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Original Article

# Analysis of the Appropriateness and Cost of Antibiotics Usage in Outpatients at Emergency Department

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ABSTRACT

Unnecessary usage of antibiotics in patients at Emergency Department (ED) is one of important issues resulting in a number of adverse consequences, namely: the occurrence of antibiotics resistance, longer medication period, death risk, and the increase of medical costs. The purpose of this research was to conduct analysis on the usage and cost of antibiotics at ED's patients who did not obtain further treatment inpatient wards.

This observational research was conducted prospectively in one of Surabaya municipal hospital EDs. The research was conducted during November-December 2015. This research was conducted by observing the outpatients' medical records to know the profile of antibiotics usage in ED. Patients' diagnosis in this research would be differentiated into infection, infection-risk, and non-infection diagnosis. The analysis of the appropriateness of antibiotics usage was conducted by comparing the actual usage of antibiotics and the recommendations from therapeutic guidelines. Patients' billing data was used as the reference of cost analysis.

Among the 385 patients obtaining antibiotics at ED, female and adult patients (>18 years old) were the most discovered. The most frequently found infection diagnosis was acute gastroenteritis (32.47%) among 194 patients with infection. Diagnosis of risk of infection most frequently found was wound (57.78%) among 99 patients with the risk of infection. Single and combined antibiotics most frequently used were *cefixime* (32.01%) and *cotrimoxazole-metronidazole* (53.14%), respectively. The appropriateness of the usage of antibiotics in terms of type of antibiotics amounted to 56.98%. Medicine interaction which occured was merely between 2 pairs of medicine, namely *ciprofloxacin-sucralfate* and *ciprofloxacin-zinc*. On average, the cost spent on antibiotics amounted to Rp 38,286.00/patient. The practice of irresponsible usage of antibiotics was still found in the ED. Further research is required to be conducted to identify the cause of the irresponsible usage of antibiotics in ED setting.

**Keywords :** antibiotics, emergency departments, appropriateness, interaction, cost.

## 1. INTRODUCTION

Emergency Department (ED) is one of the important units in the hospital as the entrance gate for the society to obtain medical service. Antibiotic is one group of medicines most frequently used in ED. A number of published articles find the practice of irresponsible usage of antibiotics taking place

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at ED. The research conducted in an ED in Morocco discovers that 57.74% antibiotics usage was classified as irresponsible usage such as: the choosing of antibiotics type, dosage, frequency, and inappropriate combination.[1] Another research conducted in an ED in Saudi Arabia exposed that there was 46.20% of irresponsible usage of antibiotics.[2]

Irresponsible usage of antibiotics will result in a number of adverse consequences, among which is antibiotics resistance. Antibiotics resistance found in ED setting is one of global health issues. A research conducted in one ED in South Korea showed that 29.26% of 229 *E.coli* cultures had been resistant towards *ciprofloxacin*, 29.65% towards *cefotaxime*, and 12.66% towards *ciprofloxacin* and *cefotaxime.* In the same research, it was discovered that antibiotics usage 3 months prior to culture examination was one of the factors causing antibiotics resistance (p=0,001).[3]

Antibiotics resistance cases will impact on deteriorating clinical outcomes of therapy, one of which is the level of patients' recovery which will result in a prolonged duration of stay in hospitals. Bacteremia patients who have been infected with *methicillin-resistant Staphylococcus aureus* (MRSA) bacteria will stay in hospitals longer than patients infected with *methicillin-susceptible Staphylococcus aureus* (MSSA), i.e. 59.90 days versus 34.80 days (p=0,01).[4]

Further consequence of irresponsible usage of antibiotics is the increase of medical cost. The medical cost for pneumonia patients using antibiotics according to therapeutic guidelines amounts to € 28.033 ± 16.574, whereas for pneumonia patients using antibiotics not according to therapeutic guidelines amounts to € 36.139 ± 20.036.[5] The huge amount of medical cost for patients using antibiotics irresponsibly should be cautioned especially if the medical cost is to be borne by the government during the period of *Jaminan Kesehatan Nasional* (JKN)/National Universal Coverage. The government is at risk of bearing the burden of unnecessary medical cost.

Considering the likelihood of the practice of irresponsible usage of antibiotics in ED and several adverse consequences which may take place, the present research is conducted with the purpose of looking into the profile of antibiotics usage at one government hospital ED in Surabaya, including the accuracy of antibiotics usage, the occurrence of medicine interaction, and medical cost spent.

