2022 [cited 2022 Aug 14]. Available from: https://www.uptodate.com/contents/gram-negative-bacillary-bacteremia-in-adults
3. Aitken SL, Tamma* PD. AMR guidance 1.0 [Internet]. IDSA Home. 2022 [cited 2022 Aug 14]. Available from: https://www.idsociety.org/practice-guideline/amr-guidance/
4. Core elements of hospital antibiotic stewardship programs [Internet]. Centers for Disease Control and Prevention. Centers for Disease Control and Prevention; 2021 [cited 2022 Aug 14]. Available from: https://www.cdc.gov/antibiotic-use/core-elements/hospital.html
5. Antibiotic use [Internet]. Centers for Disease Control and Prevention. Centers for Disease Control and Prevention; 2021 [cited 2022 Aug 14]. Available from: https://www.cdc.gov/antibiotic-use/index.html
6. Nathwani D, Varghese D, Stephens J, Ansari W, Martin S, Charbonneau C. Value of hospital antimicrobial stewardship programs [ASPs]: a systematic review. Antimicrob Resist Infect Control. 2019 Feb 12; 8:35. doi: 10.1186/s13756-019-0471-0.
7. DNV [Internet]. Accreditation Requirements, Interpretive Guidelines and Surveyor Guidance for

Hospitals - Revision 20-0. National Integrated Accreditation For Healthcare Organizations (NIAHO); 2020 [cited 2022 Aug 15]. Available from: https://brandcentral.dnvgl.com/original/gallery/10651/files/original/0d9513b108d847808df973607dd5b32e.pdf
8. Mahmood RK, Gillani SW, Saeed MW, Vippadapu P, Alzaabi MJ. Impact of pharmacist-led services on Antimicrobial Stewardship Programs: A meta-analysis on clinical outcomes. Journal of Pharmaceutical Health Services Research. 2021;12(4):615–25.
9. Fukuda T, Tanuma K, Iio S, Saito J, Komura M, Yamatani A. Impact of a Pharmacist-Led Antimicrobial Stewardship Program on the Number of Days of Antimicrobial Therapy for Uncomplicated Gram-Negative Bacteremia in a Community Hospital. Cureus. 2021 Apr 22;13(4):e14635.
10. Moehring R, Anderson D. Gram-negative bacillary bacteremia in adults [Internet]. UpToDate. Wolters Kluwer; 2022 [cited 2022 Aug 14]. Available from: https://www.uptodate.com/contents/gram-negative-bacillary-bacteremia-in-adults
11. McDermott KW, Elixhauser A, Sun R. Trends in Hospital Inpatient Stays in the United States, 2005-2014 [Internet]. Patient Trends in Hospital Inpatient Stays in the United States, 2005-2014 #225. Agency for Healthcare Research and Quality; 2017 [cited 2022Dec26]. Available from: https://www.hcup-us.ahrq.gov/reports/statbriefs/sb225-Inpatient-US-Stays-Trends.jsp
12. Davey P, Marwick CA, Scott CL, Charani E, McNeil K, Brown E, Gould IM, Ramsay CR, Michie S. Interventions to improve antibiotic prescribing practices for hospital inpatients. Cochrane Database Syst Rev. 2017 Feb 9;2(2):CD003543.
13. Products - data briefs - homepage [Internet]. Centers for Disease Control and Prevention. Centers for Disease Control and Prevention; 2022 [cited 2022 Aug 14]. Available from: https://www.cdc.gov/nchs/products/databriefs.htm
14. Havey TC, Fowler RA, Daneman N. Duration of antibiotic therapy for bacteremia: a systematic review and meta-analysis. Crit Care. 2011;15(6):R267.
