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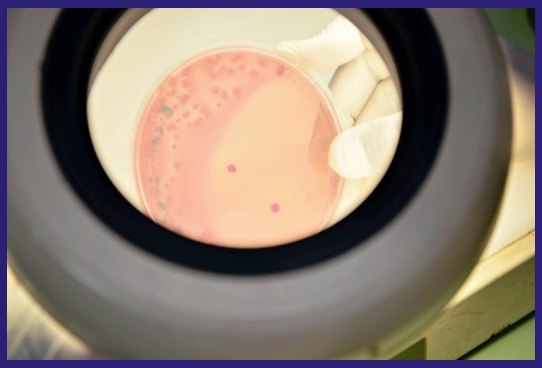


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***Original Article***

# Clinical Profiles, Laboratory, Radiological and Outcome of COVID-19 Elderly Patients in Waikabubak Regional General Hospital, West Sumba

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***ABSTRACT***

*Cases of COVID-19 in the elderly show varied clinical characteristics. Elderly patients tend to be easily infected with COVID-19 and experience more severe conditions. This study aims to analyze the correlation between clinical characteristics of elderly COVID-19 patients and severity of COVID-19 disease at Waikabubak Regional General Hospital. Retrospective study from the medical records of elderly patients with confirmed COVID-19 at Waikabubak Regional General Hospital in March 2020 – September 2021. Inclusion criteria were elderly patients with confirmed COVID-19 who underwent treatment in COVID isolation room and did rapid antigen examination. The data collected were demographics, clinical manifestations, laboratory, radiological features, comorbid, and outcomes. Data analysis using SPPS for Window 12.0 version. There were 33 patients with 18 men and 15 women. Patients aged 65-74 are the most infected with COVID-19 and experience more severe conditions. Patients with no previous vaccine history were associated with the severity of COVID-19. Elderly patients with obesity tend to experience severe COVID-19 symptoms. Elderly patients with multi-comorbidities tend to experience severe COVID-19 symptoms. Dominant clinical symptoms in elderly patients were cough (33%), shortness of breath (25%) and fever (21%). Hematologic parameters that correlated with severity were hemoglobin, platelets, NLR, ALC and RBG. The most common radiological findings were bilateral infiltrates (92%). Mortality rate of elderly COVID-19 patients treated at the Waikabubak Regional General Hospital still tends to be high (42%). Age, vaccine history, obesity, shortness of breath, multi-comorbidities, laboratory and radiology significantly influence the severity of COVID-19 infection in the elderly.*

***Keywords:*** *clinical profile; COVID-19; East Nusa Tenggara; elderly; severity*

***ABSTRAK***

*Kasus COVID-19 pada lansia menunjukkan karakteristik klinis yang bervariasi. Lansia mudah terinfeksi COVID-19 dan mengalami kondisi lebih berat. Penelitian ini bertujuan untuk menganalisis korelasi antara karakteristik klinis pasien lansia COVID-19 dengan tingkat keparahan penyakit di RSUD Waikabubak. Penelitian retrospektif, data dari rekam medis pasien lansia dengan terkonfirmasi COVID-19 di RSUD Waikabubak pada periode Maret 2020 – September2021. Kriteria inklusi pasien lansia dengan terkonfirmasi COVID-19 yang dirawat di ruang isolasi COVID, dan dilakukan pemeriksaan rapid antigen dengan spesimen swab. Data yang dikumpulkan adalah demografi, manifestasi klinis, laboratorium, gambaran radiologis, penyakit komorbid, dan luaran. Analisis data menggunakan SPPS for Window 12.0 version. Didapatkan 33 pasien dengan jumlah pria 18 orang dan wanita 15 orang. Pasien yang berusia 65-74 merupakan pasien terbanyak terinfeksi COVID-19 dan mengalami kondisi lebih berat. Pasien yang tidak memiliki riwayat vaksin sebelumnya berkaitan dengan derajat keparahan COVID-19. Pasien lansia dengan obesitas cenderung mengalami gejala COVID-19 berat.*

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*Pasien lansia dengan multikomorbid cenderung mengalami gejala COVID-19 berat. Gejala klinis yang dominan pada pasien lansia adalah batuk (33%), sesak napas (25%) dan demam (21%). Parameter hematologik yang berkorelasi dengan derajat keparahan adalah hemoglobin, trombosit, NLR, ALC dan GDS. Gambaran radiologis yang tersering didapatkan adalah inflitrat bilateral (92%). Angka kematian pasien lansia COVID-19 yang dirawat di RSUD Waikabubak masih cenderung tinggi, yaitu sebanyak 14 pasien (42%). Karakteristik klinis seperti usia, riwayat vaksin, obesitas, sesak nafas, multikomorbid, laboratorium dan radiologis berpengaruh secara bermakna terhadap tingkat keparahan dari infeksi COVID-19 pada lansia.*

***Kata kunci:*** *COVID-19; derajat keparahan; lansia; Nusa Tenggara Timur; profil klinis*

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## INTRODUCTION

The Coronavirus Disease (COVID-19) pandemic is still happening today. The first case of COVID-19 was reported in China's Wuhan Province in December 2019. The virus has infected more than 150 million people worldwide and caused more than five million deaths.[1] Indonesia is in the 16$^{th}$ position with the most COVID-19 cases in the world based on data from *Gugus Tugas Penanganan COVID-19* on January 31, 2022. Confirmed COVID-19 cases in Indonesia have reached more than 4.3 million cases. Currently, NTT COVID-19 cases have reached 64,600 cases (1.5% of all cases in Indonesia).[2]

Among the confirmed cases at the end of October in Indonesia, 11.8% were elderly patients aged 60 years and over. The elderly also contributed to 46.8% of COVID-19-related deaths nationwide. Older age and comorbidities have been noted as major factors of susceptibility to COVID-19.[3] Liu et al., stated that the mortality rate of COVID-19 patients aged 60 years and over (5.3%) was significantly higher than that of patients under 60 years (1.4%).[4] Unfortunately, data regarding the clinical profile of the elderly hospitalized with COVID-19 in Indonesia is still limited. The elderly are a population that is very at risk in a pandemic, so more attention is needed.

Waikabubak Regional General Hospital is one of the COVID-19 referral centre in West Sumba, which has integrated care and a special isolation ward for COVID-19 patients. Enforcing COVID cases in remote areas is a challenge because of the limited support. The good news is that currently rapid antigen can be used to diagnose COVID-19.

Aspects that need to be considered in reducing COVID-19 cases are treating infected patients and avoiding the spread of the virus. This study aims to analyse the correlation between clinical characteristics of elderly COVID-19 patients and the severity of COVID-19 disease. We hope that by knowing a significant relationship between the clinical characteristics and the severity of COVID-19 disease, patients will receive optimal therapy, thereby reducing mortality.