## 2. METHOD

This observational research was conducted cross-sectionally for the period of November to December 2015. The researcher had obtained a permission letter to conduct the research from the director of the hospital where the data was sought (No. 070/14708/436.7.8/2015). The researcher took notes and analysed medical records data of undertreatment ED patients. . The inclusion criteria in the present study were all patients who were given antibiotics when undergoing treatment in ED and did not continue inpatient treatment. The characteristics of observed patients thar were recorded and analyzed, were as follows: age, sex, and diagnosis. The diagnosis was classified into 3 groups, namely: infection, infection-risk, and non-infection diagnosis. The diagnosis was classified as infection diagnosis if the infection was caused by bacteria. Diagnosis was classified as infection risk diagnosis if the patients showed symptoms of infection, such as wounds, hyperpyrexia, cough, leukocytosis and fracture. The diagnosis was classified as non-infection diagnosis if the diagnosis was clearly unrelated to the infection, or infection which was most probably not caused by bacteria.

In this study, the observed characteristics of antibiotics used by patients were comprising of types of antibiotics, dosage and administration route. The observed types of antibiotics could be in the form of single antibiotics and combined antibiotics. The usage of beta-lactam antibiotics along with anti-beta-lactamase antibiotics was not classified as combined antibiotics in this research. The obtained data was analysed in terms of the appropriateness of the usage using therapeutic guidelines in accordance with each infection-related diagnosis, medicine interaction which was likely to occur, and medical cost spent by patients during medication.

The analysis of appropriateness of antibiotics usage could only be done on patients with infection diagnosis. The accuracy of antibiotics usage would be assessed based on the therapeutic guidelines published by the newest edition of Infectious Disease Society of America (IDSA). If no IDSA guidelines was found for certain diagnosis, other guidelines such as the guidelines published by the Republic of Indonesia Ministry of Health, American Academy of Family Physicians (AAFP), Scottish Intercollegiate Guidelines Network (SIGN), or other therapeutic guidelines appropriate for types of illnesses borne by patients would be used as references to determine the appropriateness of usage. The appropriateness analysis was conducted for type, dosage, and both of type and dosage of antibiotics. Appropriateness analysis of antibiotics dosage was only conducted on medical records data which clearly listed the dosage of antibiotics administered to the patients.

The analysis of medicine interaction was based on the reference of Drug Interactions Analysis and Management 2013 edition. Medicine interaction was classified into five groups in accordance to the reference. The interactions included in group 1 and 2 were classified as an interaction with clinical meaning, whereas the interactions in group 3, 4, and 5 were classified as an interaction with no-clinical meaning. Medical cost data was obtained from billing data given to the patients. Medical cost in this research only calculated the cost for antibiotics. The patients' perspective was used to calculate the cost.

## 3. RESULTS AND DISCUSSION

In total, 385 patients were given antibiotics therapy at ED throughout November -December 2015. In terms of the patients' age, 146 patients (37.92%) were 0-18 years old and

were classified as pediatric patients, and 239 other patients (62.08%) were over 18 years old,classified as adult. Among the 385 patients, 194 patients had infection diagnosis, 99 had infection-risk diagnosis, and 92 had non-infection diagnosis. Infection, infection-risk, and non-infection diagnosis mostly found in this research were acute gastroenteritis (63 patients,3247%), wounds (57 patients, 57,78%), and abdominal colic (22 patients, (23.91%), respectively. The complete details of the patients' characteristics could be found in Table 1.

**Table 1: Patients' Characteristics**

| Patients' Characteristics | | Pediatric Patients (patients) (%) | Adult Patients (patients) (%) | Number (%) |
|---|---|---|---|---|
| Age[1] | | 146 (37.92) | 239 (62.08) | 385 (100.00) |
| | Average (year) | 5.40 | 42.53 | 28.40 |
| | Range (year) | (0.02-18) | (19-83) | (0.02-83) |
| | Standard deviation (year) | 5.07 | 15.54 | 22.00 |
| Sex | | | | |
| | Male | 86 (58.90) | 124 (51.88) | 210 (54.55) |
| | Female | 60 (41.10) | 115 (48.12) | 175 (45.45) |
| Infection diagnosis | | 87 (44.85) | 107 (55.15) | 194 (50.39) |
| | Acute gastroenteritis | 23 (26.44) | 40 (37.38) | 63 (32.47) |
| | Typhoid fever | 27 (31.03) | 19 (17.76) | 46 (23.72) |
| | Upper respiratory tract infection | 21 (24.14) | 15 (14.02) | 36 (18.56) |
| | Urinary tract infection | 3 (3.45) | 17 (15.89) | 20 (10.31) |
| | Lower respiratory tract infection | 11 (12.64) | 3 (2.80) | 14 (7.23) |
| | Other infection[2] | 2 (2.30) | 13 (12.15) | 15 (7.73) |
| Infection-risk diagnosis | | 42 (42.42) | 57 (57.58) | 99 (25.71) |
| | Wounds | 18 (42.86) | 39 (68.42) | 57 (57.78) |
| | Hyperpyrexia | 21 (50.00) | 15 (26.32) | 36 (36.36) |
| | Others[3] | 3 (7.14) | 3 (5.26) | 6 (6.06) |
| Noninfection diagnosis | | 14 (15.22) | 78 (84.78) | 92 (23.90) |
| Data Completeness | | | | |
| | Complete[4] | 28 (19.18) | 34 (14.23) | 62 (16.10) |
| | Incomplete | 118 (80.82) | 205 (85.77) | 323 (83.90) |

