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Research Article

# A Multicenter Surveillance and Reporting of Antimicrobial Resistance: Focus on Ceftriaxone-Resistant *Escherichia coli* in the Year 2012 and 2013

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**ABSTRACT**
Introduction: Bacterial resistance to commonly prescribed antibiotics is increasing both in developing and developed countries. Resistance to more potent antimicrobial agents has also emerged. The present study aims to report information concerning *Escherichia coli* resistance to ceftriaxone from clinical specimens from three hospitals in Bandung, Indonesia. Method: A total of 234 specimens in 2012 and 601 specimens in 2013 were collected from all three hospitals. The results were processed to obtain the profile prevalence ceftriaxone-resistant *E. coli* and the distribution on infected specimens. Result: Increasing number of ceftriaxone-resistant *E. coli* were observed in two hospitals, hospital A from 35.38% to 43.02% and hospital C from 43.9% to 52.6%. The source of clinical specimen of E. *coli* resistant to ceftriaxone was varied in all hospital. In hospital A, pus and faeces were the predominant infected specimens. Meanwhile in hospital B, sputum was the predominant infected specimen, and in hospital C urine was the most common specimen infected by ceftriaxone-resistant *E. coli*. Conclusion: The high and increasing rate of ceftriaxone-resistant *E. coli* indicate that it is imperative to rationalize the use of antimicrobials in hospitals, use them prudently and also mandate our attention, and periodic monitoring of the trend of the resistance is crucial. A team-based approach to patient care is needed between pharmacist and prescriber to combat antibiotic resistance.

**Keywords:** *E. coli*, ceftriaxone, resistant, specimen, hospital

## INTRODUCTION

Antibiotic resistance has reached crisis point in many hospitals around the world. Multi-drug resistant (MDR) *E. coli* exhibits a high rate of resistance to various antibiotics and increases the cost of treatment, morbidity, and mortality. *Escherichia coli* is one of the most frequent causes of many common bacterial infections, especially health care-associated infections (HAIs)[1,2]. The main factor that causes increasing antimicrobial drug resistance rates is irrational antimicrobial drug usage[3]. One class of antibiotics that bacteria have increased resistance rates towards is the cephalosporin. Bacterial resistance to cephalosporin generally arises from three main mechanisms i.e. reduced cell wall penetrability, altered penicillin binding proteins and the production of beta lactamases enzyme which can hydrolyze the beta lactam ring[4]. Ceftriaxone is a broad spectrum antibiotic belonging to the third-generation cephalosporin class used to treat HAIs caused by *E. coli*[5]. *E. coli* remains relatively susceptible to third generation cephalosporin, but various studies have shown that the prevalence of ceftriaxone-resistant *E. coli* strain is higher in many countries. However, there is little information regarding the resistance pattern of *E. coli* against ceftriaxone in Indonesia. The present study was undertaken to assess the current antibiotic resistance pattern in the common pathogens isolated in three hospitals in Bandung, Indonesia, with a special emphasis on ceftriaxone.

## METHOD

This hospital record based cross-sectional study was conducted in three hospitals located in Bandung, Indonesia. The analysis was done on all isolates obtained from all specimens among hospital inpatients, admitted during the period of January to December 2012 and January to December 2013. The study was conducted on results of cultures of urine, blood, sputum, faeces, pus swab and others (eye discharge and pleura discharge). As well as *E. coli* isolates and antimicrobial susceptibility data were collected from the registration records using a standard data collection form. The microbial identification of patients' specimen based on standard microbiological methods and microbial antibiotic sensitivity test performed using the Kirby Bauer method. The results were interpreted in accordance with the guidelines on Clinical and Laboratory Standards Institute[6]. Ethical permission was not needed in this study because hospital patients were not used directly. Comparison between the rate of

