

TURNAROUND TIME OF RESULTS OF BLOODSTREAM AND WOUND INFECTIONS CAUSED BY EXTENDED SPECTRUM BETA LACTAMASE POSITIVE ESCHERICHIA COLI AT MAKERERE UNIVERSITY CLINICAL MICROBIOLOGICAL LABORATORY. A CROSS-SECTIONAL STUDY.

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Abstract **Background**

The production of extended-spectrum beta-lactamase (ESBL) enzymes is a common mechanism by which *Escherichia coli* develops resistance to antibiotics. Timely detection and reporting of ESBL-producing *E. coli* is crucial, particularly in cases of bloodstream and wound infections. Therefore, this study aimed to determine the Turnaround Time of Results of Bloodstream and Wound Infections Caused by Extended Spectrum Beta Lactamase Positive *Escherichia coli* at Makerere University Clinical Microbiological Laboratory.

Methodology

This study was a cross-sectional retrospective analysis of lab records for ESBL-positive *E. coli* isolated from blood and pus samples received between the periods of January 2019 to March 2021 at the Makerere University Clinical Microbiology Laboratory, purposive sampling technique was used to select only records for which ESBL positive *E. coli*.

Results

For bloodstream infections, out of 91 *E. coli*-positive samples received between January 2019 and March 2021, 69.23% (63 samples) were processed within the standard 3-5 days as per lab SOPs. However, 26.3% (24 samples) took 6-8 days, and 4.4% (4 samples) required 9-11 days for processing. For wound infections, out of 85 samples, 61.18% (52 samples) were processed within 3-5 days, while 21.18% (18 samples) took 6-8 days, 3.53% (3 samples) took 9-11 days, and 14.12% (12 samples) exceeded 11 days for result processing.

Conclusion

From the study findings, it was noted that most samples were processed based on the standard operating procedures (SOPS) of the lab, except for 8 blood samples that were not cultured on MAC and blood agar and 2 pus swabs whose gram stain was not indicated.

Recommendation

The samples should be processed based on the standard operating procedures (SOPS) of the lab to avoid analytical errors.

Key Words: Makerere University, Blood and Wound Infections, Turnaround Time, Beta Lactamase Positive *Escherichia coli*.

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Background of the study

Escherichia coli is a lactose fermenting gram-negative motile bacteria commonly occurring as normal flora in the gut, despite being a commensal microorganism, pathogenic strains like extraintestinal pathogenic *E. coli* (ExPEC) strains are commonly associated with wound and bloodstream infections (Leimbach et al., 2013). Globally *E. coli* is responsible for approximately 20% of

all clinically significant isolates in blood cultures and 51.2% of isolated pathogens resulting in deep wound infections and diseases like osteomyelitis. (Kumar et al., 2020; Trojan et al., 2016). A study in two tertiary hospitals in Eastern Uganda discovered that *Escherichia coli* was the most prevalent 33.9% of isolated bacteria in cultures. (Obakiro et al., 2021)

It's estimated that severe *E. coli* sepsis causes approximately 40,000 deaths per year (Sharma et al., 2011). Fatality rates for bacteremia are between 13% and 19% but may be much higher (up to 60%) in elderly persons with nosocomial infections. (Roubaud Baudron et al., 2014) Factors like: age very young or old age; underlying respiratory infections and ciprofloxacin non-susceptibility were associated with high mortality rates. (Trojan et al., 2016, Mora-Rillo et al., 2015)

Extraintestinal pathogenic *E. coli* (ExPEC) poses specific virulence factors (VFs) that play a role in enabling the bacterial cells to colonize the host, disseminate, and survive in blood and various tissues causing bloodstream and wound infections. VFs are either encoded on the bacterial chromosome or plasmids; they include adhesion molecules, iron acquisition systems, host defense-subverting mechanisms, and toxin production (Daga et al., 2019). The emergence of extended-spectrum β -lactamase (ESBL) *E. coli* strains that can produce enzymes that make them resistant to penicillins and cephalosporins of the first, second, and third generations as well as aztreonam through hydrolysis of these antibiotics presents as a challenge in the management of *E. coli* isolated from the bloodstream and wound infections.

