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A Small, Single-Center Community Hospital's Approach to Antimicrobial Stewardship in the Treatment of Patients with Escherichia coli Bacteremia

K.Anand kumar, P.Chandrashekar, .G.Thanusha, Karthan Pragathi

Samskruti College of Pharmacy

Abstract

Purpose: Inaccurate findings from antimicrobial susceptibility testing (AST), high expenses, and a lack of funding are just a few of the problems that pharmacist-led antimicrobial stewardship initiatives might face. In particular, resistance to gram-negative pathogens has grown since the COVID-19 pandemic. The majority of infections in a little community hospital with only one center are gram negative, with Escherichia coli infections being the most common. Consequently, the purpose of this research is to examine the pandemic's effects on antimicrobial stewardship initiatives aimed at fighting Escherichia coli and other ESBL pathogens, as well as the burden of gram-negative bacteremia.

Methods: Patients from a local community hospital who were 18 years old or older were examined in a retrospective cohort study. If patients' blood cultures did not show a positive result for Escherichia coli and antibiotics were not started while they were in the hospital, they were not included in the study. Determining the duration of hospital stay was the main goal. Antibiotic de-escalations, antibiotic duration, time to final antibiotic treatment, serum procalcitonin levels, blood culture availabilities, MIC breakpoints, and Clostridioides difficult occurrences are critical secondary outcomes. Among the seventy-four individuals diagnosed with gram-negative bacteremia, 41 tested positive for Escherichia coli. The duration of stay for patients with Escherichia coli bacteremia who remained in the intensive care unit was 13.6 days, according to the primary endpoint statistics. The average duration of stay for patients with bacteremia caused by Escherichia coli in a non-intensive care unit context is 7.3 days, whereas the length of stay for patients with bacteremia caused by E. septic shock in the same situation is 6.8 days.

Results: Antimicrobial stewardship programs (ASPs) in small community hospitals confront a number of obstacles; nonetheless, this particular ASP is making good use of its policies and resources to reduce hospital stays for patients with Escherichia coli bacteremia and increase the use of appropriate antibiotics.

Coli form bacterium, COVID-19, bloodstream infection, procalcitonin, and the Antimicrobial Stewardship Program are some of the related terms.

Introduction

The goal of Antimicrobial Stewardship Programs (ASP) is to reduce antibiotic resistance and the overuse of antibiotics. Acute care hospitals in the United States give antibiotics, and over 30% of those medications are either not needed or are not effective. The Antibiotic Stewardship Program (Core Elements) was introduced in 2014 by the Centers for Disease Control and Prevention (CDC) and is now being used in hospitals nationwide. Updates to the Core Elements include additional sections on hospital leadership's dedication, pharmacy knowledge and experience, taking

action, monitoring progress, reporting findings, and education.4 From 2015 to 2020, the proportion of hospitals using ASP rose from 48% to 91%.5 Along with the fight against COVID-19, Antimicrobial Stewardship Programs became an essential component of healthcare systems nationwide in 2020 and 2022. In light of the apparent link between the COVID-19 pandemic and the subsequent increase in antibiotic resistance, it was necessary to investigate regional patterns in community hospitals more thoroughly. A rise in healthcare-associated infections, an uptick in the use of antibiotics, and problems with enforcing infection control measures are all outcomes of the COVID-19 pandemic. Hospitals have been seeing sicker patients with longer lengths of stay because to the pandemic, which has led to the development of more resistant illnesses. This is especially true in hospitals, where the prevalence of enterobacterales that produce extended spectrum beta-lactamase (ESBL) has surged by 32% between 2019 and 2020.1 The majority of gram-negative bacterial infections in hospitals are caused by Escherichia coli, and gram-negative bloodstream infections are a leading cause of death and disability.2 Although the Infectious Disease Society of America (IDSA) discusses gram-negative infection

