

Original Research Article

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Predicting Carriage of Extended-Spectrum Beta-Lactamase producing Enterobacteriaceae (ESBL-E) in Intensive Care Unit Patients: A Cross Sectional Study

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ABSTRACT

The incidence of Extended-Spectrum Beta-Lactamase Producing *Enterobacteriaceae* (ESBL-E) infection is rising worldwide. ESBL-E is a group of pathogens increasingly encountered in ICU setting. Infections with ESBL-E are associated with increased morbidity and mortality. The present study was undertaken to determine the prevalence of patients colonized with Extended Spectrum Beta Lactamase producing *Enterobacteriaceae* (ESBL-E) in intensive care unit (ICU) patients and also to assess risk factors for ESBL carriage. Patients admitted or transferred to ICU were included in the study and their rectal swabs were collected on admission and discharge. The swabs were cultured and tested for ESBL-E. Out of 50 cases, 41 (82%) cases were Males and 9 (18%) cases were Females. Most of cases was in the age group of 21-30 years and above followed by that of 11-20 years. Out of these 50 cases, 29 (58%) cases were culture positive (colonised patients) and 21 (42%) cases were Culture negative (non colonised patients). Of the 29 culture-positive cases, *Escherichia coli* was isolated from 16 (32%) samples; *Klebsiella pneumoniae* was isolated from 5 (10%) samples and both were isolated from 8 (16%). The rate of subsequent development of infection was higher in colonized patients (10%) compared to non colonized patients (2%). The study revealed high rates of carriage of ESBL producers in patients admitted to the ICU. Prior colonization with ESBL-E could result in their influx and spread in ICU, challenging infection control measures. Screening of the ESBL producers in the ICU's and proper implementation of infection control measures can control the infections in ICU.

Keywords

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Introduction

Extended Spectrum Beta Lactamase producing *Enterobacteriaceae*

(ESBL-E) are found worldwide with rates varying between countries and institutions (Pena *et al.*, 2006; Canton and Coque, 2006). In intensive care unit (ICU), infection and

colonization by resistant Gram-negative bacteria increase costs, length of stay and mortality. Extended Spectrum Beta Lactamase producing *Enterobacteriaceae* (ESBL-E) is a group of pathogens increasingly encountered in ICU setting. Conditions that promote ESBL-E acquisition are not completely understood. Infections with ESBL-E are associated with increased morbidity and mortality (Stewardson *et al.*, 2013).

Early detection of ESBL-E carriage could allow timely implementation of infection control measures and the appropriate selection of antimicrobials (Harris *et al.*, 2007). On admission surveillance for ESBL-E has been associated with a reduced incidence of ESBL-E infections during hospitalization (Lowe *et al.*, 2013). However, universal screening for ESBL-E is time consuming, expensive and unlikely to be feasible (Gardam *et al.*, 2002; Thouverez, 2004). Targeted screening based on clinical prediction tools could therefore be useful. The development of such tools requires knowledge of the local epidemiology of ESBL-E (Johnson *et al.*, 2013).

Hence the present study was undertaken to determine the prevalence of patients colonized with Extended Spectrum Beta Lactamase producing *Enterobacteriaceae* (ESBL-E) in intensive care unit (ICU) patients and also to assess risk factors for ESBL carriage. The main aim of the study is to formulate a prediction tool for ESBL carriage at hospital admission and also to quantify incidence of infections for ICU patients.

Materials and Methods

This cross sectional study was conducted Department of Microbiology and Department of Medicine (Intensive care unit) at Tirunelveli Medical College Hospital, Tirunelveli, Tamil Nadu for the period of six

months from April 2018 to October 2018. The study protocol was approved by the Institutional Scientific and Ethics Committee

Study population

All patients >18 years of age consecutively admitted to Intensive Medical care unit.