## MATERIALS AND METHODS

This retrospective study used secondary data from medical record data of elderly patients with confirmed COVID-19 at Waikabubak Regional General Hospital in the period March 2020 to September 2021. The inclusion criteria were elderly patients with symptoms of COVID-19 based on the criteria of the Indonesian Ministry of Health 2020, who underwent treatment in the ward isolation of COVID and examination of nasal swab specimens using rapid antigen according to established standards.

The data collected were age, gender, epidemiological history (contact with adult patients whether suspected, probable, or positive COVID-19, and/or traveling or living in infected areas, red zone areas according to

the Ministry of Health), vaccination history, smoking history, body mass index, clinical symptoms, comorbidities, laboratories, and chest X-ray. images. Laboratory examinations and X-rays were performed using the same equipment and protocol for all patients. Patient outcomes were categorized as discharge with improvement and death. Patients were excluded from the study if data were incomplete and patients aged <65 years. The collected data were analyzed using SPPS for window 12.0 version.

## RESULTS AND DISCUSSION

### Socio-demography

During the study period, 33 patients were obtained who had complete data, consisting of 18 men and 15 women (Table 1).

**Table 1.** Demographics of Elderly Patients with COVID-19

| Parameters | | Severity | | *p* |
|---|---|---|---|---|
| | | Severe/ ARDS | Mode-rate | |
| BMI | Normal | 5 (15%) | 7 (22%) | 0,251 |
| | Overweight | 8 (24%) | 5 (15%) | 0,201 |
| | Obesity | 8 (24%) | 0 (0%) | 0,001* |
| Early symptom | Fever | 2 (6%) | 5 (15%) | 0,564 |
| | Cough | 8 (24%) | 3 (9%) | 0,153 |
| | Shortness of breath | 7 (22%) | 1 (3%) | 0,042* |
| | Chest pain | 2 (6%) | 0 (0%) | 0,274 |
| | Malaise | 0 (0%) | 2 (6%) | 0,274 |
| | Nausea and vomit | 0 (0%) | 1 (3%) | 0,553 |
| | Anosmia | 0 (0%) | 1 (3%) | 0,553 |
| | Decrease of consciousness | 1 (3%) | 0 (0%) | 0,553 |
| Comorbid | Hypertension | 3 (9%) | 6 (18%) | 0,301 |
| | Diabetes Mellitus | 1 (3%) | 2 (6%) | 0,352 |
| | Coronary arterial disease | 1 (3%) | 0 (0%) | 0,553 |
| | Tuberculosis | 2 (6%) | 1 (3%) | 0,401 |
| | Hepatitis | 0 (0%) | 1 (3%) | 0,553 |
| | Absent | 0 (0%) | 3 (9%) | 0,165 |
| | Multi-comorbid | 13 (40%) | 0 (0%) | 0,001* |

The results showed that gender did not correlate with the severity of COVID-19 (p=0.435). Patients aged 65-74 years correlated with the severity of COVID-19 (p=0.045). Patients who were exposed to cigarette smoke were also not related to the severity of COVID-19 (p=0.481). Patients who had no previous vaccine history were associated with the severity of COVID-19 (p=0.05). Patients with a history of COVID-19 contact and travel history were not associated with the severity of COVID-19 (p=0.515) and (p=0.737).

### Clinical

In the analysis of body mass index (BMI), obese patients tend to experience more severe symptoms (p=0.001) (Table 2). Patients with normal BMI and overweight did not correlate with severity (p=0.251 and p=0.201).

**Table 2.** Clinical Elderly Patients with COVID-19

| Parameter | | Severity | | *p* |
|---|---|---|---|---|
| | | Severe/ ARDS | Moderate | |
| Sex | Men | 12 (36%) | 6 (18%) | 0,435 |
| | Women | 8 (24%) | 7 (22%) | |
| Age | 65-74 | 14 (43%) | 8 (24%) | 0,045* |
| | 75-84 | 5 (15%) | 3 (9%) | 0,873 |
| | ≥85 | 1 (3%) | 2 (6%) | 0,607 |
| Smoking | Exposed | 19 (58%) | 7 (22%) | 0,481 |
| | Not exposed | 3 (9%) | 4 (12%) | |
| Vaccine history | Yes | 3 (9%) | 6 (18%) | 0,05* |
| | No | 17 (52%) | 7 (22%) | |
| COVID-19 contact history | Yes | 10 (31%) | 5 (15%) | 0,515 |
| | No | 10 (31%) | 8 (24%) | |
| Travel history | Yes | 4 (12%) | 2 (6%) | 0,737 |
| | No | 16 (49%) | 11 (34%) | |

On examination of clinical symptoms, fever did not correlate with the degree of severity (p=0.564). Cough symptoms did not correlate with severity (p=0.153). Patients with shortness of breath tended to experience severe symptoms (p=0.042). Symptoms of chest pain did not correlate with severity (p=0.274). Symptoms of weakness also did not correlate with the degree of severity (p=0.274).

Complaints of nausea and vomiting did not correlate with the degree of severity (p=0.553). Symptoms of anosmia did not correlate with severity (p=0.553). Symptoms of decreased consciousness did not correlate with severity (p=0.553).

Patients with multi-comorbidity tended to have severe symptoms (p=0.001). Patients with one or no comorbidities did not correlate with severity.

**Table 3.** Laboratory Results of Elderly Patients with COVID-19

| Parameters | | Severity | | *p* | OR (CI 95%) |
|---|---|---|---|---|---|
| | | Severe/ ARDS | Moderate | | |
| Blood routine test | | | | | |
| Low Hb level | | 11 (33%) | 5 (15%) | 0,049* | 1,833 (0,299-11.259) |
| High WBC level | | 12 (36%) | 10 (30%) | 0,411 | 1,421 (0,812-1,824) |
| Low WBC level | | 3 (9%) | 1 (3%) | 0,056 | 0,186 (0,054-1,254) |
| Thrombo-cytopenia | | 6 (18,2%) | 2 (6%) | 0,011* | 0,912 (0,785-1,341) |
| COVID-19 support parameter | | | | | |
| NLR | ≥3.13 | 20 (61%) | 7 (21%) | 0,001* | 0,561 (0,421 - 1,125) |
| | <3.13 | 0 (0%) | 6 (18%) | 0,004* | 0,462 (0,208-1,022) |
| ALC | ≥1500 | 0 (0%) | 6 (18%) | 0,001* | 8,915 (1,514-66,081) |
| | <1500 | 20 (61%) | 7 (12%) | 0,002* | 0,814 (0,456-1,208) |
| Blood glucose | | | | | |
| RBG | ≥200 | 17 (52%) | 2 (6%) | 0,001* | 0,441 (0,215-0,822) |
| | <200 | 3 (9%) | 11 (33%) | 0,042 | 2,513 (1,107-4,255) |

Note. Hb=haemoglobin; WBC=white blood cell; NLR=Neutrophil-lymphocyte ratio; ALC=Absolute-lymphocyte count; RBG=Random blood glucose.