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treatment strategies that are resistant to antibiotics, we were interested in concentrating on the management of gram-negative bacteremia caused by Escherichia coli, the most common gram-negative pathogen.3 Antibiotic resistance and gram-negative infections are on the rise at a little community hospital with only one location. Antimicrobial stewardship initiatives aimed at fighting Escherichia coli and ESBL organisms during the COVID pandemic must, therefore, prioritize an evaluation of the burden of gram-negative bacteremia. There has been a decline in healthcare-associated infections, antibiotic usage, and costs due to the growing implementation of ASP programs.6 As a basis for its governance, DNV applies the Core Elements to the small community hospital. towards certification criteria for antimicrobial stewardship.7 As per DNV's requirements, the Antimicrobial Stewardship Committee (ASC) analyses and reports ASP efforts to the Pharmacy and Therapeutics (P&T) committee every three months. Antimicrobial stewardship programs spearheaded by pharmacists have greatly enhanced patient care. Health benefits like shorter hospital stays, lower mortality rates, less unnecessary antibiotic usage, and lower healthcare expenditures may be achieved by pharmacist-led antimicrobial stewardship programs, according to previous research.8,9 While participating in healthcare system-wide interdisciplinary teams, pharmacists are able to maintain a laser-like focus on appropriate antibiotic use.10 Ultimately, helping to ensure that antimicrobials are used appropriately, which in turn leads to positive therapeutic results. A shortage of funds and other resources is only one of many obstacles that an ASP working for a little rural hospital may encounter. This is a chance to assess the present policies and instruments used by the antimicrobial stewardship program in addressing gram negative bacteremia at a small community hospital. The purpose of this literature study is to evaluate the present state of antimicrobial stewardship in local hospitals as it pertains to areas like infectious diseases The ASP of the tiny community hospital made use of a variety of methods, including those spearheaded by pharmacists and others pushed by legislation.

Methods

Study Design and Setting:

Researchers in both the intensive care unit and those outside of it used a retrospective cohort analytic approach to look at how antimicrobial stewardship policies affected the treatment of Escherichia coli bacteremia. A tiny, non-academic community hospital in Pennsylvania, USA, with 239 beds, served as the site of this research. From July 2021 to July 2022, all patients admitted to the hospital who tested positive for Escherichia coli in their blood cultures were considered. If patients' blood cultures did not show a positive result for Escherichia coli and antibiotics were not started while they were in the hospital, they were not included in the study. The process flow diagram for selecting patients with gram-negative bacteremia is shown in Figure 1. There were 74 cases of gram-negative bacteremia and 43 cases of Escherichia coli bacteremia found in the research. E. coli ESBL bacteremia (n=6), E. coli bacteremia in a non-ICU context (n=29), and E. coli bacteremia in an ICU setting (n=8) were the subcategories into which these patients were further classified. Forty-one patients were included for the study, with two patients omitted because antibiotics were not started. Finding out how long patients stayed in the hospital was the main goal (Table 2). Table 3 shows antibiotic de-escalations; Table 4 shows antibiotic duration; Table 5 shows serum procalcitonin levels; and Table 6 shows blood culture availabilities; all of these are critical secondary endpoints.

Policies and Procedures for Antimicrobial Stewardship:

Table 1a lists the interventions, policies, and tools that drive the Antimicrobial Stewardship Program (ASP) at this small community hospital, which is directed by an infectious diseases pharmacist. The program's focus is on gram negative infections and treatments. In addition to helping with the analysis of important secondary outcomes, Table 3 provides a comprehensive overview of antimicrobial stewardship strategies. Together with a multidisciplinary team, ASP developed source-specific cumulative antibiograms (for both urine and non-urine isolates) for 2021 and 2022 (See Figure 2) to evaluate resistance trends and prevalence from January 2021 to December 2022. Figure 3 shows the results of a data separation study that looked at ESBL organisms in 2021 and 2022 separately to see how their resistance manifested in urine and in non-urine antibiograms.

Gathering Information:

A de-identified data collecting form was used to capture information retrieved from the electronic medical record (EMR). The data that was gathered included basic demographic information like age and gender, as well as specific medical details like dates of admission, dates of discharge, dates of blood culture collection, dates of antibiotic treatments started, dates of antibiotics started, procalcitonin levels on admission, and dates of IV to PO conversions.

Definitions and Variables:

• De-escalation, or replacing a broad-spectrum antibiotic with a more specific one

• Accuracy—using antibiotics when needed

• Length of hospital stay—time from patient admission to discharge

• Surveillance—monitoring changes in populations of organisms to understand patterns of resistance

Analysis of Data: Demographics (Table 1b), duration of hospital stays (Table 2), broad therapy to de-escalating agents for E. coli bacteremia in non-ICU settings (Table 4), broad therapy to de-escalating agents in ICU settings (Table 4), agents utilized for ESBL-producing E. coli bacteremia in non-ICU settings (Table 5), and presence of positive blood cultures (Table 6) are the descriptive statistics and key outcome measures that were identified. As you can see below, the supporting tools included comparing antibiograms for the years 2021 and 2022.

The cumulative antibiograms for the years 2021 and 2022 are shown in Figure 2.