**Notes :**

[1]Pediatric patients were patients aged 0-18 years old, whereas adult patients were patients over 18 years old.

[2]Other infection diagnosis (n=15), namely: abscess (n=2), dysentery (n=1), furunculosis (n=2), gingivitis (n=1), gonorrhea (n=1), conjunctivitis (n=1), cellulites (n=3), sepsis (n=1), tuberculosis (n=1), and tuberculosis being treated (n=2).

[3]Other infection-risk diagnosis (n=6), as follows: cough (n=3), fracture (n=2), and leukocytosis (n=1).

[4]Complete data was data that enlists the name and/or the dosage, frequency and the amount of antibiotics given.

In this research, 353 patients (91.68%) had single antibiotics therapy and 32 patients (8,.31%) had combined antibiotics therapy. The most used single antibiotics for patients in ED at the hospital was of the third-generation *cephalosporin* group, namely *cefixime*, which was administered to 113 patients (29.35%), whereas the most used combination of antibiotics was *cotrimoxazole-metronidazole* administered to 17 patients out of the entire patients administered with combined antibiotics (53.13%). Details of antibiotics usage in pediatric and adult patients could be seen in Table 2.

**Table 2: The Characteristics of Antibiotics**

| The Characteristics of Antibiotics | | Pediatric Patients (%) | Adult Patients (%) | Total (%) |
|---|---|---|---|---|
| **Single Antibiotics** | | **144 (40.79)** | **209 (59.21)** | **353 (100.00)** |
| | Cefixime | 57 (39.58) | 56 (26.78) | 113 (32.01) |
| | Cefadroxil | 36 (25.00) | 38 (18.18) | 74 (20.96) |
| | Amoxicillin | 22 (15.27) | 12 (5.75) | 45 (12.74) |
| | Thiamphenicol | 13 (9.03) | 23 (11.00) | 37 (10.48) |
| | Cotrimoxazole | 9 (6.25) | 28 (13.40) | 36 (10.20) |
| | Ciprofloxacin | 3 (2.08) | 42 (20.10) | 34 (9.63) |
| | Metronidazole | 2 (1.39) | 4 (1.91) | 6 (1.70) |
| | Amoxicillin+clavulanic acid | 1 (0.70) | 3 (1.44) | 4 (1.13) |
| | Others[1] | 1 (0.70) | 3 (1.44) | 4 (1.13) |
| **Combined Antibiotics** | | **2 (6.25)** | **30 (93.75)** | **32 (100.00)** |
| | Cotrimoxazole-Metronidazole | 1 (50.00) | 16 (53.33) | 17 (53.13) |
| | Other combination[2] | 1 (50.00) | 14 (46.67) | 15 (46.88) |

**Notes :**

[1]Other single antibiotics (n=4), wee as follows: *erythromycin* (n=2), *levofloxacin* (n=1), and *gentamicin* (n=1).

[2]Other combined antibiotics (n=15), were as follows:

a) *cefadroxil-gentamicin* (n=3),
b) *cefixime-gentamicin* (n=3),
c) *cefadroxil-metronidazole* (n=2),
d) *cefadroxil-ceftriaxone* (n=1),
e) *cefixime-chloramphenicol* (n=1),
f) *amoxicillin-ceftriaxone* (n=1),
g) *cefixime-metronidazole* (n=1),
h) *thiamphenicol-cotrimoxazole* (n=1),
i) *ciprofloxacin-gentamicin* (n=1), and
j) *ciprofloxacin-metronidazole* (n=1).

For patients with gastroenteritis in this research, the most used single antibiotic was *cotrimoxazole* administered to 23 patients, and the most used combined antibiotic was *cotrimoxazole-metronidazole* administered to 4 patients. Combined antibiotics *cotrimoxazole-metronidazole* were also used in 9 patients with abdominal colic, and 3 patients with renal colic. The details of antibiotics usage in every diagnosis was described in Table 3.