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Table 1: The comparative prevalence between ceftriaxone-resistant E. coli to ceftriaxone-sensitive E. coli in the year 2012 and 2013

| Ceftriaxone | Hospital A | | Hospital B | | Hospital C | |
|---|---|---|---|---|---|---|
| | 2012 | 2013 | 2012 | 2013 | 2012 | 2013 |
| Resistant | 31 (47.69%) | 46 (53.49%) | 15(46.60%) | 184 (42.69%) | 68 (43.59 %) | 391 (52.06%) |
| Sensitive | 34 (52.31%) | 40 (46.51%) | 17(53.40%) | 247 (57.31%) | 88 (56.41%) | 360 (47.94%) |
| Total | 65 | 86 | 324 | 431 | 156 | 751 |

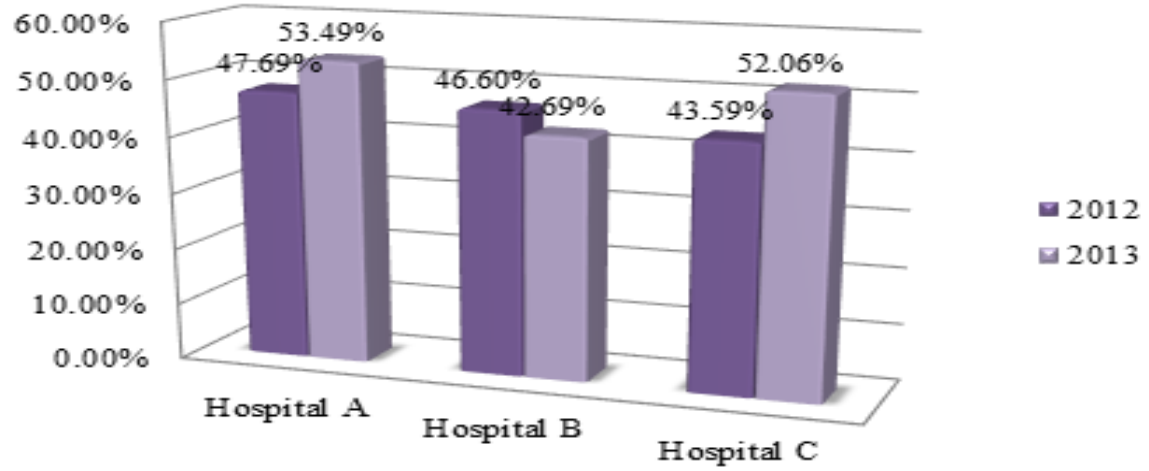


Figure 1: The prevalence of E. coli resistant to ceftriaxone towards three hospital

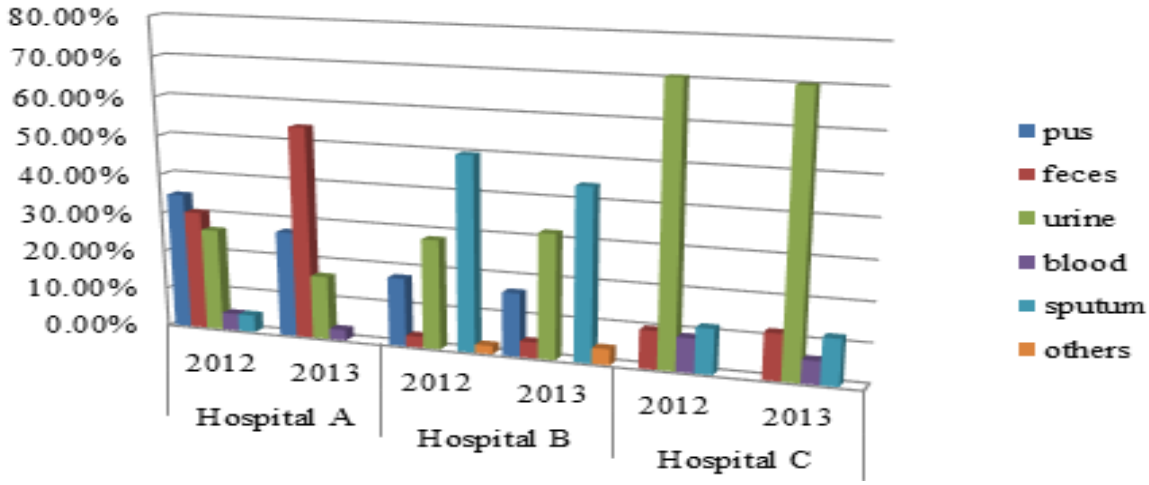


Figure 2: The distribution of infected specimen caused by ceftriaxone-resistant Escherichia coli

Ceftriaxone-Resistant *E. coli* in the year 2012 and 2013 was performed by chi-square ($\chi^2$) test. These statistical tests were performed using IBM SPSS® Statistic software 22 and the threshold for statistical significance was $p < 0.05$.