15. Chotiprasitsakul D, Han JH, Cosgrove SE, Harris AD, Lautenbach E, Conley AT, Tolomeo P, Wise J, Tamma PD; Antibacterial Resistance Leadership Group. Comparing the Outcomes of Adults With Enterobacteriaceae Bacteremia Receiving Short-Course Versus Prolonged-Course Antibiotic Therapy in a Multicenter, Propensity Score-Matched Cohort. Clin Infect Dis. 2018 Jan 6;66(2):172-177.
16. Garnacho-Montero J, Gutiérrez-Pizarraya A, Escoresca-Ortega A, Corcia-Palomo Y, Fernández-Delgado E, Herrera-Melero I, Ortiz-Leyba C, Márquez-Vácaro JA. De-escalation of empirical therapy is associated with lower mortality in patients with severe sepsis and septic shock. Intensive Care Med. 2014 Jan;40(1):32-40.
17. Lakbar I, De Waele JJ, Tabah A, Einav S, Martin-Loeches I, Leone M. Antimicrobial De-Escalation in the ICU: From Recommendations to Level of Evidence. Adv Ther. 2020 Jul;37(7):3083-3096.
18. Kutob LF, Justo JA, Bookstaver PB, Kohn J, Albrecht H, Al-Hasan MN. Effectiveness of oral antibiotics for definitive therapy of Gram-negative bloodstream infections. Int J Antimicrob Agents. 2016 Nov;48(5):498-503.
19. Thurber KM, Arnold JR, Narayanan PP, Dierkhising RA, Sampathkumar P. Comparison of intravenous and oral definitive antibiotic regimens in hospitalised patients with Gram-negative bacteraemia from a urinary tract infection. J Glob Antimicrob Resist. 2019 Sep;18:243-248.
20. Cleland DA, Eranki AP. Procalcitonin - StatPearls - NCBI Bookshelf [Internet]. Procalcitonin. StatPearls Publishing LLC.; 2022 [cited 2022 Aug 15]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK539794/
21. Assink-de Jong E, de Lange DW, van Oers JA, Nijsten MW, Twisk JW, Beishuizen A. Stop Antibiotics on guidance of Procalcitonin Study (SAPS): a randomised prospective multicenter investigator-initiated trial to analyse whether daily measurements of procalcitonin versus a standard-of-care approach can safely shorten antibiotic duration in intensive care unit patients--calculated sample size: 1816 patients. BMC Infect Dis. 2013 Apr 16;13:178.
22. Huang TS, Huang SS, Shyu YC, Lee CH, Jwo SC, Chen PJ, Chen HY. A procalcitonin-based algorithm to guide antibiotic therapy in secondary peritonitis following emergency surgery: a prospective study with propensity score matching analysis. PLoS One. 2014 Mar 4;9(3):e90539.
23. Broyles MR. Impact of Procalcitonin-Guided Antibiotic Management on Antibiotic Exposure and Outcomes: Real-world Evidence. Open Forum Infect Dis. 2017 Oct 3;4(4):ofx213.
24. Introducing blood culture identification panel 2 (BCID2) [Internet]. HNL Lab Medicine. 2021 [cited 2022 Aug 15]. Available from: https://www.testmenu.com/healthnetworklaboratories/TestDirectory/SiteFile?fileName=sidebar%5CBloodCultureIdentificationPanel2-BCID2_InfoSheet_7-21.pdf
25. Guidance for Interpretation of Rapid Nucleic Acid Amplification (NAA) Blood Culture Results (BCID2) [Internet]. HNL Lab Medicine. 2021 [cited 2022 Aug 15]. Available from: https://www.testmenu.com/healthnetworklaboratori