## Laboratory

On laboratory results (Table 3), patients with anemia tended to have severe symptoms (p=0.049; OR=1.833; 95% CI=0.299-11.259), as well as thrombocytopenia (p=0.011; OR=0.912; 95% CI=0.785-1.341). Patients with NLR ≥ 3.13 tend to experience more severe symptoms (p=0.001; OR=0.561;95% CI=0.421-1.125), while patients with NLR <3.13 tend to experience milder symptoms (p=0.004; OR=0.462; CI95%=0.208-1.022). Patients with ALC <1500 tended to experience milder symptoms (p=0.001; OR=8.915; 95% CI=1.1514-66.081), while patients with ALC <1500 tended to experience more severe symptoms (p=0.002; OR = 0.814; 95% CI = 0.456-1,208). Patients with random blood glucose (RBG) ≥200 tended to have severe symptoms (p=0.001; OR=0.441; 95% CI=0.215-0.822).

## Radiological Feature

Elderly patients with COVID-19 had abnormal radiological features as shown in Table 4, showing a tendency to experience severe symptoms (p=0.070). X-rays with bilateral infiltrates tend to have severe symptoms (p=0.024). The radiological features of pulmonary oedema were not related to the severity (p=0.530).

**Table 4.** Radiological Feature of Elderly Patients with COVID-19

| Parameter | | Severity | | *p* |
|---|---|---|---|---|
| | | Severe/ ARDS | Mode-rate | |
| X-Ray | Abnormal | 20 (61%) | 11 (33%) | 0,070* |
| | Normal | 0 (0%) | 2 (6%) | |
| Infiltrate | Unilateral | 0 (0%) | 3 (9%) | 0,024* |
| | Bilateral | 20 (61%) | 10 (31%) | |
| Pulmonary oedema | Yes | 3 (9%) | 1 (3%) | 0,530 |
| | No | 17 (52%) | 12 (37%) | |

## Outcome

Patients with severe symptoms tend to have a worse outcome than patients with moderate symptoms as shown in Table 5.

**Table 5.** Outcome of Elderly Patients with COVID-19

| Parameter | | Severity | | *p* |
|---|---|---|---|---|
| | | Severe/ ARDS | Mode-rate | |
| Outcome | Not survived | 14 (42%) | 0 (0%) | 0,0002* |
| | Survived | 6 (18%) | 13 (40%) | |

## DISCUSSION

The results of this study showed several characteristics that correlated with the severity of the patient. Based on socio-demography, ages 65-74 are the most infected patients with COVID-19 and experience more severe conditions. Aging is associated with ACE-2 overexpression, immune dysregulation, decreased sex steroids, poor nutrition, vitamin D deficiency, mitochondrial dysfunction and oxidative

stress, comorbidities, and lower physical activity. These effects result in increased viral replication, cytokine storm, and poor lung protection against viruses.[5] However, based on CDC data, 80% of deaths occur among adults aged 65 years with the highest percentage in older adults aged ≥85 years.[6]

In this study, 80% of patients were exposed to cigarettes, both active and passive smokers. However, patients exposed to cigarettes were not associated with the severity of COVID-19. It is known that recent reviews show that nicotine exposure is associated with cardiopulmonary susceptibility to COVID-19 and tobacco use is at risk of viral infection and more severe clinical symptoms.[7, 8]

From our study data, it was found that patients who had no previous vaccine history were associated with the severity of COVID-19. The COVID-19 vaccine is highly effective in preventing COVID-19-related hospitalizations in older adults. In the elderly aged 65-74 years, the effectiveness of 2 doses of the vaccine is 96%, while in the elderly aged ≥75 years it reaches 91%.[9]

Based on clinical findings, patients with obesity tend to experience more severe symptoms. Recent evidence suggests that obesity weakens the immune system, leaving the host vulnerable to infectious diseases.[10] Obesity is a risk factor for the development of severe COVID-19 with the need for hospitalization and mechanical ventilation, especially in elderly patients. Obesity causes changes in the microbiota, physiological and immune responses associated with poor viral responses.[11] While the most common symptoms were cough (33%), shortness of breath (25%) and fever (21%). A systematic review of Singhal et al, stated similarly that the most common symptoms in elderly patients were fever, cough and shortness of breath.[12]

On hematological examination, almost half of the patients were anemic (48%). This study is in accordance with Bergamaschi et al, who stated that older people are at risk for anemia and it can affect their quality of life.[13] In COVID-19 patients, inflammation can cause changes in iron hemostasis and reduced iron absorption in the intestine, resulting in reduced metal availability in the process of erythropoiesis and hemoglobin (Hb) production.[14] Several studies have focused on the relationship between anemia and the severity or mortality of COVID-19, the results are still controversial.[15, 16]

In this study, the leukocyte count was increased (66%). The results of this study are similar to those of Liu et al., the increase in white blood cell count was significantly more common in elderly patients, indicating that elderly patients infected with 2019-nCoV were more likely to have bacterial infections.[3] The increase in the number of white blood cells and neutrophils in elderly COVID-19 patients was 30.64% and 33.33%.[17] In particular, a high neutrophil count was an independent predictor of poor outcome. Neutrophilia observed during a cytokine storm caused by viral infection.[18] In the study of Betsy et al, after autopsy they showed neutrophils infiltrating the lungs in the context of a cytokine storm triggering ARDS and causing organ damage and death in COVID-19.[19]

In this study, the percentage of thrombocytopenia did not predominate, but patients with thrombocytopenia tended to experience severe symptoms. Platelets tend to be activated in viral pneumonia causing lung damage by stimulating the respiratory inflammatory response. A tendency to thrombocytopenia in elderly COVID-19 patients may indicate a worsening of the thrombotic state, which is associated with increased mortality.[20] In elderly COVID-19 patients, thrombocytopenia is associated with a 4.24-fold increased risk of death.[21]

Inflammatory biomarkers describe immune status which is a predictor of COVID-19 prognosis. Hematological ratios such as neutrophil to lymphocyte ratio (NLR) and absolute lymphocyte count (ALC) are markers of systemic inflammation that have

been extensively investigated as potential predictors of viral pneumonia. Increased NLR and decreased ALC predict poor outcome in elderly COVID-19 patients.[22] In this study, supporting examination for COVID-19 showed an increase in NLR (82%) and a decrease in ALC (82%).

