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Research Article

Extended-Spectrum β Lactamase Producing *Escherichia coli*

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ABSTRACT

Background: The incidence of nosocomial infection caused by Extended Spectrum β Lactamase (ESBL) producing bacteria is increasing worldwide. Infections caused by Extended Spectrum β Lactamase (ESBL) producers have been associated with severe adverse clinical outcomes that have led to increased mortality, prolonged hospitalization, and rising medical costs.

Aim: The main objective of this study was to determine the prevalence of Extended Spectrum β Lactamase (ESBL) production among nosocomial isolates of *Escherichia coli* (*E. coli*) and associated risk factors.

Subject and methods: A nested case-control, hospital-based study was conducted for a period of 3 months from the 1st of September 2017 to the end of November 2017. Total 192 consecutive non-duplicate clinical isolates of *E. coli* from various clinical specimens collected from adult patients admitted to Al-Hussein University hospitals in Egypt.

Results: Out of the 192 isolates, 63 (32.8%) were Extended Spectrum β Lactamase (ESBL) producers, and 129 (67.2%) as non-Extended Spectrum β Lactamase (ESBL) producers. Highest ESBLs were found in urine sample (58%) followed by wound swap (22.6%). Ventilator use, increased duration of hospital stay of >7 days and prior use of antibiotics were significantly risk factor for the occurrence of Extended Spectrum β Lactamase (ESBL) producers *E. coli* (P=0.01, 0.03 and 0.003 respectively).

Conclusion: In this study, we identified Ventilator use, increased duration of hospital stay and prior use of antibiotics was associated with the occurrence of Extended Spectrum β Lactamase (ESBL) producers *E. coli*.

Keywords: *Escherichia coli*, Extended Spectrum β-Lactamase (ESBL), Risk factors

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INTRODUCTION

Escherichia coli are a common cause of community-acquired and nosocomial bacterial infections. Extended Spectrum beta Lactamase (ESBL) producing *E. coli* infections first occurred in the nosocomial setting then spread to community-acquired infection. It is now a major public health problem (Hawser SP, *et al*., 2009). Extended Spectrum beta Lactamases (ESBLs) are a heterogeneus group of enzymes responsible for the resistance of enterobacteria to broad spectrum beta lactam antibiotics (Hsieh CJ, *et al*., 2010). The incidence of infections due to Extended Spectrum β Lactamase (ESBL) producing bacteria has increased rapidly in recent years and poses a worldwide threat to health care (Ben-Ami R, *et al*., 2009). It is recognized that Egypt has a very high Extended Spectrum β Lactamase (ESBL) rate of 60.9% (Al-Agamy MH, *et al*., 2006).

The close relationship between Extended Spectrum β Lactamase (ESBL) production and multidrug resistance leaves only a few treatment options for infections commonly caused by Enterobacteriaceae (Hawser SP, *et al*., 2009). Patients with an infection caused by Extended Spectrum β Lactamase (ESBL) producing bacteria are at risk for therapeutic failure or even death because there is often a delay before the correct antibiotic treatment is given (Schwaber MJ and Carmeli Y, 2007).

The known risk factors for colonization or onset of infection with Extended Spectrum β Lactamase (ESBL) producing Enterobacteriaceae are antibiotic use, prolonged and/or recent hospital stay, severe illness, recent surgery, bladder catheterization or other invasive medical devices, residence in a long-term care facility, international travel, and age 65 years and older (Tham J, *et al*., 2010; Tangden T, *et al*., 2010). Poor hand hygiene and lack of food hygiene facilitates the spread of Extended Spectrum β Lactamase (ESBL) producing Enterobacteriaceae (Kaier K, *et al*., 2009). It is important to identify patients who are at risk for infection with Extended Spectrum β Lactamase (ESBL) producing bacteria, especially in low endemic countries, in order to reduce mortality, to avoid spread of resistant bacteria in hospitals, and to minimize the number of patients receiving unnecessary treatment with broad spectrum antibiotics (Schwaber MJ and Carmeli Y, 2007).

