







# Antibiotic Resistance Pattern in Patients with Ulcus, Respiratory, and Digestive Tract Infection at Turi Primary Health Care Yogyakarta

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**Abstract. Background:** The incidence and development of antibiotic resistance have been shown to have an impact on the ineffectiveness of therapy and are associated with the increased morbidity and mortality, length of hospitalization, and cost of treatment. Antibiotic-resistant bacteria can spread among bacteria, from treated patients to others, or through the environment. Therefore, mapping the profile of antibiotic resistance in health care facilities such as hospitals, health centers and the surrounding environment becomes crucial. **Objective:** To determine the profile of antibiotic use, antibiotic resistance and infection-causing bacteria in the community setting. **Method:** This was a descriptive-analytical observational study with cohort design in patients with respiratory infections, acute gastroenteritis, or skin infection/ulcer at Turi Primary Health Care, Yogyakarta. **Result:** The infection-causing bacteria were *Staphylococcus aureus* (36%), *Streptococcus pyogenes* (16%), *Streptococcus beta hemolyticus* (12%), *Klebsiella pneumonia* (10%), *Escherichia coli* (6.05%), and other bacteria in amounts less than 5%. The three largest types of infections occurred were respiratory infections (20%), ulcus (18%), pharyngitis, and pyoderma (12.2%). Antibiotics used in infection therapy were amoxicillin 57%, ciprofloxacin 40%, and doxycyclin 2%. Antibiotic sensitivity test results obtained amoxicillin resistance 54%, tetracycline 50%, amoxiclav 33%, chloramphenicol 20%, and the rest were less than 10%. **Conclusion:** In this study, bacteria were resistant to 9 types of antibiotics, two of which were amoxicillin and tetracycline with a resistance percentage of more than 50%. While the majority of infection-causing bacteria was *Staphylococcus aureus* which was resistant to 6 types of antibiotics, namely penicillin, tetracycline, chloramphenicol, gentamycin, erythromycin and cefazolin.

**Keywords:** Resistance · Antibiotics · Primary health care · Bacteria · Resistance

## 1 Introduction

The incidence of antibiotic resistance is rapidly increasing and poses a major threat to public health in all countries in various sectors. The continuously increasing spread of resistance requires serious attention from the governments around the world in addressing the threat. The prescribing pattern is mainly carried out in the first-level health care facilities in remote and rural areas with very limited resources. Several strategies for addressing antibiotic resistance have shown positive results after pursuing various methods aimed at increasing knowledge, clinical, surveillance and policies on the use of antibiotics [1].

Antibiotic resistance is one of the few examples of evolution that is so evident today that conducting research on antibiotic resistance becomes crucial. The presence of antibiotic resistant genes in microorganisms in the environment greatly affects the emergence, spread, and evolution of these resistant genes. Thus, it is very necessary to have both clinical and non-clinical analysis in the habitat so that the spread can be stopped, although the main factor that is very important in resistance is the basic ability of pathogenic microorganisms to increase their immune system in order to maintain their resistance to antibiotics [2]. The spread of drug-resistant pathogens with new resistance mechanisms, leading to antimicrobial resistance, continues to threaten the ability to treat common infections. The rapid global spread of multi- and pan-resistant bacteria (superbugs) will lead to infections that cannot be treated with existing antimicrobial drugs such as antibiotics [3]. Multidrug resistant organisms have been found in several studies such as *Acinetobacter baumannii* which in various circumstances combined with resistance is closely related to healthcare associated infections (HAIs); MDR strains and XDR were reported 27.9% and 42.1%, respectively. MDR strains show sensitivity to amikacin, trimethoprim-sulfamethoxazole, tobramycin, ampicillin-sulbactam, and meropenem. *Acinetobacter baumannii* strain XDR only shows good sensitivity to amikacin [4]. MDR strains also occur in *Mycobacterium tuberculosis* which in 2017 was resistant to rifampicin, then 82% became multidrug-resistant [5]. Appropriate prescribing and the use of antibiotics based on the principles of antimicrobial stewardship accompanied by proper diagnosis and aggressive control of infection will be able to prevent the occurrence of multidrug-resistant organisms (MDRO) [6].