In our study, RBG value ≥200 mg/dL was present in most of the patients (58%). Severe hyperglycemia is common in critically ill patients and is seen as a marker of disease severity. The study of Li et al., examined COVID-19 patients with hyperglycemia who were hospitalized, consisting of 21.6% of the elderly who had a history of diabetes, 20.8% were newly diagnosed with diabetes, and 28.4% were diagnosed with dysglycemia.[23] The mechanism by which new-onset diabetes develops in the elderly with COVID-19 remains unknown, but it is possible that a number of complex etiologies exist, including disturbances in glucose disposal and insulin secretion, stress hyperglycemia, diabetes preadmission, and steroid-induced diabetes.[24]

Based on radiological results, 94% of chest X-rays had abnormal features with bilateral infiltrates (92%). Our study is consistent with the Neumann-Podczaska study, which stated that the most common radiological features in the elderly were ground glass opacities (GGO) (28.6%), or GGO + consolidation (12.9%), affecting multiple lobes (62.2%) with a bilateral distribution (58.2%). Although most studies did not specify a peripheral or central distribution specifically (93.0%), some studies tended to show a peripheral picture (4.5%) with some cases being peripheral and central (2.5%).[25]

The mortality rate for COVID-19 elderly patients treated at the Waikabubak Regional General Hospital still tends to be high, namely 14 patients (42%), which are included in the severe category. This figure is not much different from the national elderly mortality rate of 46% which was reported on January 31, 2022.[2]

## CONCLUSIONS

The results of this study indicate that clinical characteristics such as age, vaccine history, obesity, clinical symptoms (shortness of breath), multi-comorbid, laboratory (hemoglobin, platelets, NLR, ALC and GDS) and radiologically have a significant effect on the severity of COVID-19 infection in the elderly. By knowing the severity of the disease, patients will receive optimal therapy and reduce mortality. In addition, early diagnosis and supportive care are very important for elderly COVID-19 patients.

## ACKNOWLEDGEMENT

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## CONFLICT OF INTEREST

All authors declared that they do not have any conflict of interest in both the research and also in the article writing process.

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***Original Article***

# Clinical Identifiers, Comorbidities, and Outcomes among COVID-19 Confirmed Patients in Banda Aceh, Indonesia

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***ABSTRACT***

*Coronavirus disease 2019 (COVID-19) is a highly contagious disease with an increasing number of infections in Indonesia. However, hypertension and diabetes are chronic diseases with high incidence in Aceh, there is still limited information regarding the demographics and clinical data of COVID-19 patients. This study aims to explain the clinical characteristics, comorbidities, and outcomes of COVID-19 patients. A retrospective method was used to locate data from the medical record of COVID-19 patients that were admitted to the hospital between June-October 2020. The characteristics demographics, clinical data on admission, and outcomes were extracted from the medical record. In order to determine the comorbid relationship, the chi-square test was used for the laboratory tests and clinical outcomes. A total of 120 patients were included, and more than half were male 80 (60%) with 41-60 years of age at most (51.2%). Most of the patients had comorbid diabetes mellitus (40.5%), hypertension (28.9%), and chronic lung disease (8.3%). Furthermore, most COVID-19 was severe degrees 56 (46.3%). The patients with recovery are 92 (76.0%) and only 29 (24.0%) died. The neutrophilia, and comorbid had no relationship with the clinical outcome of COVID-19 (p>0.05). The Lymphopenia and degree of severity had relationship with clinical outcome (p> 0.05). Diabetes melitus and hypertension are the most common comorbid reported in the COVID-19 patients. The Inflammation markers, such as lymphocytes, can be used as an early warning to increase awareness in treating patients with severe disease.*

***Keywords:*** *clinical identifier; comorbidities; COVID19; outcomes*

***ABSTRAK***

*Coronavirus disease 2019 (COVID-19) merupakan penyakit yang sangat menular dengan jumlah infeksi yang terus meningkat di Indonesia. Hipertensi dan diabetes merupakan penyakit kronis dengan insiden yang tinggi di Aceh, masih terbatasnya informasi mengenai demografi dan data klinis pasien COVID-19. Penelitian ini bertujuan untuk menjelaskan karakteristik klinis, penyakit penyerta, dan outcome pasien COVID-19. Metode retrospektif digunakan untuk mencari data dari rekam medis pasien COVID-19 yang dirawat di rumah sakit antara Juni-Oktober 2020. Karakteristik demografi, data klinis saat masuk, dan hasil diambil dari rekam medis. Untuk menentukan hubungan komorbiditas, uji chi-square digunakan untuk uji laboratorium dan hasil klinis. Sebanyak 120 pasien dilibatkan, dan lebih dari setengahnya adalah laki-laki 80 (60%) dengan usia paling banyak 41-60 tahun (51,2%). Sebagian besar pasien memiliki penyakit penyerta diabetes mellitus (40,5%), hipertensi (28,9%), dan penyakit paru kronis (8,3%). Selanjutnya, sebagian besar COVID-19 adalah derajat berat 56 (46,3%). Pasien yang sembuh sebanyak 92 (76,0%) dan yang meninggal hanya 29 (24,0%). Neutrofilia, dan komorbiditas tidak memiliki hubungan dengan hasil klinis COVID-19 (p >0,05).*

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*Limfopenia dan derajat keparahan memiliki hubungan dengan luaran klinis (p>0,05). Diabetes mellitus dan hipertensi adalah penyakit penyerta yang paling umum dilaporkan pada pasien COVID-19. Penanda peradangan, seperti limfosit, dapat digunakan sebagai peringatan dini untuk meningkatkan kesadaran dalam merawat pasien dengan penyakit parah.*

***Kata kunci:*** *COVID19; komorbiditas; outcome; penanda klinis*

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## INTRODUCTION

*Coronavirus disease 2019* (COVID-19) is a contagious disease caused by SARS CoV2 with increasing morbidity and mortality.[1] Indonesia is one of the countries affected by SARS CoV2.[2] Clinical symptoms appear varied, asymptomatically, mild and very severe symptoms. These trigger the difficulty of disease control in the community.[3] Due to the large variety of clinical manifestations of COVID-19, and the Real-Time Reverse-Transcription Polymerase Chain Reaction (RRT-PCR) examination as the gold standard for COVID-19 is not always available in various places. Therefore, several studies are needed to describe the results of laboratory tests as a guide to determine the severity of the disease, prognosis, and clinical outcome. So, the laboratory examination results are valuable knowledge during the COVID-19 pandemic.[4]

COVID-19 patients with comorbidities such as hypertension and diabetes have a poorer prognosis, higher morbidity and mortality, and longer ICU stay.[5] Diabetes mellitus was discovered to be higher in people with obesity, and hypertension was strongly associated with diabetes mellitus in Indonesia.[6] And even the prevalence of smoking, high blood pressure, and obesity in men are increasing in Indonesia.[7] Although there have been many studies describing the clinical characteristics of patients in China and other countries,[8,9,10] a little description of the clinical characteristics of COVID-19 patients in Indonesia is very significant. A retrospective study in China showed that men with a mean age of 56 were mostly infected, while men in Italy with a mean age of 67.5 years were more infected.[11] Subsequently, there is significant differences between Indonesia and other countries based on population demographics, comorbid and clinical outcomes of patients. Therefore, this study aims to report on the clinical characteristics, comorbidities, and outcomes of COVID-19 patients in Banda Aceh, Indonesia.