## RESULT

*E. coli* was the commonest pathogen isolated from all three hospital while ceftriaxone was the commonest prescribed antibiotic (unpublished data). Table 1 shows the comparative prevalence between ceftriaxone-resistant *E. coli* to ceftriaxone-sensitive *E. coli* isolated from patients in the year 2012 and 2013. The trend numbers of *E. coli* resistant to ceftriaxone from three hospitals in the year 2012 and 2013 can be seen in Fig. 2. Hospital A and C showed increasing number although not statistically significant (p hospital A = 0.48 and p hospital C = 0,05). Each hospital showed a different pattern of the infected specimen caused by ceftriaxone-resistant *E. coli*. Two hospitals showed the same highest rate of specimen infected by ceftriaxone-resistant *Escherichia coli* in 2012 and 2013 while one hospital showed different infected specimen (Table 2).

## DISCUSSION

The major goal of this study was to document the emerging *E. coli* resistance to ceftriaxone because of the limited information available in Bandung. *E. coli* was our major concern because it is a common source of health care-associated infection in hospitalized patients with high morbidity and mortality, while ceftriaxone, which is a third generation cephalosporin, is effective in eradicating Gram-

negative bacteria including *E. coli*[5]. During the period between 2009 and 2012, there was a high prevalence of *E. coli* (4.41%) in sepsis patients in a private hospital in Bandung, and the mostly used antibiotic was ceftriaxone (10.48%). Third generation cephalosporin, including ceftriaxone, was commonly used in sepsis patients but 55% of *E. coli* were resistant to ceftriaxone[7]. From the data above, the percentage number of ceftriaxone-resistant *E. coli* during 2012-2013 is 42.69% - 52.06% in range. Two hospital which hospital A and hospital C shows increasing number of ceftriaxone-resistant *E. coli* in 2012 compared to 2013 although it is not statistically significant ($p>0.05$). However, recognizing these trends remains important to guide changes in empirical antimicrobial therapy and drug development. Many bacterial pathogens associated with epidemics of human disease have evolved into multidrug-resistant (MDR) forms following antibiotic use, including *E. coli*. It is usually a commensal bacterium of humans and animals, and its pathogenic variants can cause intestinal and extra-intestinal infections, including gastroenteritis, urinary tract infection, meningitis, peritonitis, pneumonia, and septicemia[8,9]. *E. coli* is one of the main causes of both nosocomial and community acquired infections in humans[10], and is one of the organisms most frequently isolated from blood[11-13]. The organism is, therefore, of clinical importance and can be isolated from various clinical specimens. Eventhough *E. coli* is naturally colonized in human intestine, it can egress and invade the lower respiratory tract[14]. While the lungs are continuously exposed to bacteria, including *E. coli*, infections of the respiratory system by *E. coli* do, however, occur, and may have severe implications in humans. *E. coli* lung infections or pneumonia are observed in patients with haematological diseases[15] and in patients that need mechanical ventilation in hospital ICU units[16]. Pulmonary infection caused by *E. coli* may result from hematogenous dissemination from either the gastrointestinal or urinary tracts, and from aspiration from the pharynx[17], although it rarely occurs in clinical settings. *E. coli* infection usually induces bronchopneumonia with interstitial infiltration of mononuclear cells. Risk factors of such infections include chronic illness, particularly diabetes mellitus, renal disease, and alcoholism. This organism seldom causes acute infection in patients with chronic bronchitis[17].