The emergence and development of antibiotic resistance have been shown to have an impact on ineffective and efficient treatments as they are associated with the increased morbidity and mortality, hospitalization and treatment costs. Afterwards, The United Nations on a global scale issued a World Health Assembly Resolution (WHA 68.7) titled "Global Action Plan on Antimicrobial Resistance" as a form of deep attention to this global issue [7]. The problem in Indonesia is that only limited hospitals equipped with clinical microbiology laboratory facilities. By controlling the spread of antibiotic resistance, it is expected to increase the rationality of antibiotic usage, improve the quality of infection control, and inhibit the increase of antibiotic resistance. Hospitals must provide complete facilities to control antibiotic resistance [8]. In subsequent developments, spreading control is also carried out by primary health care facilities. Apart from focusing on the inappropriate use of antimicrobials, the quality of the drug is another important thing worth to consider; drugs with a lower dose of the active ingredient may cause resistance. Strategies aimed at overcoming antimicrobial resistance include

ensuring the availability, proper management of existing antimicrobials and the quality of drugs. Overall, the emergence of AMR in primary health care has been linked to the prescription and use of high-volume antibiotics [9]. Efforts to prevent and handle the further spread of resistance are directed to control the use of antibiotics and map the pattern of antibiotic resistance in the health service facilities and the surrounding environment.

The Indonesian government, through the Regulation of the Minister of Health of the Republic of Indonesia No. 8 of 2015, has required every hospital to carry out the antimicrobial resistance control program optimally through the formation of implementation team, the formulation of antibiotic policies and guidelines, the implementation of the appropriate use of antibiotics, and the implementation of the principles of infection control prevention [10]. This study aims to determine the pattern of antibiotic resistance in primary health care in infectious diseases including respiratory infection, gastrointestinal infection and ulcers in outpatients so that it can be a reference material for the prevention and treatment of antibiotic resistance.

## **2 Methods**

This was a descriptive research with an observational study design and an analytical approach. Data collection was taken prospectively using patient medical record data as well as data on the results of antibiotic sensitivity and sensitivity tests from the microbiology laboratory to specimens from patients according to the type of infection.

## **3 Materials**

The instrument utilized in this study was a research data collection form, consisting of patient identity, diagnosis, the drugs given and swabs to be carried out. The material used was the medical record of the patient who met the inclusion criteria and transport media used to carry specimens from patients to be tested in the microbiology laboratory.

## **4 Research**

The first step of this study was the selection of patients who met the inclusion criteria and were willing to participate as a research subject by filling in the informed consent, followed by data collecting identities and providing treatments, then taking specimens including nasal swabs from ari patients, skin swabs from ulcer patients and feces from patients with gea. specimens with swab collection were carried with transport media while fecal specimens were placed in sterile containers. All specimens would be tested microbiologically to determine the infectious bacteria as well as for sensitivity and resistance tests for further analysis.

## 5 Results and Discussion

The study was conducted on 49 respondents, with almost equal sex disparity between male and female; 55.1% were females and 44.9% were males (Fig. 1). The age group of late adolescence (17–25 years Old) was the largest group (24.49%). Meanwhile, most respondents were housewives and students with 26.53 and 28.57%, respectively.

This study was conducted prospectively with inclusion criteria of patients diagnosed with one of the infections based on the International Classification Diseases (ICD)-10, namely Upper Respiratory Tract Infection, acute gastroenteritis (GEA), ulcers or skin infections. In accordance with these inclusion criteria, 15 types of infections were obtained, and the 4 largest groups in a row were respiratory infection, ulcus pyoderma, pharyngitis, and bacterial scabies. Moreover, the next type of infection with a smaller percentage was infection with dermatitis, bronchitis, dysentery impetigo, parotid and rhinitis (Fig. 2). The antibiotics used to treat such infections consisted of amoxicillin (57.4%), ciprofloxacin (40.82%) and doxycycline (2.04%).

One of the most common diseases experienced by patients in primary health services was pharyngitis. 30% to 60% of acute pharyngitis cases were caused by viruses, but in practice, antibiotics were given [11]. In this study, 75% pharyngitis were given ciprofloxacin therapy for 5 days while the rest were given amoxicillin for 5 days combined with paracetamol, methylprednisolone and acetylcysteine according to the symptoms experienced by the patients.

The second largest type of infection was ulcus and the majority were diabetic ulcus. In several health care facilities, diabetic ulcus has become a serious problem that continues to develop which lead to the increased morbidity and the incidence of lower extremity amputations. The results of the tissue culture test are very useful to be a reference for the determination of antibiotic therapy given. The results showed that the gram-positive bacteria causing ulcers were *Staphylococcus aureus*, while those in the gram-negative group were *Pseudomonas aeruginosa* [12]. In this study, the bacteria causing ulcers were not only those two bacteria, but also *Salmonella enterica* sp Arizona, *Klebsiella oxytoca*, *Citrobacter koseri*, *Citrobacter freundii*, and *Burkholderia cepacia*. *B. cepacia* is an aerobic gram-negative bacillus found in various aquatic environments and is often found in fluids used in hospitals.