Currently, the prevalence of blood bloodstream and wound infections caused by ESBL-producing *E. coli* is estimated to be at 94.6 % and 60% respectively. (JCDR - Drug Resistance, Multiple, Bacterial, *Escherichia coli* Infections/Microbiology, n.d.; Kibret & Abera, 2011)

In a study done in Uganda to determine the prevalence of ESBL producers in cultures, 60% of the isolates were *Escherichia coli* isolates. Without early detection of ESBL-producing *E. coli* in the lab, treatment failure and disease complications may arise. (Kasango et al., 2018)

Therefore, timely and accurate detection of extended-spectrum beta-lactamase-producing *Escherichia coli* in blood and pus cultures is crucial in in-patient management and is dependent on quality control in all phases of the lab to prevent errors. However, the increase in the prevalence of diagnostic errors presents a challenge to the accurate and timely detection of extended-spectrum beta-lactamase *Escherichia coli*-positive samples. These Diagnostic errors could occur in either the pre-analytical, analytical, or post-analytical phase of lab diagnosis and may result in misdiagnosis, inappropriate therapeutic interventions, unnecessary investigations, diagnostic delays, mix-up of patient results, prolonged hospital stay, delays in reporting, unnecessary re-draws/re-tests, decreased customer satisfaction, increased costs, incorrect diagnosis, injury and occasionally death. (Green, 2013; State, 2015) The highest error rates were found in Blood (25.57 %), and wound cultures (12.06%)(PDF) Analysis on the Errors in the Pre-Analytical Process in a Clinical Microbiology Laboratory/ Bir Mikrobiyoloji Laboratuvarındaki Preanalitik Süreçteki Hataların Analizi, n.d.; Nichols, n.d. Valenstein, et al., n.d.). Hence, this study sought to determine the Turnaround Time of Results of Bloodstream and Wound Infections Caused by

Extended Spectrum beta-lactamase-positive *Escherichia coli* at Makerere University Clinical Microbiological Laboratory.

Methodology

Study Design

This study was a cross-sectional retrospective analysis of lab records for ESBL-positive *E. coli* isolated from blood and pus samples received between the periods of January 2019 to March 2021 at the Makerere University Clinical Microbiology Laboratory.

Study Area

The study was conducted at Makerere Clinical Microbiology Laboratory using lab records for ESBL-positive *E. coli* isolated from pus and blood samples. The Microbiology Clinical laboratory is found at the College of Health Sciences, Makerere University. It's a level 2 biosafety laboratory, accredited by the College of American Pathologists (CAP number 7225593) under the department of medical microbiology.

Study Population

The study population included all records of ESBL-positive *E. coli* isolated from blood and pus cultures obtained from patient test results from the period of January 2019 to March 2021 at the Makerere Clinical Microbiology Laboratory, College of Health Sciences, Makerere University.

Study selection criteria

Inclusion criteria

All records of ESBL-positive *E. coli* isolated from blood and pus cultures collected between the periods of January 2019 to March 2021 at the Makerere Clinical Microbiology Laboratory were included in this study.

Exclusion criteria

Records of other *E. coli* phenotypes isolated from blood and pus cultures were excluded from this study.

Sample Size Determination

The sample size was calculated using the Kish-Leslie formula (1965) below

$N =$

$N =$

$N = 148$ samples

Where, N = the desired sample size.

Z = the standard normal deviation 1.96, at a 95% confidence interval.

P = 44.4% prevalence of diagnostic lab errors as identified by a study done to determine errors in sample processing in the lab (Carraro & Plebani, 2007).

$Q = 1 - P$

$d2$ = maximum error the investigator is willing to allow, (8%).

Study variables

Dependent variables

This variable was the timely and accurate reporting (turnaround time) of samples positive for ESBL *E.coli* isolated from blood and pus cultures.

Independent variables

The independent variables included;

Prevalence of ESBL-positive *E. coli*.

Pre-analytical errors like missing information on the lab request form e.g. missing age, name, sex, lab identification number, specimen type, test, and initials of recipient.

Analytical errors due to non-conformity with standard operating procedures for processing blood and pus samples e.g. missing gram stain, subculture, biochemical test, antimicrobial susceptibility test results, and initials of lab personnel who carried out the test

Post analytical errors like wrong data entry and increased turnaround time of results.

Other factors beyond control e.g., electricity, water, reagents shortages.

Sampling technique

A purposive sampling technique was used to select only records for which ESBL-positive *E.coli* were reported by the lab between the period January 2019- March 2021.

Data collection tools

A checklist was used to collect data on lab errors occurring at the different stages of the lab cycle from sources like the sample reception, blood, and pus culture books.

For the preanalytical phase, data was collected using the sample reception book and the laboratory request forms to identify any errors that occurred like missing age, name, sex, lab identification number, specimen type, test, and initials of the recipient.

For the analytical phase, data was collected from the blood culture book and Pus swab book of the Makerere Clinical Microbiology Laboratory and used to identify any errors that occurred due to failure to follow standard operating procedures while processing the samples like; missing gram stain, subculture, biochemical test, antimicrobial susceptibility test results and initials of lab personnel who carried out the test.

The blood culture book and Pus swab book were used to monitor turnaround time which was calculated as the difference in time between when the sample was received at the lab and the time the results were reported or dispatched.

