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Prevalence of extended-spectrum ß-lactamase-producing *Escherichia coli* in companion dogs in animal clinics, Surabaya, Indonesia

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Abstract

Background and Aim: The practice of keeping animals as pets is becoming increasingly common. The upsurge of extended-spectrum β-lactamase (ESBL)-producing organisms of animal origin is a health threat globally. This study aimed to identify the presence of extended-spectrum β-lactamase-producing *Escherichia coli* in companion dogs in animal clinics in Surabaya, Indonesia.

Materials and Methods: A total of 85 rectal swab samples were collected from companion dogs at five animal clinics in different regions of Surabaya, Indonesia. The presence of *E. coli* was identified from the samples using standard methods, followed by antibiotic sensitivity testing. The resistant isolates were examined for the presence of ESBL using the double-disk synergy test method. The phenotypically identified ESBL-producing *E. coli* was further confirmed with an automated system using Vitek-2.

Results: The rectal swab samples (n=85) tested were 100% positive for *E. coli* isolates. Eight (9.41%) out of the 85 *E. coli* obtained from rectal swabs were extended-spectrum β-lactamase producers. All eight ESBL-producing *E. coli* were identified by automated Vitek-2 confirmatory tests.

Conclusion: This study provides insight into the prevalence of ESBL-producing organisms isolated from companion dogs in Indonesia. This work indicates the need for the general public to be more aware of the role of companion animals in disseminating pathogenic organisms, since they serve as potential reservoirs in the spread of antibiotic resistance affecting human health.

Keywords: animal clinics, companion dogs, extended-spectrum β-lactamase, *Escherichia coli*, human health.

Introduction

Extended-spectrum β-lactamase (ESBL) is an enzyme produced by Gram-negative bacteria (family Enterobacteriaceae), which is a threat to health in the fields of human and veterinary medicine globally [1]. The production of this enzyme by these bacteria confers resistance to cephalosporin and monobactam, but not to cephamycin or carbapenem, and it is inhibited by β-lactamase inhibitors such as clavulanate, sulbactam, and tazobactam [2]. Resistance caused by ESBL is often associated with resistance to other groups of antibiotics commonly used in human medicine [3]. As a result, there is growing concern that ESBL-producing bacteria in companion animals can potentially spread directly through resistant pathogens from animals to humans or indirectly through resistance genes [4].

One approach to promote human and animal health is to limit antibiotic resistance, especially that in animals living in close proximity to humans [5]. ESBL-producing *Escherichia coli* has been well documented in humans, livestock, wild animals, and non-clinical isolates [6], but the role of companion animals is not well known in terms of the spread of resistance [1].

The ESBL test, a combination of Vitek-2 and an advanced expert system, is an automated system that is used to show the phenotype of the isolates tested and able to determine the sensitivity or resistance of an isolate to an antibiotic [7]. It is hoped that this method can rapidly detect the presence of antibiotic resistance, enabling administration of the appropriate treatment to prevent the spread of antibiotic resistance.

This study aimed to assess the presence of extended-spectrum β-lactamase-producing *E. coli* in companion dogs in animal clinics in Surabaya, Indonesia.

Materials and Methods

Ethical approval

Rectal swabs were used in this study; hence, ethical approval was not necessary. Rectal swab samples were collected from animal clinics, Surabaya, Indonesia, as per standard collection procedure.

Study period, location, and sample collection

The study was conducted from February to April 2019. A total of 85 rectal swabs were collected from companion dogs attending animal clinics in five different regions (Central, Northern, Eastern, Southern, and Western) of Surabaya, Indonesia. The samples were collected aseptically using sterile cotton swabs moistened in sterile normal saline and immersed in 1% peptone water (E. Merck, Darmstadt, Germany). They were stored in a cool box and immediately taken to the laboratory in the Department of Veterinary Public Health, Faculty of Veterinary Medicine, Airlangga University, Indonesia, for examination [8].

Isolation and identification of *E. coli*

The rectal swab samples in 1% peptone water medium (E. Merck, Darmstadt) were inoculated onto already-prepared MacConkey Agar (MCA) (E. Merck) plates and incubated at 37°C for 24 h. After incubation, the growth of organisms was inspected on MCA medium (colonies were round, smooth, red, and surrounded by cloudy zones) for the isolation of *E. coli.* Gram staining and biochemical characterization were performed to identify the suspected *E. coli* [9]. Furthermore, positive isolates of *E. coli* were further purified by inoculation onto Eosin Methylene Blue Agar (EMBA) plates and incubated at 37°C for 24 h. Metallic green colonies on EMBA were identified as *E. coli* [10].