The most used antibiotic as single therapy in this research was third generation *cephalosporin* (3GC), i.e. *cefixime* (113 patients,32.01%). Ironically, out of the 113 patients, 25 patients (31.65%) were given *cefixime* for non-infection risk. The irresponsible usage of 3GC, including in non-infection patients may lead to the risk of resistance of the bacteria that can produce extended-spectrum beta lactamase or ESBL. The relationship between 3GC usage and ESBL-*Klebsiella pneumoniae* (ESBL-KP) bacteria resistance level in hospitals in Czechoslovakia proves that ESBL-KP bacteria resistance fluctuates according to the rise and fall of 3GC usage. In 1997, 3GC usage amounted to 1.79 DBD (defined daily dose per 100 bed-days), and 8.00% ESBL-KP bacteria isolates were found. The amount of 3GC usage reached its peak in 2007, amounting to 2.40 DBD with total ESBL-KP bacteria isolates 18.00% .[6] Infection caused by ESBL producing bacteria can no longer treated with 3GC thus requires antibiotics with higher activity spectrum, for instance antibiotics of *carbapenem* group. The cost for administering antibiotics of *carbapenem* group is higher compared with 3GC. Considering this fact, 3GC usage has to be controlled to prevent the increase of ESBL bacteria resistance cases and to suppress unnecessary medical cost.

The most frequent infection-related diagnosis found in this research was acute gastroenteritis (63 patients, 32.47%). The most used antibiotic by patients with gastroenteritis was *cotrimoxazole*, in 23 patients. The high usage of *cotrimoxazole* for gastroenteritis patients was also found in a

published research with ED setting in Nicaragua, Guatemala.[7] *Cotrimoxazole* is chosen as the antibiotic for gastroenteritis patients as it has good activity to eradicate the bacteria causing gastroenteritis ssuch as: *Salmonella*, and *Shigela*.[8] Although it might be used for gastroenteritis patients, the usage of *cotrimoxazole* requires serious attention in regards to a few things, namely: 1) the risk of resistance towards *cotrimoxazole*, and 2) the most common cause of gastroenteritis is virus. A research shows that 15 out of 24 *E. coli* isolates have been resistant towards *cotrimoxazole* and 12 out of 36 *S. aureus* isolates have been resistant towards *cotrimoxazole*.[9]

**Table 3: Antibiotics usage for Every Diagnosis**

| Diagnosis | Single antibiotics | | | | | | | | | Combined antibiotics | | TOTAL |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Cefixime | Cefadroxil | Ciprofloxacin | Cotrimoxazole | Thiamphenicol | Amoxicillin | Metronidazole | Amoxicillin + clavulanic acid | Others | Cotrimoxazole + Metronidazole | Other combination | |
| **Infection diagnosis** | **60** | **26** | **18** | **31** | **25** | **16** | **4** | **2** | **1** | **5** | **6** | **194** |
| Gastroenteritis | 13 | 7 | 2 | 23 | 5 | 2 | 4 | 1 | 0 | 4 | 2 | 63 |
| Typhoid Fever | 15 | 2 | 0 | 5 | 19 | 5 | 0 | 0 | 0 | 0 | 0 | 46 |
| Upper Respiratory Tract Infection | 16 | 11 | 1 | 0 | 1 | 5 | 0 | 1 | 1 | 0 | 0 | 36 |
| Urinary Tract Infection | 4 | 0 | 11 | 3 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 20 |
| Lower Respiratory Tract Infection | 8 | 4 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 14 |
| Other infection | 4 | 2 | 4 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 4 | 15 |
| **Infection-risk diagnosis** | **28** | **28** | **7** | **2** | **6** | **15** | **2** | **2** | **1** | **0** | **8** | **99** |
| Wounds | 14 | 17 | 6 | 0 | 0 | 11 | 0 | 1 | 0 | 0 | 8 | 57 |
| Hyperpyrexia | 12 | 9 | 1 | 1 | 6 | 4 | 2 | 1 | 0 | 0 | 0 | 36 |
| Other Infection-Risk | 2 | 2 | 0 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 6 |
| **Non-infection Diagnosis** | **25** | **20** | **20** | **4** | **5** | **3** | **0** | **0** | **2** | **12** | **1** | **92** |
| Abdominal Colic | 5 | 2 | 2 | 3 | 0 | 1 | 0 | 0 | 0 | 9 | 0 | 22 |
| Renal Colic | 5 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 3 | 0 | 10 |
| Other Non-Infection | 15 | 17 | 18 | 1 | 5 | 2 | 0 | 0 | 1 | 0 | 1 | 60 |
| **TOTAL** | **113** | **74** | **45** | **37** | **36** | **34** | **6** | **4** | **4** | **17** | **15** | **385** |