The prevalence of ESBL-positive *E.coli* was calculated using results recorded in the blood and pus culture books of the clinical microbiology laboratory.

Data Analysis and presentation

The data collected was checked for correctness and completeness. The data was then entered into a data capture tool (EPIDATA), validated, and exported to STATA version 13 for analysis.

This statistical analysis aimed at establishing the prevalence of ESBL-positive *E.coli* and determining the effect of laboratory errors on the accurate and timely reporting of bloodstream and wound infections caused by extended-spectrum beta-lactamase-positive *Escherichia coli* over the stated study period.

Quantitative data was then presented in the form of pie charts, tables, graphs, and written information.

Quality control

Data was extracted by two people to ensure accuracy and consensus, this made certain that no details were left eliminated or repeated.

Ethical consideration.

The study got ethical clearance from the higher degree and graduate research ethics committee (HDREC) of the School of Biomedical Sciences, Makerere University College of Health Sciences.

Permission to collect data was sought from the laboratory director through the Head of the department of medical microbiology and the laboratory Manager of the clinical microbiology laboratory to carry out a research study within their premise.

A waiver of consent was applied for from the laboratory management. This research only commenced after approval by the Institutional Review Board.

The patient details were kept with utmost confidentiality and were only accessed by study investigators who returned the documents to the laboratory immediately after use.

Data entries and results were identified by unique codes generated in the laboratory rather than patient names.

Results

Effect of Laboratory Errors on the Accurate and timely reporting of Bloodstream Infections Caused by extended-spectrum beta-lactamase *Escherichia coli* Turnaround time of reporting ESBL-positive *E.coli* bloodstream infections.

The majority of 63(69.23%) of the samples were processed within the stipulated time of 3-5 days as per the lab sops from the time of reception, while a few of them 24(26.3%) took 6-8days before results were sent out. A small percentage of 4(4.4%) samples took 9-11 days to be processed as shown in Figure 1.

Figure 1: Turnaround time of reporting ESBL-positive E.coli bloodstream infections. (N=91)

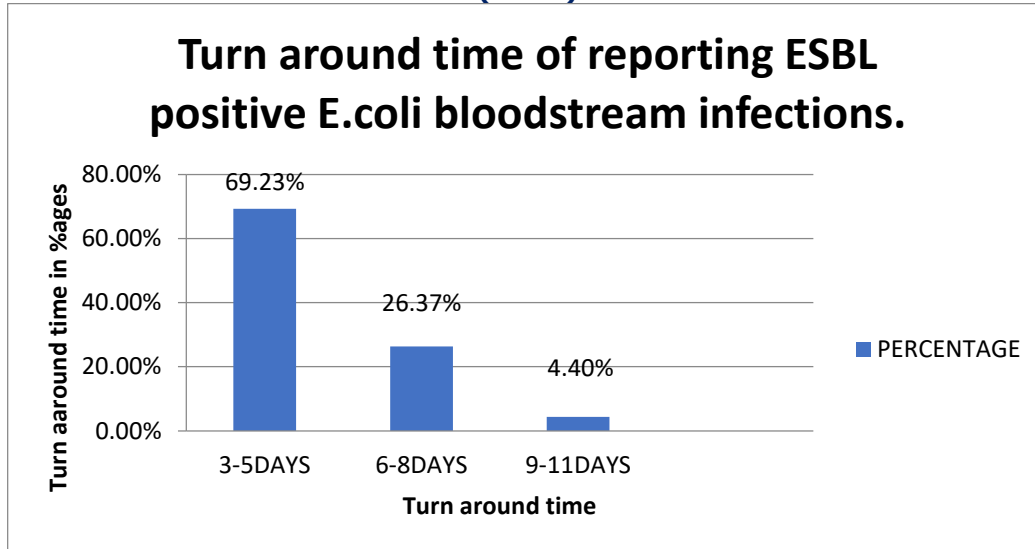


Figure 1 shows the turnaround time of reporting ESBL-positive *E. coli* stream infections. The majority 63(69.23%) of the samples were processed within the stipulated time of 3-5 days as per the lab sops from the time of reception. The minority 4(4.4%) of samples took 9-11 days to be processed.

Effect of laboratory errors on the accurate and timely reporting of wound infections

caused by extended-spectrum beta-lactamase positive Escherichia coli Turnaround time of reporting ESBL-positive E.coli wound infections.

The majority 52(61.18%) of the samples were processed within the stipulated time of 3-5 days as per the lab sops from the time of reception, while 18 (21.18%) took 6-8days, 3 (3.53%) took 9-11days and 12 (14.12%) took greater than 11days before results were sent out as shown in figure 2.