DOI: https://doi.org/10.24926/iip.v14i4.5526

es/TestDirectory/SiteFile?fileName=sidebar%5CBloodCultureIdentificationPanel2_BCID2-Guide_7-21.pdf
26. Statement from the Infectious Diseases Society of America (IDSA) [Internet]. The Infectious Diseases Society of America (IDSA). 2016 [cited 2022 Aug 15]. Available from: https://www.idsociety.org/globalassets/idsa/policy--advocacy/current_topics_and_issues/diagnostics/statements/idsa-statement-to-senatehelp-committee-on-laboratory-developed-tests-pdf
27. M100ED32: Performance standards for antimicrobial susceptibility testing, 32nd edition [Internet]. Clinical & Laboratory Standards Institute. Clinical and Laboratory Standards Institute; 2022 [cited 2022 Aug 15]. Available from: https://www.clsi.org/standards/products/microbiology/documents/m100/
28. Prinzi A. Updating breakpoints in antimicrobial susceptibility testing [Internet]. The American Society for Microbiology. The American Society for Microbiology; 2022 [cited 2022 Aug 15]. Available from: https://asm.org/Articles/2022/February/Updating-Breakpoints-in-Antimicrobial-Susceptibili

DOI: https://doi.org/10.24926/iip.v14i4.5526

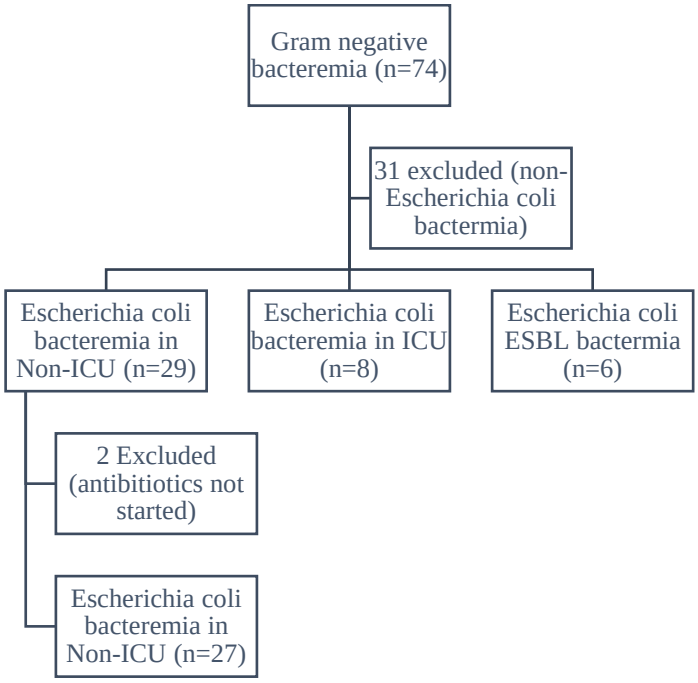

Figure 1: Flowchart of patients included in the study

DOI: https://doi.org/10.24926/iip.v14i4.5526

Figure 2: Cumulative Antibiograms
Year 2021:

ANTIBIOGRAM - NON-URINE
(MAY 2022)
01/01/2021 to 12/31/2021

Non-Urine (Gram Negatives)	# ISOLATES	AMIKACIN	AMPICILLIN	AMPICILLIN/SULBAC TAM	AZTREONAM	CEFAZOLIN	CEFEPIME	CEFTAZIDIME	CEFTRIAXONE	CIPRO	GENTAMICIN	MEROPENEM	PIPTAZO	TRIMETHOPRIM-SUL
ENTEROBACTER CLOACAE COMPLEX	23	100			96		100	96	96	100	100	100	95	96
ESCHERICHIA COLI	122	100	57	64	99	94	98	99	99	84	92	100	98	77
KLEBSIELLA PNEUMONIAE	41	100		90	100	100	100	100	100	100	100	100	95	98
PROTEUS MIRABILIS	34	97	82	88	100	90	100	100	97	82	88	100	100	82
PSEUDOMONAS AERUGINOSA	75	99					89	88		89	93	91	90	
SERRATIA MARCESCENS	11	100			100		100	100	100	100	100	100		100