In this research, the combination of *cotrimoxazole* and *metronidazole* is also used in patients with abdominal colic diagnosis (9 patients, 52.94%) and renal colic diagnosis (3 patients,17.65%). The usage of combined antibiotics in these groups of patients can be classified as inaccurate antibiotics usage. Considering the cause, abdominal colic and renal colic are not necessarily caused by bacteria. Colic is a sharp pain, and is located in the abdominal area and is usually related to the organs inside. Should the pain occur in upper right quadrant of the abdomen, the most commonly found cause are gallstones in the bile duct (*cholelithiasis*) or the presence of embolism in the lungs, although it may also be caused by bacteria such as *pyelonephritis* in the kidney or *pneumonia* in the lungs..[10] Renal colic is specific pain caused by a blockage of urinary tract due to stones known as *nephrolithiasis.* The first given treatment should *neprolithiasis* occur is fluid therapy, antiemetic, and anti-pain of NSAID group and opioid group.[11] Based on those sources, further examination is required to ensure the presence of infection in patients with *colic*, hence antibiotics usage can be minimized especially for non-infection colic patients group.

Most commonly found infection-risk diagnosis in ED in this research are wounds 57 (57.78%) out of the total of 99 patients who had infection-risk diagnosis. In this research, the most used antibiotic for patients with wounds diagnosis was *cefadroxil* (17, 29.31%). C*efadroxil* is the first generation of *cephalosporin*. The usage of the first generation *cephalosporin* antibiotics for indications of wounds was also found in another research.[12] One of the microorganisms able to enter wound tissue is *Staphylococcus aureus*, which is a normal flora in human skin tissue.[13] Moreover, the first generation *cephalosporin* group such as *cefadroxil* has good activity to eradicate positive gram bacteria, one of which is *S. aureus.*[8]

The usage of the first generation *cephalosporin* antibiotics in patients with wounds is presumed to prevent infection caused by positive gram bacteria such as *S. aureus.* However, not all wounds have the potential to result in infection. A wound can develop into infection if: 1) it is a bite wound on the hands or face, 2) it is an injury, and 3) it is in contact with *lymphedematous* tissue which is marked by the presence of pus or contaminated by saliva, faeces, or vaginal fluid. Further assessment is required to ensure that the antibiotics are administered on patients with wounds who truly require them.[14] Hyperpyrexia, cough, fracture, and leukocytosis was also classified as infection-risk diagnosis and was present in 36 (36,36%), 3 (3,03%), 2 (2,02%), 1 (1,01%) patients respectively. The cause of those diagnosis is not always related to infection. Hyperpyrexia can be caused by infection, malignancies condition, autoimmune diseases, medicine consumption, and hypersensitivity reaction (allergy).[15] Whereas cough can be caused by several conditions, such as: asthma, chronic obstructive pulmonary disease (COPD), gastroesophalangeal reflux disease (GERD), or the usage of medicine from *Angiontensin Converting Enzyme Inhibitors* group (ACEI).[16] Fracture is known as broken bone condition with infection risk, especially in open fracture. Whereas in closed fracture, infection is hardly ever found. Considering the possibility of non-infection causes in hyperpyrexia, cough, and fracturas clinical conditions, professional medical staff can delay the administration of antibiotics in patients with the condition. A practice known as delayed antibiotic prescription, a practice that delays the administration of antibiotics, can be considered to be implemented in ED. The practice has been proven not to endanger the patients.[17]

Leukocytosis is another diagnosis which is classified as a condition potential to infection and is one of commonly used clinical parameters as the guidelines of administering antibiotics. Leucocytosis itself can be caused by either infection or non-infection clinical condition. A research states that leukocytosis is defined as a condition in which the number of leukocytes exceeds 15.000 cells/mm$^3$, and in

52.00% patients, it is confirmed that the cause is infection. Moreover, leukocytosis can also be caused by non-infection factors, such as: stress (38%), medicine side effects (11%), hematology disruption (6%), inflammation or necrosis (6%), unknown exact cause (4%).[18] From the research, it can be concluded that leukocytosis is not the only cause of infection, but it can also be caused by non-infection cause. Hence, further examination has to be conducted to obtain the exact cause of patients' leukocytosis, prior to the administration of antibiotics. This has to be done as an effort to prevent the occurrence of antibiotics resistance.