Sample collection

Every patient was underwent rectal swab screening for ESBL-E carriage at admission and then twice a week until ICU discharge performed by ward nurses. A swab is defined as “on admission” if it had been performed within 48 h of admission to an internal medicine unit. A “discharge swab” was performed within 36 h of discharge. “In-hospital acquisition” was established if patients had an ESBL-E identified on a discharge swab where the admission swab had been negative. Enhanced hygiene measures (protective gowns, gloves, ESBL-E announcing stickers) were applied in the case of patients colonized and/or infected by ESBL-E and preventively in patients considered at risk for ESBL-E carriage. Demographic data was collected. Patient records were reviewed retrospectively to obtain data on co-morbid conditions and antibiotic use.

Microbiological Methods

Screening test for ESBLs

Screening for ESBL-E was performed by inoculating rectal swabs directly onto HiChrome ESBL agar and was incubated at 37°C for 18–24hrs. Antibiotic susceptibility was tested using Disc diffusion method on Mueller-Hinton agar according to CLSI guidelines. The following antibiotics were tested: Ampicillin, Cefoxitin, Cefotaxime, Ceftazidime, Imipenem, Ertapenem,

Meropenem, Gentamicin, Amikacin, Nalidixic acid, Ciprofloxacin and Co-trimoxazole.

Confirmatory tests for ESBLs

The ESBL producers were confirmed by simultaneously performing the Clinical and Laboratory Standards Institute confirmatory test for the detection of ESBL using double-disk synergy method (CLSI, 2017). This test requires the use of a third-generation cephalosporin antibiotic disk alone and in combination with clavulanic acid.

In this study, a disk of Ceftazidime (30µg) alone and a disk of Ceftazidime + Clavulanic acid (30 µg/10 µg) were used.

Both the disks were placed at least 25 mm apart, centre to centre, on a lawn culture of the test isolate on Mueller Hinton Agar (MHA) plate and incubated overnight at 37°C. Difference in zone diameters with and without clavulanic acid was measured. Interpretation: When there is an increase of ≥ 5 mm in inhibition zone diameter around combination disk of Ceftazidime + Clavulanic acid versus the inhibition zone diameter around Ceftazidime disk alone, it confirms ESBL production. All ESBL-E producing isolates were stored at -80°C .

Statistical analysis

Data from this study was analyzed descriptively using chi squared tests for categorical variables and student t tests for interval variables.

Factors potentially associated with previously unknown carriage of ESBL-E on admission and ESBL-E acquisition on discharge was first evaluated using univariate logistic regression. Variables were retained if the P-value was <0.2 .

Results and Discussion

Fifty patients were included in the study and their rectal swabs were cultured. Out of these 50 cases, 41 (82%) cases were Males and 9 (18%) cases were Females. Most of cases was in the age group of 21-30 years and above followed by that of 11-20 years. Age wise Distribution of Samples was depicted in Table 1.

Out of these 50 cases, 29 (58%) cases were culture positive (colonised patients) and 21 (42%) cases were Culture negative (non colonised patients). Of the 29 culture-positive cases, *Escherichia coli* was isolated from 16 (32%) samples; *Klebsiella pneumoniae* was isolated from 5 (10%) samples and both were isolated from 8(16%) by HiChrome ESBL agar method (Table 2).

The overall prevalence rate of ESBL-E was 58%.The most commonly isolated organism was *E. coli* (32%) isolates, *Klebsiella* isolates (10%) and both (16%) were ESBL-E positive by Double disc diffusion method (Table 3).

All 29 ESBL isolates were resistant to 3rd Generation cephalosporins, Trimethoprim-sulfamethoxazole, Ciprofloxacin while resistance rates to Amikacin, Gentamicin, Ampicillin were 86.2% (25/29), 93.1% (27/29), 86.2% (25/29) respectively (Table 4). All isolates were susceptible to Imipenem, Meropenem and Ertapenem.