Non-Urine (Gram Positives)	# ISOLATES	AMPICILLIN	CEFTAROLINE	CIPRO	CLINDAMYCIN	DAPTOMYCIN	ERYTHROMYCIN	LEVOFLOXACIN	LINEZOLID	OXACILLIN (NAFCILLIN)	RIFAMPIN	TETRACYCLINE	TRIMETHOPRIM-SUL	VANCOMYCIN
ENTEROCOCCUS FAECALIS	32	100		85		100			100					100
METHICILLIN RESISTANT STAPHYLOCOCCUS AUREUS	97		100	24	60	100	16	26	100		100	87	87	100
STAPHYLOCOCCUS AUREUS	185		99	88	74	99	61	89	100	100	99	94	97	100
STAPHYLOCOCCUS EPIDERMIDIS	16			69	69		44	69	100	38	94	94	81	100
STAPHYLOCOCCUS HOMINIS	10				80		40	80	100	64	100		90	100

Year 2022:

ANTIBIOGRAM - NON-URINE
(MAY 2023)
01/01/2022 to 12/31/2022

Non-Urine (Gram Negatives)	# ISOLATES	AMIKACIN	AMPICILLIN	AMPICILLIN/SULBAC TAM	AZTREONAM	CEFAZOLIN	CEFEPIME	CEFTAZIDIME	CEFTRIAXONE	CIPRO	GENTAMICIN	MEROPENEM	PIPTAZO	TRIMETHOPRIM-SUL
ENTEROBACTER CLOACAE COMPLEX	17	100			88		100	88	88	100	100	100	94	100
ESCHERICHIA COLI	116	100	65	72	99	97	99	99	99	89	94	99	97	85
KLEBSIELLA PNEUMONIAE	17	100		88	100	100	100	100	100	100	100	100	100	100
PROTEUS MIRABILIS	28	100	89	93	100	96	100	100	100	89	93	100	100	89
PSEUDOMONAS AERUGINOSA	50	100					90	88		92	96	98	98	
SERRATIA MARCESCENS	10	100			100		100	100	100	100	100	100		100

Non-Urine (Gram Positives)	# ISOLATES	AMPICILLIN	CEFTAROLINE	CIPRO	CLINDAMYCIN	DAPTOMYCIN	ERYTHROMYCIN	LEVOFLOXACIN	LINEZOLID	OXACILLIN (NAFCILLIN)	RIFAMPIN	TETRACYCLINE	TRIMETHOPRIM-SUL	VANCOMYCIN
ENTEROCOCCUS FAECALIS	27	100		81		100			100					100
METHICILLIN RESISTANT STAPHYLOCOCCUS AUREUS	80		100	27	69	100	14	33	100		100	80	80	100
STAPHYLOCOCCUS AUREUS	138		100	87	68	100	51	88	100	96	100	91	99	100
STAPHYLOCOCCUS EPIDERMIDIS	9			44	44	100	11	44	100	33	100	56	56	100
STAPHYLOCOCCUS HOMINIS	8			25	38	100	38	25	100	25	100	63	63	100

DOI: https://doi.org/10.24926/iip.v14i4.5526

Figure 3:
Segregated Data Analysis – ESBL organisms
Figure 3. ESBL organisms URINE AND NON-URINE Antibiogram:

Year 2021:

Segregated Data Analysis - ESBL organisms
URINE AND NON-URINE
(MAY 2022)
01/01/2021 to 12/31/2021

URINE	# ISOLATES	AMIKACIN	AMPICILLIN	AMPICILLIN/SULBACTAM	AZTREONAM	CEFAZOLIN	CEFEPIME	CEFTAZIDIME	CEFTRIAXONE	CIPRO	GENTAMICIN	MEROPENEM	NITROFURANTOIN	PIP/TAZO	TRIMETHOPRIM-SUL
ESCHERICHIA COLI ESBL PRODUCER	69	99		41						20	86	100	91	91	54
KLEBSIELLA PNEUMONIAE ESBL PRODUCER	19	95		16						47	53	100		63	11
KLEBSIELLA OXYTOCA ESBL PRODUCER	2	100										100	50	50	
PROTEUS MIRABILIS ESBL PRODUCER	4	100		75						25	100	100		100	75