The analysis of the appropriateness of the type of antibiotics in this research revealed that antibiotics had been accurately administered in 106 (54.64%) out of 194 patients with infection diagnosis. The appropriateness of the dosage was conducted among patients with complete data. In total there were 44 patients with complete data whom could be analysed in terms of the dosage accuracy. The dosage of antibiotics was accurate for 24 (54.54%) out of 44 patients. The details of the accuracy of antibiotics usage for every diagnosis could be seen in Table 4.

**Table 4: The Accuracy of Antibiotics usage**

| Infection diagnosis | Type | | Dosage | | Type and Dosage | |
|---|---|---|---|---|---|---|
| | Accurate (patients) | Inaccurate (patients) | Accurate (patients) | Inaccurate (patients) | Accurate (patients) | Inaccurate (patients) |
| Gastroenteritis | 24 | 39 | 6 | 4 | 0 | 10 |
| Typhoid Fever | 41 | 5 | 4 | 4 | 5 | 3 |
| Upper Respiratory Tract Infection | 15 | 21 | 5 | 5 | 3 | 7 |
| Lower Respiratory Tract Infection | 2 | 12 | 3 | 3 | 0 | 6 |
| Urinal Tract Infection | 20 | 0 | 6 | 2 | 6 | 2 |
| Other Infection | 4 | 11 | 0 | 2 | 0 | 2 |
| Total | 106 | 88 | 24 | 20 | 14 | 30 |
| Percentage (%) | 54.64 | 45.36 | 54.54 | 45.46 | 31.82 | 68.18 |

In terms of the appropriateness of the usage of antibiotics types in patients with acute gastroenteristis diagnosis, the accuracy was only found in 24 (38.10%) out of 63 patients with acute gastroenteritis. Antibiotics usage was categorized in accordance with therapeutic guidelines if the patients with acute gastroenteritis are treated using recommended antibiotics including: for adult patients *cotrimoxazole* or *fluoroquinolone*, and for pediatric patients *cotrimoxazole*.[19] Recommended antibiotics usage was based on the bacteria causing gastroenteritis which was mainly caused by aerobic negative gram bacteria i.e. *E. coli*. A research states that 62 isolates (9.90%) of *Suspected Diarrheagenic E. coli* bacteria was found. However, it does not eliminate the possibility that acute gastroenteritis is caused by virus. A research discovers that 202 isolates (32.20%) of *novovirus* virus was found in 627 isolates patients suffering from acute gastroenteritis.[20] In this research, the usage of *cotrimoxazole* was classified in accordance to the guideline with the consideration that it was impossible for the medical staff in ED to perform cultures. If cultures were conducted, the results of the process would be obtained after 4 days, hence it could not be applied in the outpatient context. Nonetheless, although antibiotics usage was accurate, further examination is required, considering that gastroenteritis can also be caused by virus.

The medicine interaction occured at ED was only found in 2 pairs of medicine (0.14%) namely *ciprofloxacin-sucralfate,* and *ciprofloxacin-zinc*, out of 1348 pairs of medicine. These two pairs of medicine are in class 3 interaction, which is an interaction with no-clinical meaning. For other pairs of medicine, totaling 1346 pairs (99.86%), the information related to their interaction was unknown. The details of the medicine interaction taking place in ED could be seen in Table 5.

**Table 5: Medicine Interaction with Medicine at ED**

| Category | Number (%) | Drug Pairs | Number (%) |
|---|---|---|---|
| 1 | 0 | - | |
| 2 | 0 | - | |
| 3 | 2 (0.14) | *Ciprofloxacin-sucralfate*<br>*Ciprofloxacin-zinc* | 1 (0.07)<br>1 (0.07) |
| 4 | 0 | | |
| 5 | 0 | | |
| NI* | 1346 (99.86) | *Cefixime-Acetaminophen*<br>*Cefixime-Ambroxol*<br>*Cefadroxil-Acetaminophen*<br>*Cefixime-Mefenamic Acid*<br>*Ciprofloxacin-Mefenamic Acid*<br>Other interaction | 62 (4.60)<br>30 (2.23)<br>28 (2.08)<br>27 (2.00)<br>27 (2.00)<br>1172 (86.95) |
| Total | 1348 (100.00) | | 1348 (100.00) |

**Note :**

*****NI stands for No Information, the medicine pair used simultaneously is not listed within the Drugs Interactions Analysis and Management 2013 edition literature.