Figure 3: ESBL organisms in urine and non-urine antibiograms for the years 2021 and 2022—

Results

During the 2021 COVID-19 pandemic, the major aim was to find out how antimicrobial stewardship actions guided by pharmacists affected the duration of hospital stays for patients with Escherichia coli bacteremia. Table 2 shows that the longest duration of stay for patients with Escherichia coli bacteremia was 6.8 days for those with ESBL E. coli bacteremia, the shortest duration of stay for patients with Escherichia coli bacteremia in the non-ICU setting was 7.3 days, and the longest duration of stay for patients with Escherichia coli bacteremia in the ICU setting was 16.6 days. Time to final antibiotic treatment, serum procalcitonin levels, antibiotic duration, antibiotic de-escalations, and blood culture availabilities are critical secondary outcomes. According to Table 4, cephalosporins are the most often used de-escalating drugs in both the non-ICU and ICU settings. As a result of the ASP's efforts, 61% of patients had their agents de-escalated. In Table 3 you will find a comprehensive overview of the treatments related to antimicrobial security. The majority of the 1061 antimicrobial stewardship interventions concentrated on broad-spectrum antibiotics such as cefepime, levofloxacin, meropenem, and carbapenem de-escalation, accounting for 13.3% of the total. This indicates that there has been a noticeable increase in efforts to combat resistance by utilizing one of the most extensive classes of intravenous antibiotics.

Table 4 shows that 18 de-escalations occurred out of 27 patients with E. coli bacteremia in a non-ICU environment. The average duration to de-escalate was 3.3 days, and de-escalations did not occur in 9 patients due to broadening treatment or the use of exclusively wide antibiotics. Table 4 shows that seven de-escalations happened out of eight patients with Escherichia coli bacteremia in an intensive care unit environment. One patient did not have a de-escalation when treatment was expanded. The de-escalation process took an average of 3.6 days.

The antibiotics that were started or switched for six individuals with ESBL E. coli bacteremia are shown in Table 4. Three patients were prescribed carbapenems, the right medications, while the other three were given the wrong ones. For 29 patients, serum procalcitonin levels were available at admission. The PCT analysis did not include one patient since their PCT level was higher than 100. All patients included in the study had blood cultures taken. Thirteen individuals were the only ones whose blood cultures were repeated.

Discussion

Based on the data that was separated, the antibiogram for gram-negative organisms other than urine that were reported from January to December 2021 showed that the most common organism at our institution was Escherichia coli (122). Thirty isolates were found to be ESBL producers in the Non-Urine group, according to the antibiogram study. We found 20 E. coli isolates that produced Escherichia coli ESBL. We concentrated on de-escalation strategies and therapies used for patients with bacteremia caused by Escherichia coli, gram negative bacilli, since these organisms pose a significant risk to hospitalized patients and because there is a high incidence of Escherichia coli-ESBL producers in the non-urine group. Death rates range from 12–38%, with the exact figure dependent on the antibiotics used.2 Therefore, blood culture testing, procalcitonin monitoring, and ASP-led therapies were the primary foci of this investigation.

Shortening patients' stays in the hospital has many benefits, including better patient outcomes, lower death rates, and lower healthcare expenditures.11 Patient outcomes including duration of stay, re-admissions, and death are affected by antibiotic stewardship initiatives. Research published in 2017 in the Cochrane database found that hospitalized patients whose antibiotic use was reduced had lower death rates and shorter hospital stays.12 Additionally, the CDC stresses that ASPs may aid in better antibiotic dosing, which in turn can enhance clinical results while minimizing patient risks.4 The duration of hospital stay for patients in the intensive care unit was greater in our patient cohort, as anticipated given the illness load and comorbidities. Sepsis patients were in the hospital for 43% longer than their non-septic counterparts, according to data from the CDC's National Hospital Discharge Study.13 Patients in the non-ICU environment had a much lower average duration of stay for Escherichia coli bacteremia and ESBL Escherichia coli. This might be because these patients are not as unwell and need less antibiotics overall. The average length of time a patient was prescribed an antibiotic was 2.6 days. Treatment for simple gram-negative bloodstream infections typically lasts between seven and fourteen days. In patients treated for bloodstream infections, there is no difference in clinical outcomes between shorter and longer courses of antibiotic treatment, according to many retrospective investigations and reviews. This is particularly true for individuals with urinary tract infections.14, 15 We found that additional infections were present in the urine of most of the individuals in our research. Because the data only records antibiotics administered in hospitals, it does not take into consideration how many days a patient may have been sent home on medication, which is why the treatment length was much less than 7 days. To reduce needless and extended antibiotic treatment, the ASP software automatically sets a 7-day stop date for all antibiotics started in patients. Reduced antibiotic use and duration, as a result of infectious disease stewardship initiatives and automatic 7-day end dates, has reduced antibiotic resistance and selection pressure.