During the study there were 49 patients who met the respondent inclusion criteria. From the results of microbiology test, 65 isolates were obtained where 3 isolates did

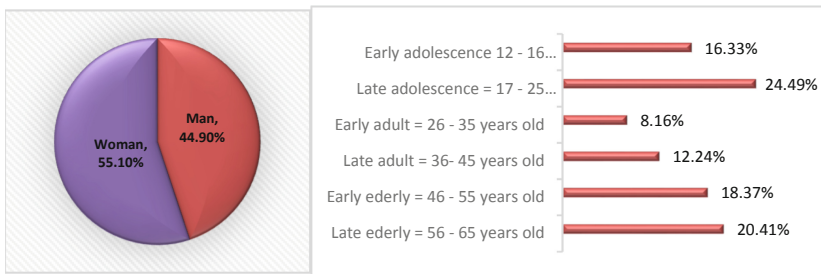
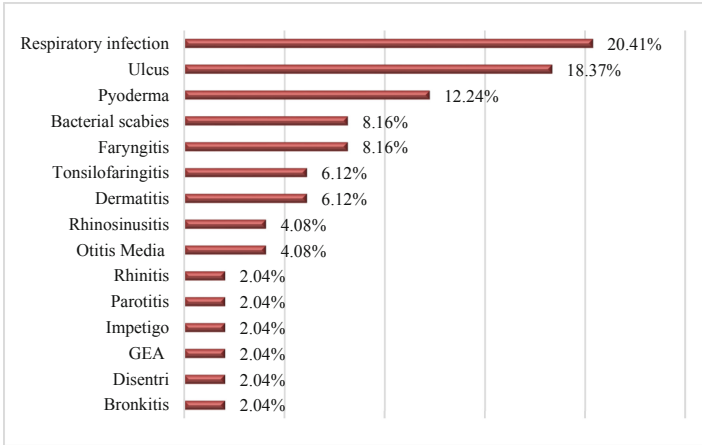
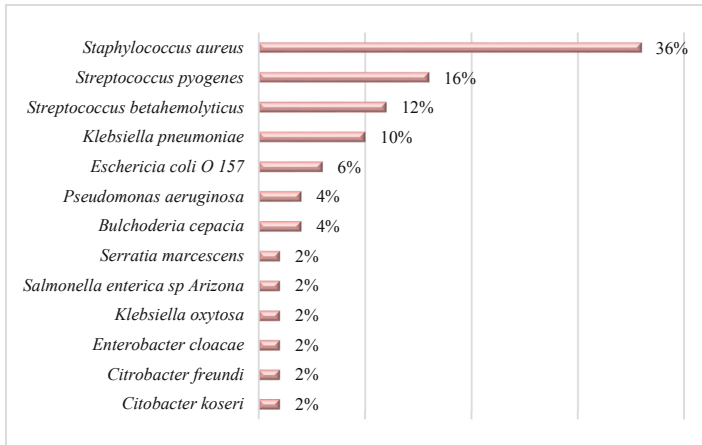


Fig. 1. Characteristics of respondents.



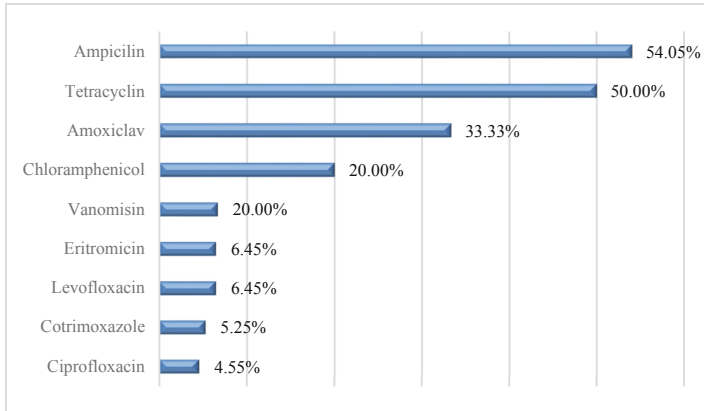
**Fig. 2.** Infectious disease patterns.