## MATERIALS AND METHODS

### Setting Study

This is an observational analytical study with a retrospective method using medical data from the medical records of confirmed COVID-19 patients. Furthermore, this study was conducted at the dr. Zainoel Abidin General Hospital Banda Aceh from October 2021. This study was admitted by Institutional Review Board of the School of Medicine, Universitas Syiah Kuala, Banda Aceh (377/EA/FK-RSUDZA/2021) and National Ethics Commission the Ministry of Health of the Republic of Indonesia (#1171012P. Data were collected from the medical records of patients diagnosed with COVID-19 confirmed by positive reverse transcriptase PCR examination from nasal swabs, which were analyzed molecularly in the hospital virology unit according to WHO.[12]

### Variable Definitions

This study collected demographic data (gender, age, and occupation), and clinical data (clinical symptoms, comorbidities, chest X-rays, laboratory tests). Basic demographic, comorbid and clinical symptoms are fully

documented in the medical record. The definition of clinical outcome is a patient that has completed his treatment in the hospital, either recovered or died. The severity of the disease is divided only into four categories based on the WHO guidelines, namely mild, moderate, and severe, and critically ill or very severe.[13]

### Statistic Analysis

Exploratory statistical analysis was performed to determine characteristic variables of potential patients, clinical symptoms, laboratory results, and clinical outcomes. The association between comorbid, laboratory results and clinical outcomes was assessed using the Chi-square test. For statistical analysis, lymphopenia when the lymphocyte percentage is < 20, Absolute Lymphocyte Count (ALC) decreases when < 1500, Neutrophil Lymphocyte Ratio (NLR) decsreases when < 13.5, and increases > 13.5. Neutrophils percentage decrease when the neutrophil percentage is < 55 and increases > 70. The significance for all data analyzed was $\alpha = 0.05$. All statistical analyzes were performed using SPSS (Statistical Package for Social Sciences) for Windows version 25.0 (IBM SPSS Inc., USA).

## RESULTS AND DISCUSSION

This study collected medical record data for 120 confirmed COVID-19 patients that received diagnostic examinations and treatment. The majority were male 80 (66%) with the age of 41-60 years at most (51.2%) and 31.4% of the patients were over 60 years old. Most of the patients had comorbid diabetes mellitus (40.5%) and hypertension (28.9%), only 8.3% patient had chronic lung disease. Immunodeficiency cases such as Human Immunodeficiency Virus (HIV), Systemic Lupus Erythematosus (SLE), and congenital abnormalities like Congenital pulmonary anomaly and cardiac malformation were absent. Fever is the most common clinical symptom found in treated 89 patients (73.6%). Almost all chest X-rays have bilateral pneumonia (95.9%). Moderate COVID-19 was mostly reported in 32 patients (26.4%) and severe degrees in 56 (46.3%) patients. All patients were well treated, and most of the patients treated out of the hospital in stable condition (recovery) were 209 (87.1%) and only 31 (12.9%) patients died. (Table 1).

**Table 1.** Baseline Characteristics

| Characteristic Demographic | n | % |
|---|---|---|
| **Age** | | |
| < 20 years | 0 | 0.0 |
| 20 - 40 years | 21 | 17.4 |
| 41 - 60 years | 62 | 51.2 |
| >60 years | 38 | 31.4 |
| **Gender** | | |
| Male | 80 | 66 |
| Female | 41 | 34 |
| **Comorbid** | | |
| **Hypertension** | | |
| Yes | 35 | 28.9 |
| No | 86 | 71.1 |
| **Diabetes mellitus** | | |
| Yes | 49 | 40.5 |
| No | 72 | 59.5 |
| **Chronic Lung Disease** | | |
| Yes | 10 | 8.3 |
| No | 111 | 91.7 |
| **Fever** | | |
| Yes | 89 | 73.6 |
| No | 32 | 26.4 |
| **Cough** | | |
| Yes | 96 | 79.3 |
| No | 25 | 20.7 |
| **Shortness of Breath** | | |
| Yes | 79 | 65.3 |
| No | 42 | 34.7 |
| **Anosmia** | | |
| Yes | 15 | 12.4 |
| No | 106 | 87.6 |
| **Chest Radiograph** | | |
| Pneumonia Bilateral | 116 | 95.9 |
| Without Pneumonia | 5 | 4.1 |
| **Sore Throat** | | |
| Yes | 30 | 24.8 |
| No | 91 | 75.2 |
| **Headache** | | |
| Yes | 8 | 6.6 |
| No | 113 | 93.4 |
| **Anorexia** | | |
| Yes | 76 | 62.8 |
| No | 45 | 37.2 |
| **Degree of Severity** | | |
| Mild | 5 | 4.1 |
| Moderate | 32 | 26.4 |
| Severe | 56 | 46.3 |
| Very Severe | 28 | 23.2 |
| Outcome | 28 | 23.1 |
| Recover | 92 | 76.0 |
| Died | 29 | 24.0 |
| **Absolute Lymphocyte Count (ALC)** | | |
| Normal | 39 | 32.2 |
| Decrease | 82 | 67.8 |
| **Netrophyl Lymphocyte Ratio (NLR)** | | |
| High | 24 | 19.8 |
| Low | 97 | 80.2 |
| **Total** | 121 | 100.0 |

A number of studies showed that the incidence of SARS-CoV and SARS-CoV-2 infection is higher in men than in women.[14,15] Based on the history of the influenza epidemic, there is a variable risk of gender, where men are more susceptible to infection than women.[16] Men generally had worse clinical outcomes and higher mortality rates in the SARS and MERS epidemics.[14] Likewise, a number of studies showed that they are at greater risk of being infected with COVID-19 and most are hospitalized.[17] Some of the mechanisms that put men at a higher risk of contracting the disease than women are gender hormones and gene X-related activity, which play a role in modulating innate and adaptive immune responses to viral infections.[18] The main route of SARS-CoV-2 infection is via the ACE2 receptor, and therefore the biological differences in the angiotensin-converting enzyme 2 (ACE2) receptor also play a role, with men shown to have more ACE2 expression in the circulation and lungs than women.[17] This is consistent with the findings that most men infected with COVID-19 received treatment in the hospital.