Table 3 shows that in both the non-ICU and ICU settings, cephalosporins were the most prevalent de-escalating drugs. As a result of the ASP's efforts, 61% of patients had their agents de-escalated. Since the degree of the illness and other co-morbidities determine whether antibiotics are de-escalated or not, this did not happen in all patients. Blood culture panels, culture and susceptibility reports, and antibiotic appropriateness assessments are all done by the ASP, who then de-escalates treatment. The infectious disease stewardship team has plenty of time to de-escalate treatment for narrower coverage in order to minimize resistance since, on average, culture and susceptibility data come back in 2.8 days. Treatment de-escalation took an average of three days. Lower mortality and less resistance are outcomes of de-escalating antibiotic treatment, according to studies.16, 17 Data on oral step-down treatment with cephalosporins for gram-negative bacteremia is scarce. But there are studies that show that hospitalized patients with gram negative bacteremia may be effectively treated with oral antibiotics that have a high bioavailability.18 In terms of bioavailability, cephalexin (Keflex) is by and away the most effective oral cephalosporin. To increase patient safety and reduce the risk of cannula-related infections, it is crucial to de-escalate treatment from intravenous to oral administration. Treatment failure rates were comparable for patients who went from intravenous antibiotics alone to oral antibiotics.19 Antibiotic de-escalation from intravenous to oral use should be carefully considered for patients. The most prevalent oral-step-down agents were cephalexin and oral fluoroquinolones; among 43 patients, 16 (37.2%) required this transition from intravenous to oral administration. Because of their high absorption, oral fluoroquinolones and cephalexin are useful in treating gram-negative bacteremia in hospitalized patients. Because of factors including clinical stability and bacteremia load, less than 50% of patients ultimately received oral antibiotic treatment. The infectious disease stewardship team can safely transition hospitalized patients from intravenous antibiotics to oral equivalents once they reach clinical stability, according to the ASP's IV to PO policy. The American Society of Pharmacy is working hard to reduce the expenses associated with intravenous antibiotic usage and the risks associated with it.

One of the most important biomarkers for detecting bacterial infections early on is procalcitonin (PCT). Because serum PCT levels are not increased in viral infections, it is an excellent biomarker for detecting bacterial infections, in contrast to other biomarkers like C-reactive protein (CRP), which do not distinguish between bacterial and non-bacterial infections with any degree of specificity. When the serum level is higher than 0.25 ng/mL, it may suggest the presence of bacteria. Reducing morbidity, mortality, and antibiotic usage may be achieved with early diagnosis of bacterial infections using PCT. Sera with high PCT levels are associated with sepsis and positive blood cultures.20 In order to address antimicrobial stewardship initiatives, this research also examined PCT levels at baseline in patients with Escherichia coli bacteremia in both non-ICU and ICU settings at a small community hospital. A total of 29 patients had their serum procalcitonin levels taken upon admission. The PCT analysis did not include 1 patient since their PCT level was higher than 100. Patients whose PCT levels were higher than 2ng/mL stayed an average of 9.6 days. Patients with other co-morbidities were not excluded from this research, therefore it is possible that other causes, such as impaired renal function, malignancy, or spinal cord injuries, are responsible for this rise. In the intensive care unit, PCT levels averaged 23 ng/mL, which was much greater than the 10 ng/mL levels seen in the non-intensive care unit. Given that septic shock and sepsis were more often treated in the intensive care unit, this is not surprising. Patients with PCT levels over 2.0 ng/mL are at high risk for sepsis and/or septic shock, according to the ASP policy on systemic bacterial infections. On average, it took 3 days for intensive care unit (ICU) patients and 4 days for non-ICU patients to reduce antibiotic dosages when PCT levels exceeded 2 ng/mL. Using procalcitonin levels as a guidance for de-escalation may reduce antibiotic duration without causing issues, according to studies.21-23 Antibiotic usage and appropriateness are further evaluated by the implementation of the procalcitonin policy by the ASP.