Out of 1348 observed pairs of medicine in this research, only 2 pairs of medicine possessed interaction-related data. Those two pairs were *ciprofloxacin-sucralfate* and *ciprofloxacin-zinc*. In terms of their interaction, *sucralfate* and *zinc* will bind with *ciprofloxacin* hence cannot be absorbed by the body. As an effort to prevent interaction from taking place, the two types of medicine have to be consumed with a certain time interval. Other interactions without any data in literatures need further research, to ensure the safety and efficacy when the combination of medicines are given to patients.[21] The absence of information related to the interaction between two medicines makes the medical staff's role in monitoring patients' development has to be optimized in order to minimize the potential unwanted medicine reaction.

The total cost spent by the patients on medication with antibiotics amounted to Rp 2,373,733.00, with average cost spent on antibiotics alone was 38,286.00 (with the range from Rp 816.00 to Rp 197,610.00). Adult patients spent greater average cost on antibiotics than pediatric patients totaling Rp 44,963.00. The details of medical cost on antibiotics could be seen in Table 6.

**Table 6: Antibiotics Medical Cost Spent by Patients at ED**

| Notes | Infection Diagnosis Cost (Rp) | Infection-risk Diagnosis Cost (Rp) | Non Infection Diagnosis Cost (Rp) | Total Cost (Rp) |
|---|---|---|---|---|
| All Patients | | | | |
| Number | 1,077,139.00 | 622,558.00 | 646,436.00 | 2,373,733.00 |
| Average | 29,920.00 | 62,255.00 | 40,402.00 | 38,286.00 |
| Minimum | 816.00 | 2,254.00 | 2,040.00 | 816.00 |
| Maximum | 195,500.00 | 197,610.00 | 195,500.00 | 197,610.00 |
| SD | 46,208.00 | 61,845.00 | 66,391.00 | 55,370.00 |
| Pediatric Patients | | | | |
| Number | 425,649.00 | 300,886.00 | 204,686.00 | 844,971.00 |
| Average | 26,603.00 | 42,983.00 | 34,114.00 | 33,177.00 |
| Minimum | 2,254.00 | 2,254.00 | 3,510.00 | 2,254.00 |
| Maximum | 86,250.00 | 86,250.00 | 86,250.00 | 86,250.00 |
| SD | 31,948.00 | 35,105.00 | 40,821.00 | 32,963.00 |
| Adult Patients | | | | |
| Number | 651,490.00 | 321,672.00 | 437,710.00 | 1,528,762.00 |
| Average | 32,574,50 | 107,224.00 | 48,634.00 | 44,963.00 |
| Minimum | 816.00 | 6,762.00 | 2,040.00 | 816.00 |
| Maximum | 195,500.00 | 197,610.00 | 195,500.00 | 197,610.00 |
| SD | 55,775.00 | 95,822.00 | 83,378.00 | 68,385.00 |

Apart from resistance-related issues, antibiotics usage in conditions where antibiotics are not or have not yet required may result in the increase of medical cost. The average cost spent on antibiotics by patients amounted Rp 38,286.00/patient. This cost was merely for the antibiotics and did not include other medicines which were also needed by the patients should they be given more than 1 type of medicine. The medicine cost may be borne by the patients themselves or by an insurance. Moreover, in the era of *Jaminan Kesehatan Nasional* (JKN)/ National Universal Coverage implementation per 2014, the medical cost of the patients, who previously are the policy holders, will be borne by the government. Unnecessary usage of antibiotics will increase medical cost without giving any benefits for the patients.

## 4. CONCLUSION

Antibiotics usage in ED's patients who later undergo outpatient treatment has to be optimised. The practice of irresponsible usage of antibiotics is still found, i.e. in patients with unclear indications of infection, requires attention from all related parties, as not only does it have the potential to increase the risk of antibiotics resistance, but also it can squander cost budget without clear benefits. This will definitely be an irony for Indonesians who are now implementing *Jaminan Kesehatan Nasional*/National Universal Coverage. Moreover, the ongoing discovery of antibiotics usage not in accordance with therapeutic guidelines established from developed countries is an invitation for health academicians and practitioners to provide therapeutic guidelines which are suitable to Indonesia condition. The identification of pathogens causing infection along with the sensitivity test towards several types of antibiotics will be the preliminary step to make therapeutic guidelines which will be in accordance with the Indonesian context. Substantial cost is required to begin the process of promoting responsible use of antibiotics, however, the cost will be lower compared to all consequences which might take place amidst the Indonesian society.