Diabetes is one of the top causes of morbidity and mortality, and relationship with infection has long been allowed. Infections such as pneumonia are generally seen in type 2 diabetes mellitus (T2DM) people. China and Italy reported that older patients with diabetes were at higher risk for more serious COVID-19 and mortality.[19,20] Patients with comorbid cardiovascular disease are at higher risk of severe symptoms when infected with SARS-CoV-2. Hypertension is a major risk factor related with poor clinical outcomes in COVID-19.[21] According to this study, it was shown that Diabetes mellitus and hypertension was the most common comorbid disease but it was not significantly related to the clinical outcome ($p < 0.05$). This happens because the prevalence of diabetes mellitus and hypertension is quite high in Indonesia and half of the hypertensive patient are unaware of the dangers of this comorbid.[7] It is not unexpected that immunity and metabolism have coevolved in such proximity. Cellular stressors in diabetes mellitus, such as endoplasmic reticulum stress, oxidative stress, and others, might exacerbate inflammatory responses.

In COVID-19, When SARS-CoV-2 infects diabetic patients with the aforementioned cellular stressors, the decreased immune response may result in significant lung and other pathology and frequently results in mortality.[22] The worse outcomes in COVID-19 patients can be partially attributed to hypertension, which plays a significant role in the control of RAAS, inflammation, immunological responses, and the gastrointestinal tract. Because of this, patients who have both hypertension and SARS-CoV-2 infection may suffer a double blow.[23]

Most patients admitted to the hospital had a complaints of, coughing 96 (79.3%), and Shortness of breath 79 (65.3%), and only 8 patients had a headache. The laboratory examinations results at the hospital showed that the mean levels of leukocytes were 11.276 x $10^3$/uL, lymphocytes percentage 14.6, neutrophils percentage 81.2, NLR 6.7, and ALC 1375 (Table 2).

**Table 2.** Clinical and Laboratory Findings on Admission

| Parameter | Min. | Max. | *Mean* | SD |
|---|---|---|---|---|
| Systolic (mmHg) | 14.00 | 194.00 | 130.4628 | 22.32974 |
| Diastolic (mmHg) | 48.00 | 275.00 | 79.9669 | 20.60014 |
| Heart Rate (x/i) | 71 | 130 | 95.13 | 11.272 |
| Respiratory Rate (x/i) | 18 | 40 | 25.51 | 4.384 |
| SaO2 Without O2 (%) | 40 | 99 | 87.69 | 9.930 |
| Leukocytes x $10^3$/uL ( normal range 4.0-10.0) | 1100 | 34400 | 11276.03 | 6576.904 |
| Lymphocyte percentage, normal range 25-40 | 2 | 47 | 14.60 | 12.128 |
| Neutrophyl Lymphocyte Ratio (NLR) | .00 | 47.50 | 6.7660 | 9.58457 |
| Neutrofil percentage, normal range 50-70 | 26.00 | 126.00 | 81.2231 | 15.17591 |
| Absolute Lymphocyte Count (ALC) | 77.00 | 7082.00 | 1375.4380 | 1109.49531 |
| Systolic (mmHg) | 14.00 | 194.00 | 130.4628 | 22.32974 |
| Diastolic (mmHg) | 48.00 | 275.00 | 79.9669 | 20.60014 |

A meta-analysis of patients with COVID-19 had a fever as the most common initial symptom (88.8%), dry cough (68%), and fatigue (33%). Other symptoms reported were productive cough (28.5%), shortness of breath (17%), muscle aches (14.4%), sore throat (11.4%), and headache (10.2%). During the first week of the virus phase when the body becomes infected, fever is a manifestation of the body's immune response to virus replication.[24] In line with the findings, it shows that cough and fever are the clinical symptoms most complained of by COVID-19 patients.

The results show that most cases of COVID-19 are hospitalized in severe cases and the majority return to home in stable condition. This is most likely due to increased health worker awareness about signs, symptoms, early diagnosis, and identification of disease more quickly to reduce the severity of the disease that may occur.[25] Therefore, this had an impact on the clinical outcome as most of the patients treated were able to return home in a stable condition.

Neutrophylia and Comorbid had no significant relationship with the clinical outcome of patients ($p > 0.05$), and there is a significant relationship between Lymphocyte and the degree of severity with clinical outcome ($p < 0.05$). (Table 3).

**Table 3.** The Relationship of Clinical Characteristics and Outcomes

| | | Clinical Outcome | | | | Total | *p* |
|---|---|---|---|---|---|---|---|
| | | Died | | Recover | | | |
| Hypertension | No | 17 | 19.8% | 69 | 80.2% | 86 | 0,09 |
| | Yes | 12 | 34.3% | 23 | 65.7% | 35 | |
| Diabetes Mellitus | No | 13 | 18.1% | 59 | 81.9% | 72 | 0.065 |
| | Yes | 16 | 32.7% | 33 | 67.3% | 49 | |
| PPOK | No | 28 | 25.2% | 83 | 74.8% | 111 | 0.280 |
| | Yes | 1 | 10.0% | 9 | 90.0% | 10 | |
| ALC | Decreased | 23 | 28.0% | 59 | 72.0% | 82 | 0,127 |
| | Normal | 6 | 15.4% | 33 | 84.6% | 39 | |
| NLR | Low | 22 | 22.7% | 75 | 77.3% | 97 | 0,505 |
| | High | 7 | 29.2% | 17 | 70.8% | 24 | |
| Degree Of Severity | Mild | 0 | 0.0% | 5 | 100.0% | 5 | 0,000 |
| | Moderete | 0 | 0.0% | 32 | 100.0% | 32 | |
| | Severe | 12 | 21.4% | 44 | 78.6% | 56 | |
| | Very Severe | 17 | 60.7% | 11 | 39.3% | 28 | |
| Neutrofil | Decrease | 0 | 0.0% | 9 | 100.0% | 09 | 0,101 |
| | Normal | 1 | 10.0% | 9 | 90.0% | 10 | |
| | Increase | 28 | 27.5% | 74 | 72.5% | 102 | |
| Limfosit | Decrease | 28 | 30.8% | 63 | 69.2% | 91 | 0.002 |
| | Normal | 1 | 3.3% | 29 | 96.7% | 30 | |
| **Total** | | 29 | 24,0% | 92 | 76,0% | 121 | |

Based on the laboratory tests in this study, Sars CoV2 infection affected the mean level of leukocytes, lymphocytes, and neutrophils (Table 2). Therefore, there is a significant relationship between the decrease in lymphocyte levels and the patient's clinical outcome. Our findings confirm the potential use of lymphocytes in disease severity in COVID-19. As is well known, Sars CoV2 primarily acts on T lymphocytes and further disrupts the stability of neutrophils in the immune system.[26] A meta-analysis showed that lymphopenia and neutropenia are associated with poor clinical outcomes in COVID-19.