**Fig. 3.** Types of bacteria that cause infection.

not grow and 12 isolates were normal flora of the body. The pattern of infection-causing bacteria can be seen in Fig. 3, consisting of 13 types of species with *Staphylococcus aureus* as the majority type. This bacterium is one of the most frequent causes of morbidity and mortality and is the cause of various diseases, ranging from moderately severe skin infections to fatal pneumonia and sepsis. Systemic infection of *S. aureus* begins with the entry of bacteria through the skin barriers or the spread of biofilms formed on the medical device used. In the bloodstream, bacteria can actively attack and eliminate immune cells such as neutrophils through cytolytic toxins or persist in those cells to achieve systemic distribution [13].

*Escherichia coli*, *Klebsiella (pneumoniae/oxytoca)*, *Enterobacter spp.*, *Pseudomonas aeruginosa*, *Acinetobacter spp.*, *Bacteroides spp.*, and *Proteus spp.* Were gram-negative

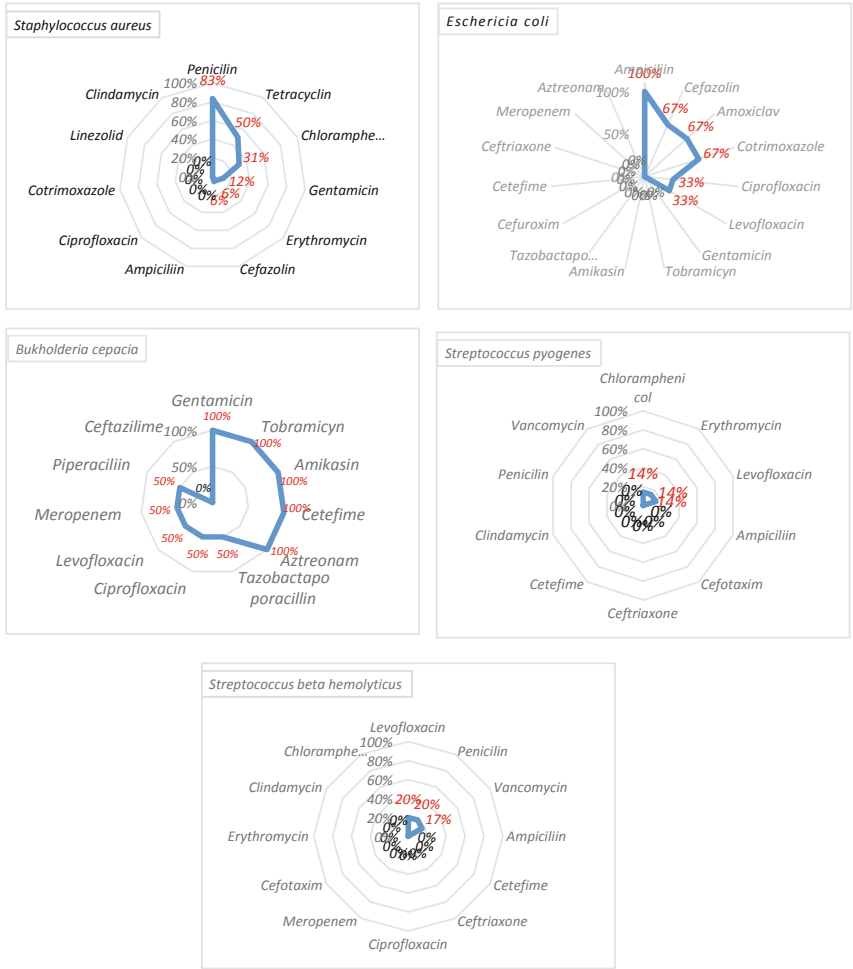


**Fig. 4.** Antibiotic resistance.

bacteria that often cause various types of infections including: catheter-associated urinary tract infections (CAUTIs), bloodstream infection (BSI), ventilator-associated pneumonia (VAP), hospital-acquired pneumonia (HAP), and surgical site infection (SSI) [14].

Antibiotic susceptibility testing (AST) was carried out in all isolates from specimens taken from respondents. Specimens were taken in an appropriate way for each type of infection, namely ulcers with wound swabs, respiratory infection with nasal or throat swabs and gastroenteritis infections with fecal samples. Additionally, 68 isolates were obtained from the specimen and antibiotic resistance data are shown on the antibiogram (Fig. 5). The percentage of ampicillin resistance had the highest rate of 54.05%, followed by tetracycline at a rate of 50.00%, amoxiclav 33.33%, chloramphenicol 20.00% as well as vancomycin, erythromycin, levofloxacin, cotrimoxazole and ciprofloxacin at a resistance rate of less than 10% (Fig. 4). This was similar to previous research conducted at Jetis primary health center, Yogyakarta which showed resistance in gram-negative bacteria such as *Klebsiella pneumoniae* and *H. influenzae* to tetracycline antibiotics, penicillin and chloramphenicol. In this study, there was also antibiotic resistance of tetracycline, penicillin and clindamycin for gram-positive bacteria, such as *Staphylococcus aureus* and *Streptococcus pneumoniae*. Penicillin resistance was affected by the overuse of penicillin antibiotics in the community as they were easily obtained from drugstores [9].