## 5. REFERENCES


1. Armel B, Berechid K, Himmich S, Tadili J, Kettani A, Faroudy M, et al. ED antibiotic use in a developing country. American Journal of Emergency Medicine 2014; 32(2):179-181.
2. Alanazi MQ, Al-Jeraisy MI, Salam M. Prevalance and predictors of antibiotic prescription errors in an emergency department, Central Saudi Arabia. Drug, Health and Patient Safety 2015; 4(7):103-111.
3. Park KH, Oh WS, Kim ES, Park SW, Hur JA, Kim YK, et al. Factors associated with ciprofloxacin- and cefotaxime-resistant Escherichia coli in women with acute pyelonephritis in the emergency department. International Journal of Infectious Disease 2013; 23:8-13.
4. Park SY, Son JS, Oh IH, Choi JM, Lee MS. Clinical impact of methicillin-resistant Staphylococcus aureus bacteremia based on propensity scores. Infection 2011; 39(2):141-147.
5. Wilke MH, Grube RF, Bodmann KF. Guideline-adherent initial intravenous antibiotic therapy for hospital-acquired/ventilator-associated pneumonia is clinically superior, save lives and is cheaper than non guideline adherent therapy. European Journal of Medical Research 2011;16(7):315-323.
6. Urbánek K, Kolár M, Lovecková Y, Strojil J, Santavá L. Influence of third-generation cephalosporin utilization on the occurrence of ESBL-positive Klebsiella pneumoniae strains. Journal of Clinical Pharmacy and Therapeutics 2007; 32(4):403-8.
7. den Engelsen C, van der Werf C, Matute AJ, Delgado E, Schurink CAM, Hoepelman AIM. Infectious diseases and the use of antibiotics in outpatients at the emergency department of the University Hospital of León, Nicaragua. International Journal of Infectious Diseases 2009; 13(3):349-354.
8. Gallangher JC, MacDougall C. Antibiotic Simplified, Third edition, Jones and Bartlett Learning, United States of America, 2013.
9. Raza MS, Chander A, Ranabhat A. Antimicrobial susceptibility patterns of the bacterial isolates in post-operative wound infections in a tertiary care hospital, Kathmandu, Nepal. Journal of Medical Microbiology 2013; 3(3):159-163.
10. Cartwright SL, Knudson MP, Evaluation of acute abdomen pain in adult. American Family Physicians 2008; 77(7):971-978.
11. Virapongse A. Nephrolithiasis, Hospital Medicine Clinic 2016; 5(1):43–57.
12. Ong S, Moran GJ, Krishnadasan A, Talan DA. Antibiotic prescribing practices of emergency physicians and patient expectations for uncomplicated

lacerations. Western Journal Emergency Medicine 2011; 12(4):375-380.
13. Mandel GL, Bennett JE, Dolin R. Mandell, Douglas, Bennett's principles and practice of infectious disease, Seventh edition, Elsevier Churchill Livingstone, Philadelphia, 2010.
14. Nicks BA, Ayello EA, Woo K, Nitzki-George D, Sibbald RG. Acute wound management: revisiting the approach to assessment, irrigation, and closure considerations, Review Article. International Journal Emergency Medicine 2010; 3(4):399-407.
15. Roth AR, Basello GM. Approach to the adult patient with fever of unknown origin, American Academy of Family Physicians 2003; 68:2223-2228.
16. Patella V, Florio G, Adiletta G, Santus P. Cough of unknown origin: an often serious, unmet clinical problem. Journal of Allergy and Therapy 2015; 6:210.
17. Little P, Moore M, Kelly J, Williamson I, Leydon G, McDermott L, et al. Delayed antibiotic prescribing strategies for respiratory tract infections in primary care: pragmatic, factorial, randomised controlled trial. British Medical Journal 2014; 348:g1606.
18. Wanahita A, Goldsmith EA, Musher DM. Conditions associated with leukocytosis in a tertiary care hospital, with particular attention to the role of infection caused by Clostridium difficile. Infectious Disease Society of America 2002; 34(12):1585-1592.
19. Guerrant RL, Gilder TV, Steiner TS, Thielman NM, Slutsker L, Tauxe RV, et al. Practice guidelines for the management of infectious diarrhea. Infectious Diseases Society of America 2001; 32:331-350.
20. Lai CC, Ji DD, Wu FT, Mu JJ, Yang JR, Jiang DDS, et al. Etiology and risk factors of acute gastroenteritis in a Taipei emergency department: clinical features for bacterial gastroenteritis. Journal of Epidemiology 2016; 26(4): 216-223.
21. Hansten PD, Horn JR. Drug interaction analysis and management 2013, Eighth edition, Fact & Comparison, United States of America, 2013.

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