This study was undertaken to determine the prevalence of Extended Spectrum β Lactamase (ESBL) production among nosocomial isolates of *E. coli* and risk factors associated with contracting this type of infection.

MATERIALS AND METHODS

A nested case control, hospital based study was conducted for a period of three months (from September 2017 to November 2017). A total number of 192 consecutive, non-duplicates, clinical isolates of *E. coli* were obtained from the cultures of specimens from patients aged >18 years hospitalised for >48 hours in El-Hussein University Hospitals in Egypt. The source of these isolates was urine (82), wound swap (33), pus exudates (53), sputum (32) and vaginal swab (14). Bacterial isolates of *E. coli* were subjected to antibiotics susceptibilty testing by disc diffusion technique. The combination disc test using ceftazidime; alone and in combination with clavulanic acid, was performed for the detection of Extended Spectrum β Lactamases (ESBLs) according to Clinical and Laboratory Standards Institute guidelines (Wayne PA, 2010).

Cases were defined as patients diagnosed with Extended Spectrum β Lactamase (ESBL) producing *E. coli* from September 2012 and November 2012. Controls were randomly selected from the same patients diagnosed with non-Extended Spectrum β Lactamase (ESBL) producing *E. coli* during the same time period. The following data were collected, age, gender, duration of hospital stay, previous antibiotic therapy, stay in Intensive Care Unit (ICU), presence of invasive device such as urinary catheter or intravenous devices, and use of ventilator or corticosteroid and presence of underlying diseases such as diabetes mellitus, renal failure, liver cirrhosis and malignancy.

Statistical analysis

Data analyses were performed using SPSS, version 12. Categorical variables were compared using Fisher's exact or Pearson's chi-square tests where appropriate. The Student's t-test was used to test for statistical significance of the continuous variables. With 95% Confidence Intervals (95% CI) a P-value of <0.05 was considered statistically significant.

RESULTS

Out of the 192 isolates, 63 (32.8%) were Extended Spectrum β Lactamase (ESBL) producers, and 129 (67.2%) as non-Extended Spectrum β Lactamase (ESBL) producers. Highest ESBLs were found in urine sample (58%) followed by wound swap (22.6%). Ventilator use, increased duration of hospital stay of >7 days and prior use of antibiotics were significantly risk factor for the occurrence of Extended Spectrum β Lactamase (ESBL) producers *E. coli* (P=0.01, 0.03 and 0.003 respectively).

Distribution of Extended Spectrum β Lactamase (ESBL) positive isolates in different clinical samples showed in *Table 1*:

A total of 192 consecutive non-duplicate clinical isolates of *E. coli* from various clinical specimens collected from different wards of Al-Hussein and Damietta University hospitals. Disk diffusion method detected 63 (32.8%) isolates as Extended Spectrum β Lactamase (ESBL) producers and 129 (67.2%) as non-Extended Spectrum β Lactamase (ESBL) producers. Highest Extended Spectrum β Lactamases (ESBLs) were found in urine sample (58%) followed by wound swap (22.6%).

The results of the risk factor analysis listed in *Table 2*:

Mean age ± SD of patients with Extended Spectrum β Lactamase (ESBL) producing isolates was 41.7 ± 19.6 years compared to 39.2 ± 17.4 years for Extended Spectrum β Lactamase (ESBL) non producer patients.

There was a significant difference between the Extended Spectrum β Lactamase (ESBL) positive and Extended Spectrum β Lactamase (ESBL) negative groups with regard to prior use of a ventilator (P=0.01), duration of hospital stay >7 days (P=0.03) and prior use of antibiotics (P=0.003) and presence of invasive device and underlying illness were not significant risk factors in this study.