Sputum was a dominant source of *E. coli* infection in two hospitals in 2012 and 2013. Sputum cultures are usually positive in the bacteremic form of *E. coli* pneumonia related to pulmonary infection[11]. Pneumonias due to *E. coli* are uncommon and are usually hospital-acquired, accounting for 9% of cases reported[18]. In one hospital in Iraq, *E. coli* was found in sputum in about 12% of intubated ventilated patients[19]. In one of the hospitals studied, urine was the largest source of *E. coli*. One of the most important abilities related to their pathogenicity, especially in the case of *E. coli*, is the ability of this bacteria to adhere to the mucous membranes in the urinary tract. Uropathogenic *E. coli* (UPEC) is present within bowel flora and can infect the urinary tract by expressing specific virulence factors that permit adherence and colonization of the lower urinary tract. Adherence of *E. coli* is dependent on three important environmental characteristics, namely the bacteria own adhesive characteristics, the receptive features of the urothelium, and the fluid present between both surfaces. *E. coli* will migrate proximally and precipitate a host-derived inflammatory response after adhering to the mucosal surface. Adhesins found on the surface of the bacterial membrane are responsible for initial attachment onto urinary tract tissues[20].

The resistance of *E. coli* against third generation cephalosporin, including ceftriaxone, is due to the production of beta lactamase, especially *Extended Spectrum Beta Lactamase* (ESBL) and AmpC groups. Subtypes of ESBL produced by these bacteria include BlaSHV-11, BlaSHV-12, BlaSHV-27, BlaTEM-63, BlaCTX-M-14, and BlaCTX-M-15, while the most common AmpC beta lactamase was CMY-2, found not only in *E. coli* but also in *Salmonela enterica*. They were found in many countries such as the United States, Taiwan, Malaysia, and Africa. Other studies have also reported that CMY-2 beta lactamase was responsible for ceftriaxone resistance in *Salmonella enterica* and *Escherichia coli*[21-25]. Ceftriaxone is included in the National Formulary of Indonesia and it's usage are more prevalent as empirical antibiotics. The high resistance of *E.coli* against ceftriaxone should be in concerned because ceftriaxone is first line antibiotics to eradicate *E.coli*. The findings of this study may help clinicians to formulate their first line empirical antibiotic treatment regimens, especially for the patients with infection caused by *Escherichia coli* and also periodic monitoring of antimicrobial susceptibility in the hospital settings is recommended. There is an urgent need to develop and strengthen antimicrobial policy, standard treatment guidelines, national plan for containment of antimicrobial resistance and research related to public health aspects of Antimicrobial resistance at community and hospital level in Indonesia. Although antibiotic are increasing in hospital settings, it is the pharmacist who has the last contact with the patient before he or she receives an antibiotic medicine and, thus, the pharmacist acts as the gatekeeper. The pharmacist's role to combat antibiotic resistance i.e. to provide proper counselling and appropriate written information when dispensing antimicrobials; encourage patients to take the full prescribed regimen and, if not possible, to dispose of any unused antimicrobial medicines appropriately; work with prescribers so that dosages prescribed are sufficient for the completion or continuation of a course of therapy; recommend therapies other than antimicrobials for minor ailments; provide updated information on antimicrobial medicines to prescribers as well as health-care professionals who administer or otherwise influence the use of medicines; be actively involved in matters of hygiene and infection control in all health-care settings; effectively monitor the supply and use of antimicrobials by their patients[26]. Maintaining and improving professional performance should be conducted between pharmacist to doctors in the interpretation of culture results and compliance with standards/procedures[27]. Improved communication between the two in relation to diagnosis, type of antibiotics prescribed and dosage is one way to

ensure appropriate prescribing. In addition, patients should be well counselled on the need for and use of antibiotics, adverse effects, consequences of incomplete dosage and the growing problem of antimicrobial resistance. Thus, a team-based approach to patient care is needed. Pharmacists are key health professionals with the skills and training required to contribute to the reduction of antimicrobial resistance. It is important to recognize and use their potential. While, in many countries of Europe, pharmacists already have the capacity to take on additional roles and responsibilities to foster the prudent use of antibiotic medicine, in some, a special effort will be necessary to update the pharmacist curriculum and ensure that it includes antibiotic stewardship[27].

***Conflict Of Interests***

Declared None

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