NON-Urine	# ISOLATES	AMIKACIN	AMPICILLIN	AMPICILLIN/SULBACTAM	AZTREONAM	CEFAZOLIN	CEFEPIME	CEFTAZIDIME	CEFTRIAXONE	CIPRO	GENTAMICIN	MEROPENEM	PIP/TAZO	TRIMETHOPRIM-SUL
ESCHERICHIA COLI ESBL PRODUCER	20	100		55						25	90	100	100	40
KLEBSIELLA PNEUMONIAE ESBL PRODUCER	6	83								50	50	100	33	
KLEBSIELLA PNEUMONIAE, extended spectrum beta-lactamase (ESBL)/carbapenemase producer (CRE)	2	100								50	100			50
PROTEUS MIRABILIS ESBL PRODUCER	2	100		50							50	100	100	50

Year 2022:

Segregated Data Analysis - ESBL organisms
URINE AND NON-URINE
(MAY 2023)
01/01/2022 to 12/31/2022

URINE	# ISOLATES	AMIKACIN	AMPICILLIN	AMPICILLIN/SULBACTAM	AZTREONAM	CEFAZOLIN	CEFEPIME	CEFTAZIDIME	CEFTRIAXONE	CIPRO	GENTAMICIN	MEROPENEM	NITROFURANTOIN	PIP/TAZO	TRIMETHOPRIM-SUL
ESCHERICHIA COLI ESBL PRODUCER	71	99		30						25	80	100	93	97	48
KLEBSIELLA PNEUMONIAE ESBL PRODUCER	19	100		11						68	47	100	5	68	16

NON-Urine	# ISOLATES	AMIKACIN	AMPICILLIN	AMPICILLIN/SULBACTAM	AZTREONAM	CEFAZOLIN	CEFEPIME	CEFTAZIDIME	CEFTRIAXONE	CIPRO	GENTAMICIN	MEROPENEM	PIP/TAZO	TRIMETHOPRIM-SUL
ESCHERICHIA COLI ESBL PRODUCER	14	100		29						14	86	100	100	64
KLEBSIELLA PNEUMONIAE ESBL PRODUCER	7	100		29						29	29	100	57	29

DOI: https://doi.org/10.24926/iip.v14i4.5526

Strategies for "Antibiotic Time outs" and "Prospective audits" for combating gram-negative infections	
Interventions	• Aztreonam surveillance • Bug-drug mismatch review • Carbapenem-de-escalation • Cefepime de-escalation • Cefepime discontinuation • Levofloxacin-appropriateness • Other ASP Interventions • Renal dosing for antimicrobials (ASP surveillance) • Zosyn- monitor C&S (empiric) Info • Zosyn-de-escalation
Policies	• Antimicrobial renal dosing by pharmacists • Automatic 7 day stop dates for antibiotic durations • Guidelines for extended infusion of Zosyn • IV to PO conversion • Procalcitonin guidelines • Reporting resistant isolates (Blood cultures)
Tools	• Institution specific antibiogram • Rapid diagnostics such as blood culture identification panels (BCID) • Software such as Theradoc, Soarian Clinical, and Cerner Pharmacy

Table 1a. Strategies for "Antibiotic Time outs" and "Prospective audits" for combating gram-negative infections

Demographics (n=41)	
Female	63.4%
Male	36.6%

Table 1b. Demographics

DOI: https://doi.org/10.24926/iip.v14i4.5526

Setting (n=41)	Average Length of Hospital Stay	Standard deviation
Age	74 years	σ =15.610493
E. coli bacteremia in ICU	13.6 days	σ =9.9398189
E. coli bacteremia in Non-ICU	7.3 days	σ =6.7486382
ESBL E. coli bacteremia in Non-ICU	6.8 days	σ =4.5490524
PCT levels >2ng/mL	9.6 days	σ =7.9945969