Table 1: Distribution of Extended Spectrum β Lactamase (ESBL) positive isolates in different clinical samples

Type of samples	Isolates tested		ESBLs producers	
	No.	%	No.	%
Urine	88	45.8	51	58
Wound swab	31	16.2	7	22.6
Pus	40	20.8	5	12.5
Sputum	17	8.9	0	0
Vaginal swab	14	7.3	0	0
Total	192	100	63	32.8

Table 2: Demographic data and risk factors for ESBL-producing *E. coli*

Variables	ESBL +ve (63)		ESBL -ve (129)		OR	Confidence Interval (95%)	P value
	No.	%	No.	%			
Age (mean ± SD yrs)	41.7+19.6		39.2+17.4		-	-8.0-3.0	0.37
Sex (male)	43	68	74	57.4	1.6	0.8-3.2	0.15
Invasive devices							
Urinary catheter	26	41.3	53	41	1	0.5-2.0	0.98
Intravenous devices	29	46	61	47.3	1	0.5-1.8	0.87
Use of ventilator	23	36.5	25	19.4	2.4	1.2-4.9	0.01
Duration of hospital stay							
>7 days	41	65	63	48.8	2.5	1.3-4.8	0.03
<7 days	22	35	66	51.2			
Use of antibiotics	37	58.7	47	36.4	2	1.0-3.8	0.003
Use of corticosteroid	19	30.1	39	48.8	1	0.5-2.2	0.83
Underlying diseases							
Liver cirrhosis	31	30.2	59	45.7	1.1	0.6-2.2	0.65
Diabetes	34	54	65	50.4	1.2	0.7-2.2	0.64
Renal failure	22	35	33	25.6	1.7	0.8-3.2	0.18

DISCUSSION

Nosocomial infections caused by Multi Drug Resistant (MDR) gram negative bacteria expressing Extended Spectrum Beta lactamases (ESBL) pose serious therapeutic challenge to clinicians due to limited therapeutic options. Our study found that the prevalence of Extended Spectrum β Lactamase (ESBL) producing *E. coli* was 32.8%. The current study findings are similar to that reported in Saudi Arabia (31.0%) (Memon JI, *et al*., 2009).

The highest rate of Extended Spectrum β Lactamase (ESBL) production was found in isolates from urine samples (40%), followed by wound swabs (18.75%). This is similar to another study (Kader AA and Kumar A, 2005).

Similar to previous study, the present study showed long hospital stay was significantly associated risk factor for infection with Extended Spectrum β Lactamase (ESBL) producing bacteria (Shanthi M and Sekar U, 2010).

Also prior use of antibiotics prior and use of a ventilator were significant risk factors associated with the occurrence of Extended Spectrum β Lactamase (ESBL). These risk factors were similar to those identified in other studies (Lautenbach E, *et al*., 2001; Graffunder EM, *et al*., 2005).

While urinary and vascular catheterization were not significantly associated with Extended Spectrum β Lactamase (ESBL) in our study. Our findings are similar to the findings of few other authors (Harris AD, *et al*., 2007; Shanthi M, and Sekar U, 2010) while other studies have found the opposite results (Ankur G, *et al*., 2009; Memon JI, *et al*., 2009).

Also patient sex, gender, underlying illness and prior use of corticosteroid were not significant risk factors associated with the occurrence of Extended Spectrum β Lactamase (ESBL). Other studies have shown the same results (Memon JI, *et al*., 2009; Shanthi M, and Sekar U, 2010).

CONCLUSION

Highest ESBLs were found in urine sample (58%) followed by wound swap (22.6%). Ventilator use, increased duration of hospital stay of >7 days and prior use of antibiotics were significantly risk factor for the occurrence of Extended Spectrum β Lactamase (ESBL) producers *E. coli* (P=0.01, 0.03 and 0.003 respectively). In this study, we identified ventilator use, increased duration of hospital stay and prior use of antibiotics was associated with the occurrence of Extended Spectrum β Lactamase (ESBL) producers *E. coli*.

RECOMMENDATION

There is a need to review antibiotic prescription practices to reduce the risk of occurrence of Extended Spectrum β Lactamase (ESBL) producers *E. coli*.

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