Figure 2: Turnaround time of reporting ESBL-positive E.coli wound infections. (N=85)

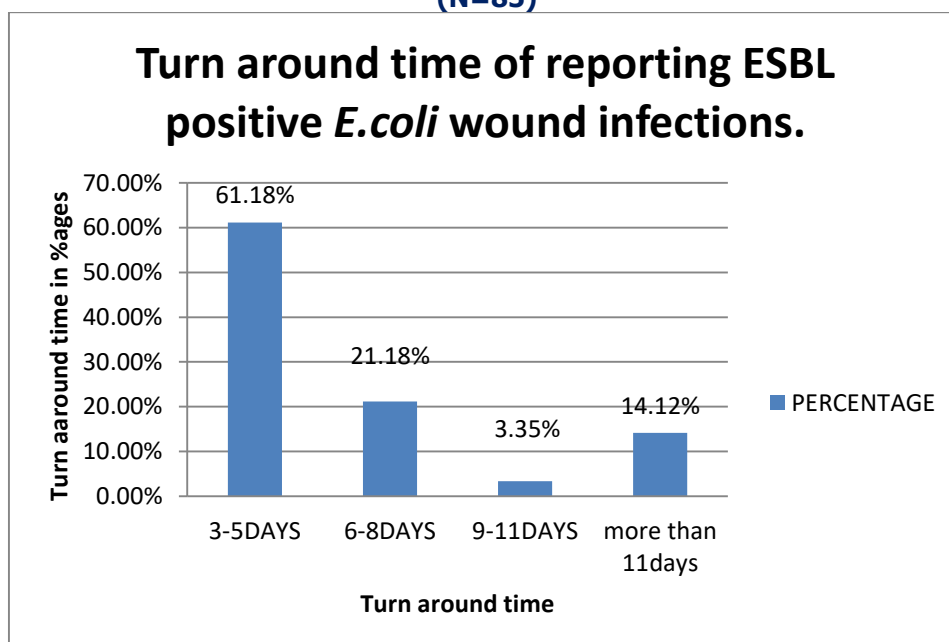


Figure 2, shows the turnaround time of reporting ESBL-positive *E.coli* wound infections.

The majority 52(61.18%) of the samples were processed within the stipulated time of 3-5 days as per the lab sops from the time of reception. The minority 3(3.35%) of samples took 9-11 days to be processed.

Discussion

Effect of turnaround time on accurate and timely detection of ESBL positive *E.coli* in blood and wound infections.

In this study of the 91 blood culture samples, 28(30.76%) had a long turnaround time greater than 5 days as stipulated by the lab sops. 8 (28.57%) of these also had missing details in the lab request forms and 5(17.86%) had no culture results for Mac and BA recorded in the lab bench book. While 33(38.82%) of the 85 pus swab samples were also found to have a turnaround time greater than 5 days of these (10) 30.30% had missing details on the request forms and 2 (6.06%) had no gram stain result recorded. These findings clearly show that lab errors occurring at other phases of the lab cycle could indirectly prolong the turnaround time for results. In cases of prolonged turnaround time and the isolated organism was ESBL positive *E.coli* as is the case in this study where 13(46.43%) and 12(36.36%) blood cultures and pus swabs respectively were ESBL positive *E.coli* and had turnaround time greater than 5 days patient may affect patient outcome leading to increased mortality and morbidity, inappropriate medication and inappropriate admission to i.c.us and unnecessary.

Conclusion

Of the 91 blood cultures and 85 pus swab results reviewed, most of them were processed within the stipulated time as per the lab SOPS which is 3 days, 63 (69.23%) for blood cultures and 52 (61.18%) for pus swabs obtained from wound infections. However, a few of the samples had prolonged turnaround time; 28 blood cultures and 33 pus samples. Of these 28 (30.76%) blood cultures had long turnaround and 8 (28.57%) of these also had missing details in the lab request forms while 5(17.86%) had no culture results for Mac and BA recorded in the lab bench book. While 33(38.82%) of the 85 pus swab samples had long turnaround time (10) 30.30% had missing details on the request forms and 2 (6.06%) had no gram stain result recorded.

Recommendation

The samples should be processed based on the standard operating procedures (SOPS) of the lab to avoid analytical errors.

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List of Abbreviations

E.coli; *Escherichia coli*
ESBL; Extended Spectrum Beta Lactamases
Expt; Extraintestinal pathogenic *Escherichia coli*
Lab; Laboratory
VF; virulence factor
MAC; MacConkey agar
BA; Blood agar
AST; Antimicrobial susceptibility test
Abx; Antibiotics

Source of funding

The study was not funded.

Conflict of interest

The author declares no conflict of interest.

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