ESBL confirmation by double-disk synergy test (DDST)

The pure culture of potential ESBL-producing *E. coli* isolate was standardized to 0.5 McFarland standard equivalents to 1.5×10^8 colony-forming unit/mL. The isolates were inoculated onto the surface of Muller–Hinton agar plates. Antibiotic disks (Oxoid, Basingstoke, UK) containing 30 µg of amoxicillin+clavulanic acid (CT0223), 30 µg of ceftazidime (CT0412), and 30 µg of cefotaxime (CT0166) were placed in parallel on the Muller–Hinton Agar medium using sterile forceps at a center-to-center distance of 15 mm and incubated for 24 h at 37°C. The positive ESBL-producing *E. coli* were confirmed by observing an increase in the inhibition zone of the antibiotic disc of cefotaxime and ceftazidime toward amoxicillin/clavulanic acid, which gives the effect of increasing the zone of inhibition according to the Clinical and Laboratory Standards Institute [11].

Detection of ESBL using automated Vitek-2 system

All *E. coli* isolates that were identified as ESBL producers using DDST were further subjected to phenotyping using the automated Vitek-2 system (bioMerieux, France). Confirmation of ESBL-producing *E. coli* using the automated Vitek-2 system (bioMerieux) was performed in accordance with the manufacturer's protocol. The results were automatically provided as a printout [12].

Results and Discussion

A total of 85 rectal swab samples were collected from companion dogs attending five animal clinics in different regions of Surabaya, Indonesia. Equal numbers of samples were collected from Central, Northern, Eastern, Southern, and Western Surabaya. All collected samples were positive for *E. coli* (Figure-1). Eight (9.41%) out of the 85 (100%) positive *E. coli* samples were identified as containing ESBL-producing *E. coli*. In the DDST method, there appears to be an enlargement of the ESBL zone with the synergistic pattern of the three antibiotics (Figure-2). The ESBL-producing *E. coli* isolates obtained using DDST were further characterized using the automated Vitek-2 system (bioMerieux), which identified all eight isolates as ESBL producers. ESBL-producing *E. coli* was recovered from Central (one *E. coli*), Eastern (two *E. coli*), Southern (three *E. coli*), and Western regions (two *E. coli*), while none was

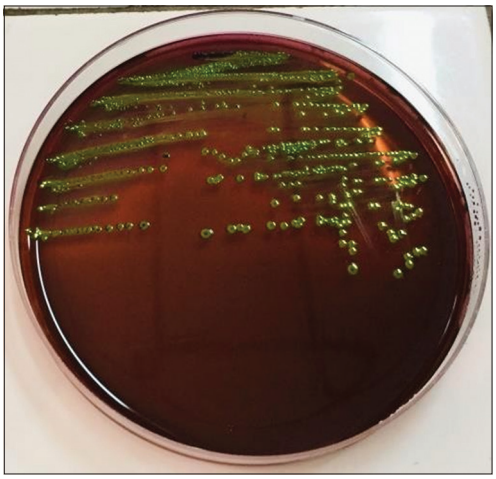

Figure-1: *Escherichia coli* on EMBA media.

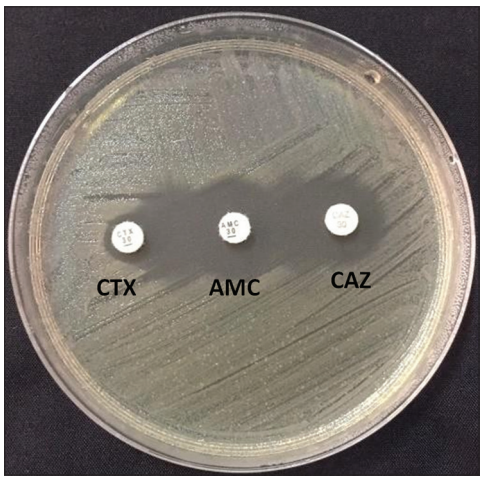

Figure-2: ESBL confirmation test using the DDST method. CTX = Cefotaxime, AMC = Amox + Clav, and CAZ = Ceftazidime.

Table-1: Data on ESBL isolates from dogs from Surabaya animal clinics.

Location	Number of samples	Positive *E. coli*	ESBL Confirmation by DDST	ESBL Confirmation by Vitek-2
Central Surabaya	17	17	1	1
Northern Surabaya	17	17	0	0
Eastern Surabaya	17	17	2	2
Southern of Surabaya	17	17	3	3
Western Surabaya	17	17	2	2
Total	85 (100%)	85 (100%)	8 (9,41%)	8 (9,41%)

ESBL=Extended-spectrum beta-lactamase, *E. coli=Escherichia coli*, DDST=Double-disk synergy test

discovered from Northern Surabaya, Indonesia (Table-1). The observation of ESBL-producing *E. coli* in companion dogs is worrisome and could endanger the health of pet owners. Pets or companion animals could be a potential reservoir for the spread of antibiotic resistance in humans and their environment [13,14].