Lymphopenia can cause interference with adaptive immunity and cytokine storms that trigger Acute Respiratory Distress Syndrome (ARDS).[27] Furthermore, low absolute lymphocyte levels can be used as a characteristic marker of diagnosis and describe the prognosis of the disease.[11]

Lymphopenia and Neutrophylia observed can be the cause of the poor clinical outcome in COVID-19 because there is a disruption in the balance of the immune system in response to viral infection, leading to hyperinflammation and death. Because of the defensins and neutrophil elastase (NE) that are generated after excessive neutrophil activation during Sars CoV2 infection, blood arteries may become more permeable. Additionally, NET formation may actively harm vascular tissue or significantly contribute to the activation of endothelial cells aggravating the inflammatory circuit and activating alveolar macrophages for clearance.[28]

## CONCLUSIONS

Diabetes melitus and hypertension are the most common comorbid reported in the COVID-19 patients. Furthermore, lymphocyte can be used as markers of disease severity that influence the clinical profile of patients with COVID-19. Majority of the patients return home with a stable condition, most likely because health worker awareness is quite good regarding this disease.

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## CONFLICT OF INTEREST

This research has no conflict of interest.

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***Original Article***

# Analysis of COVID-19 Surveillance System at Makassar City Health Office 2020

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***ABSTRACT***

*One of the infectious diseases that emerged in Indonesia in 2020 has been designated as a COVID-19 pandemic since March 11, 2020, and until now, the pandemic has not been completed. Surveillance has a role in providing information on targeted disease control activities; analyzed the COVID-19 surveillance system based on the current system approach at the Makassar City Health Office. Methods This research is a descriptive observational study conducted in September-October 2020. Data collection was carried out using in-depth interviews with people who were key informants of COVID-19 surveillance activities. There are four informants in this study. In addition, secondary data was obtained from the P2P field regarding COVID-19 cases. In general, the Input component has not been fulfilled; HR has multiple tasks, the job desk is irregular, and several important forms are not used in the methods section. The process component has been running but has not been maximized because there are still incomplete data, no reports based on the PE form, the All-Record TC-19 information system has not been used, and data analysis is still incomplete, data analysis is not equipped with data interpretation. In the Output component, the success rate for public health surveillance criteria has not been evaluated, and the dissemination of information has been carried out well across sectors. The implementation of COVID-19 surveillance at the Makassar City Health Office has been carried out well, but some things are still not optimal.*

***Keywords:*** *COVID-19; input; output; proses; surveillance*

***ABSTRAK***

*Salah satu penyakit menular yang muncul di Indonesia pada tahun 2020 telah ditetapkan sebagai pandemi COVID-19, sejak tanggal 11 Maret 2020 dan sampai saat ini pandemi belum selesai. Surveilans memiliki peranaan untuk memberikan informasi terhadap kegiatan pemberatasan penyakit tujuan ; melakukan analisis sistem surveilans COVID-19, berdasarkan pendekatan sistem yang sedang berjalan di Dinas Kesehatan Kota Makassar. Metode Penelitian ini merupakan penelitian deskriptif observasional yang dilakukan pada bulan September-Oktober 2020. Pengumpulan data dilakukan dengan cara indepth interview kepada orang yang sebagai informan kunci dari kegiatan surveilans COVID-19. Informan dalam penelitian ini ada 4 orang. Data sekunder diperoleh dari bidang P2P tentang kasus COVID-19. Pada komponen Input secara umum belum terpenuhi; SDM memiliki tugas rangkap, jobdesk yang tidak teratur, pada bagian metode terdapat beberapa formulir penting yang tidak digunakan. Pada komponen proses sudah berjalan namun belum maksimal karena masih ada data yang kurang lengkap, tidak ada laporan berdasarkan form PE,sistem informasi All- Record TC-19 belum digunakan, analisis data masih ada yang kurang lengkap, analisis data belum dilengkapi dengan interpretasi data. Pada komponen Output belum dievaluasinya angka keberhasilan kriteria surveilans kesehatan masyarakat dan penyebaran informasi telah dilakukan dengan baik dengan*

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*lintas sector. Dalam pelaksanaan surveilans COVID-19 di Dinas Kesehatan Kota Makassar telah terlaksana dengan baik, namun masih terdapat beberapa hal yang belum maksimal.*

***Kata kunci:*** *COVID-19; input; output; proses; surveilans*

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## INTRODUCTION

Coronavirus Disease 2019 is one of the infectious diseases that coincide in Indonesia and other countries.[1] Based on research conducted by the CDC, China found that the cause of pneumonia in this group of patients was a new species of coronavirus, namely SARS CoV 2.[2] The coronavirus is spherical with a diameter of about 125mm as depicted in a study using cryo-electron microscopy.[3]

Covid-19 spreads through droplets released by an infected person and is symptomatic/symptomatic through coughing or sneezing. In addition to symptomatic people, this virus can also be transmitted to asymptomatic people. Cases of transmission from symptomatic hosts are generally because the host has a history of contact with positive COVID-19 people.[4] The CDC says that all people who have been in close contact with someone with COVID-19 should be quarantined for 14 days after their last contact with that person unless they meet the requirements.[5]

Around 80% of cases of COVID-19 are mild and moderate symptoms, 13.8% are seriously ill, and 6.1% are critical cases. The percentage of subjects with no symptoms can not be known. The typical clinical symptoms of this patient are fever, dry cough, difficulty breathing, headache, and pneumonia. Other symptoms that can be found are productive cough, shortness of breath, sore throat, headache, chills, nausea/vomiting, diarrhea, abdominal pain, hemoptysis, and conjunctival congestion.[6]

Coronavirus Disease 2019 (COVID-19) is an infectious disease caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). On December 31, 2019, the WHO China Country Office reported a case of pneumonia of unknown etiology in Wuhan City, China. On January 7, 2020, China identified the case as a new type of coronavirus. On January 30, 2020, WHO designated the incident as a Public Health Emergency of International Concern (PHEIC). On March 11, 2020, WHO declared COVID-19 a pandemic. Indonesia reported its first case on March 2, 2020. Cases continued to increase and spread rapidly throughout Indonesia. As of October 16, 2020, the Ministry of Health reported 353,461 confirmed cases with 12,347 deaths.[7]

The high inflow of tourists from abroad has caused Indonesia to Sulawesi, particularly vulnerable to the spread of transnational diseases such as COVID-19. South Sulawesi is one of Indonesia's provinces with a relatively high number of COVID-19 cases as of October 16, 2020, with 17,286 confirmed cases with 442 deaths.[8] Makassar is one of the big cities in South Sulawesi and has the most significant number of COVID-19 cases. Based on the Makassar City Health Service Report on October 17, 2020, 9,098 cumulative positive COVID-19 with 282 positive cases died. Makassar city has 16 sub-districts.