All the fifty patients screened were followed for the development of infection during ICU period and 4 (8%) developed Blood stream infection in colonized patients. No infection developed in non colonized patients.

The widespread indiscriminate use of antimicrobials has led to the emergence and spread of antibiotic resistance. The prevalence of ESBL-producing isolates has increased in

the past few decades. Outbreaks of infections in the health-care settings have been linked to higher rates of faecal carriage of ESBL-producing isolates.

The present study showed a rate of 58% faecal carriage of ESBL producers. The prevalence of faecal carriage of ESBLs in this study was similar to the study conducted by Mulki *et al.*, (2017). In a study done by Paniagua *et al.*, (2010) the rates of faecal carriage of ESBL producers had increased from 0.3% to 11.8% from 1991 to 2003. The higher rate of carriage in this study may be due to increased exposure

of antibiotics over the years. All the fifty patients screened were followed for the development of infection during ICU period and 4 (8%) developed Blood stream infection in colonized patients. No infection developed in non colonized patients. The previous studies have reported 65% carriage rate in patients with urinary tract infection and 8.5% carriage rate in healthy individuals (Rodríguez-Baño *et al.*, 2008). A study by Reddy *et al.*, showed that 8.5% of the ESBL colonizers developed a subsequent ESBL bloodstream infections (Reddy, 2007).

Table.1 Age wise distribution of samples

Age	No of patients
11-20	11
21-30	13
31-40	11
41-50	6
51-60	4
61-70	3
<70	2

Table.2 Organism wise distribution of samples

Organism	No of growth	Percentage
<i>Escherichia coli</i>	16	32%
<i>Klebsiella pneumoniae</i>	5	10%
<i>Escherichia coli</i> & <i>Klebsiella pneumoniae</i>	8	16%

Table.3 Frequency of ESBL production in Gram negative isolates among carriers

Sl. no	Organism	Percentage
1	<i>Escherichia coli</i>	32%
2	<i>Klebsiella pneumoniae</i>	10%
3	<i>Escherichia coli</i> & <i>Klebsiella pneumoniae</i>	16%

Table.4 Proportion of anti microbial resistance among 29 ESBL producing *Escherichia coli* and *Klebsiella pneumoniae*

Anti microbial agent	<i>E. coli</i>	<i>Klebsiella pneumoniae</i>
Amikacin	81.25%	92.3%
Gentamicin	93.75%	92.3%
Ciprofloxacin	100%	100%
Trimethoprim-sulfamethoxazole	100%	100%
Ampicillin	100%	69.2%

The rates of colonization with multi resistant isolates have shown an alarming rise over the past few decades. The matter of concern is the emergence and spread of ESBL-producing isolates. The rectal surveillance for *ESBL-producing Enterobacteriaceae* will play a pivotal role in infection control. The ESBL-colonized patients act as source of infection to the other hospitalized patients in high-risk areas.

Asymptomatic colonization of ESBLs can thus be a threat to the subsequent development of infection, especially in the ICU settings. The surveillance of rates of faecal carriage of *ESBL-producing Enterobacteriaceae* may be helpful to track and monitor the spread of these organisms in the hospital settings. The rates of infection can be controlled by following strict infection control measures.

This study focuses on screening for faecal carriage of *ESBL-producing Enterobacteriaceae* members using rectal swab cultures in patients admitted to ICU of a tertiary care hospital and follows the patients for the subsequent development of infections with ESBL-producing organisms in the gut flora. The study revealed high rates of carriage of ESBL producers in patients admitted to the ICU. Prior colonization with ESBL-E could result in their influx and spread in ICU, challenging infection control measures. Gut colonization with these strains may be a

source of endogenous infection and horizontal transfer of these genes in future. Carriage of ESBL-producing commensal strains of *Enterobacteriaceae* is a threat as it can get transferred to the pathogenic strains. Screening of the ESBL producers in the ICU's and proper implementation of infection control measures can control the infections in ICU.

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