In general, screening ESBL-producing and carbapenem-resistant bacteria are limited to humans and hospital environments, but studies have recently shown the emergence of resistant pathogens in livestock, poultry, companion animals, and animal feed [14-19]. Given that companion animals live in very close proximity to their owners, a cycle of transmission of multidrug-resistant bacteria can occur, by which these pathogens can circulate in humans and their environment [20-24].

Pets, especially dogs, are attracting attention as a potential source of the spread of ESBL-producing Enterobacteriaceae due to their physical closeness and frequent close contact with their owners. The present study revealed the prevalence of ESBL-producing *E. coli* isolated from companion dogs to be 9.41%. In surveillance studies of sick dogs and cats across Europe, 1.6% carried ESBL-producing Enterobacteriaceae in feces, most of which contained bla_{CTX-M}, but only included 2 *E. coli* ST131 isolates, suggesting that domesticated animals may be a source of transmission of ESBL in general, but may not be the main source of epidemic clones [25]. The findings may raise public health concerns because the gut microbiome of these animals can form a reservoir for resistance genes encoding ESBL/AmpC, which can be transmitted to humans [26]. The food chain is also a source of transmission [27-29], but transmission resulting from close contact between humans and animals on farms could also occur. Veterinarians are occupationally exposed to animals, and there are also opportunities where humans come into contact with animals in domestic situations such as on farms, zoos, or by owning pets [26,30-33].

Research on the frequency of multidrug-resistant *E. coli* in dogs and cats in Poland showed a prevalence of 66.8% in the isolates studied [34]. In other studies, the prevalence of ESBL-producing strains in clinical isolates of Enterobacteriaceae originating from dogs and cats ranged from 3.1% to 54.4% [35,36], whereas in healthy animals, a rate as high as 20% were reported [37,38]. The above reports are in agreement with the findings of the present study on companion dogs in Surabaya, Indonesia, which reported a prevalence rate of 9.41%.

Research conducted at a veterinary clinic at the University of Zurich, Switzerland, during 2012-2016 identified ESBL-producing Enterobacteriaceae with a prevalence rate of 20.8% in clinical samples of dogs and cats [39]. This rate is much higher than those found in similar studies of companion animals in the United Kingdom (7%) [40], the Netherlands (2%) [41], France (3.7%) [42], and Europe (1.6%) [25].

The automated Vitek-2 compact system (bioMerieux, Marcy l'Etoile, France) is a bacterial identification and semi-automatic resistance testing system that enables the rapid determination of minimum inhibitory concentration by analyzing the kinetics of bacterial growth with antimicrobials on test cards [7,12]. In a comparative study with the Clinical and Laboratory Standards Institute method in detecting ESBL, Vitek-2 showed a sensitivity of 100% and specificity of 99.3-100%, while disk diffusion methods and Etest also showed similar results [43]. The use of Vitek-2 for detection of ESBL producing *E. col*i showed sensitivity and specificity of 98.5% and 98.9%, respectively [44,45]. This is in accordance with the findings of this study that observed 100% sensitivity for ESBL-producing *E. coli* isolated from companion dogs using the automated Vitek-2 system. From several previous reports and the results of the study, Vitek-2 compact can be used as a reliable tool for detecting ESBL-producing Enterobacteriaceae.

The presence of ESBL-producing *E. coli* from companion dogs as proven using Vitek-2 is clearly a source of zoonotic bacterial infections that can emerge and affect humans. Bacterial zoonotic diseases can be transferred from animals to humans in various ways, including through animal bites and scratches [16,46,47], or zoonotic bacteria originating from animal feed can reach humans through the direct fecal–oral route, contaminated pet food products, inappropriate food handling, and inadequate cooking [18,48]. Thus, in the One Health concept, humans who are close to pets would be able to contract zoonotic pathogenic bacteria and spread them to other humans in the community [49].

Conclusion

The prevalence of ESBL-producing *E. coli* in companion dogs was found to be 9.41% using DDST

and automated Vitek-2 confirmation tests. This indicates that companion animals have the potential to spread antibiotic resistance and thus adversely affect animal and public health. The data also show that the prevalence of ESBL-producing *E. coli* in companion dogs at veterinary clinics is increasing in Indonesia. Therefore, further molecular studies using random amplified polymorphic DNA analysis are recommended to understand the clonal relationship of ESBL-producing *E. coli* isolates of animal and human origin.

Authors' Contributions

MHE and LK: Conceptualization. MHE, AMW, and DKW: Data curation. LK and AMW: Formal analysis. MHE and LK: Funding acquisition. AMW and DKW: Investigation. MHE and AMW: Methodology. MHE and AMW: Project administration. MHE, AMW, and DKW: Resources. MHE and LK: Supervision. MHE and ENU: Validation. LK and AMW: Visualization. MHE, LK, and ENU: Writing original draft. MHE and ENU: Writing – review and editing. All authors read and approved the final manuscript.

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Competing Interests

The authors declare that they have no competing interests.

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