Table 2. Length of hospital stay

	Antibiotic	Antimicrobial Stewardship interventions (n = 1061)	N	%
Targeted Antibiotics	Cefepime	• Cefepime de-escalation • Cefepime discontinuation	26	2.45%
	Zosyn	• Zosyn-monitor C&S (empiric) Info, • Zosyn-de-escalation	79	7.44%
	Meropenem, Ertapenem	• Carbapenem-de-escalation	141	13.3%
	Levofloxacin	• Levofloxacin-appropriateness	41	3.86%
	Aztreonam	• Aztreonam surveillance,	47	4.42%
Policies	Policy-driven dosage adjustments	• Renal dosing for antimicrobials (ASP surveillance)	364	34.3%
	Surveillance – Antimicrobial Stewardship	• Bug-drug mismatch review	76	7.16%
		• Other ASP Interventions (i.e., Procalcitonin monitoring)	287	26.3%

Table 3. Antimicrobial Stewardship Interventions

DOI: https://doi.org/10.24926/iip.v14i4.5526

Broad Therapy	Cefepime	Ceftriaxone	Piperacillin/Tazobactam	Meropenem	Vancomycin
Non-ICU	Cefazolin (n=1)	Cefazolin (n=2)	Ceftazidime / Avibactam (n=1)	Cefazolin (n=1)	ceftriaxone (n=1)
	Ceftriaxone (n=2)	Tobramycin (n=1)	Ceftriaxone (n=1)	Cefuroxime (n=1)	
	Levofloxacin (n=1)	Amoxicillin (n=1)		Amoxicillin (n=1)	
	Ciprofloxacin (n=1)	Ciprofloxacin (n=1)			
		Cephalexin (n=1)			
		Azithromycin (n=1)			
ICU	Cefuroxime (n=1)	Cefazolin (n=1)	Cefazolin (n=2)	Cefazolin (n=1)	
	Ceftriaxone (n=1)		Cefepime (n=1)		

Table 4. Comparison of Broad therapy to De-escalating Agents for E. Coli bacteremia in Non-ICU setting vs. ICU setting

	Procalcitonin levels on admission (n=28)	Average	Standard deviation
Non-ICU	Procalcitonin level (ng/mL)	10	14.749707
ICU	Procalcitonin level (ng/mL)	23	13.621686
Non-ICU	Total number patients with PCT levels greater than 2	13	16.816132
ICU	Total number patients with PCT levels greater than 2	5	13.621686
Non-ICU	Average time for de-escalation with PCT levels greater than 2 (days)	4	0.96076892
ICU	Average time for de-escalation with PCT levels greater than 2 (days)	3	0.63245553
Patients with ESBL-producing E. Coli	Procalcitonin levels in ESBL E. coli bacteremia (ng/mL)	0.03	0.205
	Total number of patients with PCT levels greater than 2 in ESBL E. coli bacteremia	0	N/A

Table 5. Procalcitonin levels on admission

DOI: https://doi.org/10.24926/iip.v14i4.5526

Blood Cultures (n=43)		Standard deviation
Average time between blood culture collected and BCID posted (days)	1.2	0.59347852
Average time between blood culture collected and C&S posted (days)	2.8	0.78940022
Total number of repeat blood cultures (clinical cure)	13	N/A

Table 6. Blood Cultures

DOI: https://doi.org/10.24926/iip.v14i4.5526

IV to PO conversions (n=16)	
Cephalexin	4
Cefuroxime	2
Levofloxacin	2
Ciprofloxacin	2
Amoxicillin	3
Azithromycin	1
Sulfamethoxazole/trimethoprim	1
Metronidazole	1

Table 7. IV to PO conversions

DOI: https://doi.org/10.24926/iip.v14i4.5526