In a short amount of time, blood culture identification panels make it easy for doctors to understand positive blood culture findings. For example, the CTX-M gene, which is present in Enterobacterales that produce ESBL, is one example of an antibiotic resistance gene that the BCID panel looks for. Empirical treatment selection is guided by BCID panels.24 If blood culture findings reveal the presence of Escherichia coli without resistance indicators, the HNL Lab Medicine BCID panel recommends initiating empiric treatment with ceftriaxone. As an empirical treatment, meropenem should be used in cases where Escherichia coli with CTX-M is found.25 In order to determine the most effective use of antibiotics by eliminating the possibility of antibiotic-resistant microorganisms, our facility use blood culture identification panels (BCID). The average period for BCID panels to be submitted is 1.2 days, giving the ASP enough time to reduce antibiotic dosage (Table 6). This is of the utmost importance since the decrease in mortality and morbidity may be attributed to the quick start of the right antibiotic treatment.26 The antimicrobial stewardship team may quickly initiate the right antibiotic regimen or even reduce the dosage with a turnaround time of around 1 day. As an added bonus, this may lessen the likelihood of unpleasant side effects from medications, such as Clostridioides difficile infections. Due to the timely and accurate information they provide on pathogens, these quick diagnostic tests enhance patient care.26

Clinicians may use minimum inhibitory concentrations (MIC) to choose the best antibiotic for their patients. The Clinical and Laboratory Standards for Antimicrobial Resistance (CLSIR) classifies MICs as Susceptible (S), which indicates that the organism may be suppressed by the commonly used antibiotic at the acceptable dosage. One kind of antibiotic resistance is known as susceptible dose dependent (SDD), which occurs when the level of inhibition varies with the dosage of the drug. If the response rates of the organism's isolates are lower than those of the susceptible isolates, we say that the isolates are intermediate (I). This group demonstrates the clinical effectiveness of antibiotics at concentration locations or at doses above the recommended maximum. When the appropriate dosage of an antibiotic fails to stop the growth of an organism isolate, we say that the organism is resistant (R).27 Table 3 shows that of all the de-escalating agents used, cephalosporins were the most prevalent. The two most prevalent drugs used to reduce the effectiveness of cephalosporin's were ceftriaxone and cefazolin. At present, two groups—the Clinical and Laboratory Standards Institute in the United States and the European Committee on Antimicrobial Susceptibility Testing—are responsible for setting and publishing clinical MIC breakpoints. Oral cephalosporin's may be tested using cefazolin as a substitute. When administering a dosage of 1g every 8 hours, the CLSI guidelines for AST state that the minimum inhibitory concentration (MIC) of cefazolin for the treatment of simple UTIs is ≤16 μg/ml. Nineteen individuals had co-infections with Escherichia coli in their urine. We concentrated on bloodstream infections even though some patients also had urinary tract infections; this was because the CLSI recommendations for MIC breakpoints were revised to encompass illnesses other than UTIs. The MIC breakpoint for cefazolin, when used to treat infections other than simple UTIs caused by Escherichia coli, was determined to be less than or equal to 2 μg/ml according to CLSI guidelines for AST, which were based on a dosage of 2g per eight hours.27 The susceptibility testing for the small community hospital environment is conducted by the HNL lab. In 29 patients, the minimum inhibitory concentration (MIC) of cefazolin for systemic infections caused by Escherichia coli was found to be less than or equal to 4 µg/ml. The MIC value reported by our local lab is greater than what CLSI recommends. This is due to the fact that laboratories using FDA or commercial MIC susceptibility testing systems encounter several obstacles when trying to include new MIC breakpoints. Due to the length of time required for the FDA to approve the susceptibility testing systems that include the updated CLSI breakpoints, the implementation of new MIC breakpoints may be postponed for many years. This is because the system makers are unable to ship the necessary equipment to evaluate these breakpoints.28 Regardless of this obstacle, understanding how the CLSI updated breakpoints affect patient treatment is a crucial responsibility for ID experts and pharmacists. Hospital stays may be reduced via the efforts of the infectious disease stewardship team, which collaborates with the local HNL lab to enhance infection control measures and optimize antibiotic usage.

Conclusion

Antimicrobial stewardship programs (ASPs) in small community hospitals confront unique challenges; nonetheless, one such program is working to improve antibiotic appropriacy and shorten hospital stays for patients with Escherichia coli bacteremia by implementing a number of policies and tools. The ASP is greatly influenced by pharmacists because of the important responsibilities they play in implementing numerous initiatives to enhance health outcomes. The research has some limitations, such as a small sample size, a retrospective methodology, and the possibility of confounding variables due to varied main diagnoses. It may be challenging to forecast the findings' extrapolability to other facilities due to these restrictions. A more rigorous study design using a multicenter method on a bigger population sample may be the focus of future research. This research has highlighted the different pharmacist-led treatments that a small community hospital employs to enhance patients' healthcare, despite its constraints.

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.