Antibiotics can inhibit the growth of bacteria after penetrating the cell envelope and reaching their target at adequate concentrations. However, bacteria then fight back and find new ways to survive. Target modification can be achieved by resistance to target mutations (e.g. quinolone resistance), target replacement (occasional beta-lactam resistance due to acquisition of penicillin-binding proteins), enzymatic modification of the target (e.g. resistance to vancomycin), or target protection (e.g. resistance to quinolones) [2]. The presence of resistant pathogenic bacteria will affect the patient in several different ways. Resistance genes can alter the immunity of pathogenic bacteria; it will make it more or less virulent; it will cause delays in the administration of appropriate antibiotics; and the antibiotics given may be toxic or inadequate [15].



**Fig. 5.** Multidrug-resistant Organisms (MDRO) in a community setting.

*Staphylococcus aureus* was found to be the bacterium that caused the most infections in primary health centers. The AST showed 100% resistant to amoxicillin, and resistant to cefazolin, amoxiclav and cotrimoxazole reached 67%. Furthermore, Saito (2017) reported that the excessive bacterial resistance to ampicillin and amoxicillin (97%) was dominated by *S. Aureus*, and was found also in *Acinetobacter spp.*, *Enterobacter spp.*, *E.coli*, and *Klebsiella* [16]. Each bacteria found in this study had different resistance pattern, as illustrated in Fig. 5. Most bacteria were resistant to more than 2 types of antibiotics, even some of which were included in the category of multidrug-resistant organisms (MDRO). In addition, there were two bacteria, namely *P. aeruginosa* and *Salmonella sp.*, which were still sensitive to all antibiotics tested.

*Enterococcus*, *S. aureus*, *K. pneumoniae*, *A. baumannii*, *P. aeruginosa*, and *E. coli* are bacteria that cause the majority of infections in health care facilities around the globe. Antibiotic resistance in these bacteria is strongly associated with increased morbidity, mortality and the threat of economic problems [17]. Some of the mechanisms that are common in gram-negative bacteria include the destruction of antibiotic molecules, decreased penetration of antibiotics by reducing permeability, increased antibiotic efflux, mutation of the target location, or changes in antibiotic chemistry [14].

The result of this study showed that *K. pneumoniae* was one of the bacteria that caused respiratory infection. The bacterium is a type of gram-negative opportunistic pathogenic bacteria that can lead to respiratory infections, urinary tract infections, nosocomial infections, and even mortality up to 10% in humans. This type of bacteria is easily found in human body fluids, including blood, urine, and sputum [18]. Additionally, antibiotic resistance also occurred at Sanglah Central General Hospital Denpasar where *K. pneumoniae* was resistant to beta-lactam antibiotics due to the expression of resistant genes, namely the blaCTX-M-1 gene group (83.33%) [19]. Other results obtained were *Enterobacter cloacae*, *Klebsiella oxytoca*, *Serratia marcescens*, each of which only found one isolate, so that the resistance pattern per bacterium was not visible.

In general, infections caused by resistant bacteria lead to produce two times higher adverse outcomes than similar infections caused by susceptible bacteria. These adverse outcomes may be clinical (death or treatment failure) or economic (cost of care, length of stay) and reflect treatment delays and failure of antibiotic treatment to cure infection [20]. Management of patients infected with resistant bacteria is to provide the appropriate antibiotics by considering clinical efficacy, sensitivity, cost, clinical condition of the patient, prioritizing first-line/narrow-spectrum antibiotics, and the availability of antibiotics in health care facilities [21].

## 6 Conclusion

IN this study, bacteria were resistant to 9 types of antibiotics, two of which were amoxicillin and tetracycline with a resistance rate of more than 50%. Meanwhile, the majority of infection-causing bacteria was staphylococcus aureus which was resistant to 6 types of antibiotics, namely penicillin, tetracycline, chloramphenicol, gentamycin, erythromycin and cefazolin.

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