The highest COVID-19 cases occurred in the Rappocini sub-district, with 1,153 cases. The distribution of positive cases of COVID-19 by age group can be seen that the highest number of positive cases of COVID-19 occurred in the age group of 31-40 years, with 2303 cases, and the least number of positive cases of COVID-19 occurred in the age group > 80 years which is 28 cases.[9]

Maintenance of efforts prevention and control of infectious and non-infectious data support is required information through an epidemiological surveillance system disease routinely and integrated as part of the health

epidemiological surveillance system.[10] Surveillance is in the form of continuous and systematic observation for the sake of prevention.[11] The morbidity and mortality rates due to COVID-19 are increasing. Therefore, prevention and control efforts are needed, one of which is epidemiological surveillance.[12] Surveillance is crucial to provide information on disease control activities. The concept adopted by surveillance is the principle of epidemiology in identifying diseases based on variables of person, place, and time.[13]

Surveillance is an essential component of the health system in producing epidemiological information for health services so that diseases and risk factors can be detected early and effective and efficient responses can be made to health services. Surveillance activities are an inseparable part of quarantine. During the quarantine period, surveillance is carried out to monitor changes in the condition of a person or group of people.[14]

Surveillance also enables decision-makers to lead and manage effectively. Public health surveillance provides decision-makers and managers with early warning information about health problems that need attention in a population. The performance of the health epidemiological surveillance system is measured by input, process, and output indicators. The three indicators are one unit, where the weakness of one of these indicators indicates the performance of the surveillance system is not yet adequate. Evaluation is an essential tool for policymakers that help to improve the performance and productivity of health programs.[15] Evaluation surveillance system showed that the system was overall effective in estimating morbidity and mortality and monitoring the disease trend.[16] The rationale for evaluating public health surveillance systems is to determine if the disease is being observed efficiently and effectively.

Every surveillance system should be evaluated periodically with recommendations to improve the surveillance system's usefulness, quality, and efficiency.[17] All surveillance components such as collection, processing, analysis, and interpretation of data, follow-up, and feedback must be carried out in a systematic and organized manner.[18] Sensitive surveillance in detecting disease trends and being active in finding cases of COVID-19 is very important in efforts to handle and monitor close contacts and people at risk.[19]

The COVID-19 problem requires adequate and comprehensive control efforts. These efforts must be supported by providing precise and accurate data and information systematically and continuously through a good surveillance system.[20] The results of surveillance activities will be used as input to reduce morbidity and mortality and improve health status.[21]

In general, the goal is to describe the COVID-19 Surveillance system based on a system approach (input, process, output) to analyze the existing health condition so that priority problems can be determined at the Makassar City Health Office in 2020.

The specific objectives to be achieved include: Obtain an overview of the regional situation at the Makassar City Health Office; Get an overview of the COVID-19 surveillance system at the Makassar City Health Office; Obtain an overview of the implementation of the COVID-19 surveillance program at the Makassar City Health Office based on a systems approach; Studying the problems of the COVID-19 surveillance program related to identifiable health problems and the quality of the data collected. Determining priorities for the COVID-19 Surveillance Program problem at the Makassar City Health Office. And planning an alternative solution to the COVID-19 Surveillance Program at the Makassar City Health Office.

## MATERIALS AND METHODS

This research design uses a descriptive observational design that aims to describe the

activities of the COVID-19 Surveillance Program at the Makassar City Health Office through problem identification and represents the priority of the problem determined based on the method used and alternative problem-solving.

The location of this research is at the Makassar City Health Office, which will be held from 26 September to 11 October 2020.

Data collection was carried out using in-depth interviews with the holders of the COVID- 19 surveillance program, the Head of the Surveillance & Immunization Section, and employees involved in COVID-19 activities at the Makassar City Health Office, which was carried out on several people who were considered key informants of the COVID-19 Surveillance activity.[22]

Four informants in the activity consisted of 1 coordinator of the COVID-19 surveillance program, namely the Head of the Surveillance and Immunization Section and staff who joined the COVID-19 surveillance program, and one student.

The technique of determining the priority of the problem in this study is to use the CARL method. The CARL method is C is Capability (availability of resources), A is Accessibility (easiness), R is Readiness (readiness of implementing personnel and target readiness), and L is Leverage (how much influence one criterion has on another in problem-solving). This method aims to determine the problems that will be prioritized from the results of problem identification.[23]

The presentation of data in this activity report is in the form of tables, graphs, and images which are then analyzed using a straightforward narrative.

## RESULTS AND DISCUSSION

### Overview of the Makassar City Health Office Situation

Makassar City Health Office Vision "Healthy and Comfortable Makassar for All Towards a World City." And Makassar City Health Service Mission: Improving quality and affordable health services based on technology. Improving public health and community empowerment. Ensure public health through the health insurance system. And creating a healthy environment.

### Overview of the COVID-19 Surveillance System at the Makassar City Health Office

*(The flow of Reporting and Feedback on COVID-19 Case Management at the Makassar City Health Office).*

The mechanism for reporting and feedback on the COVID-19 surveillance program as shown in Figure 1.

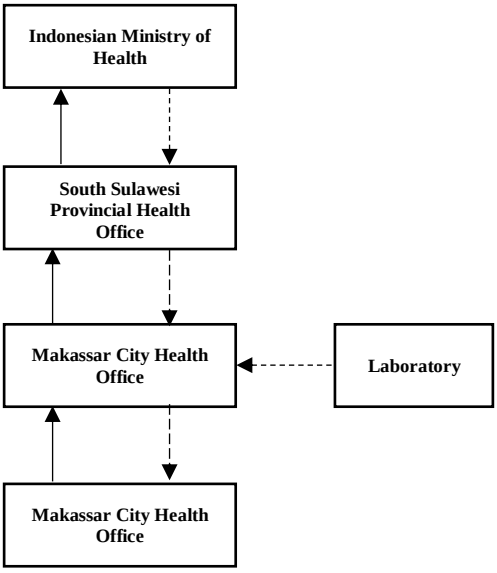


**Figure 1.** COVID-19 Surveillance Reporting & Feedback Mechanism[9]

### The Importance of COVID-19 Surveillance

The high number of COVID-19 cases in Makassar City has caused the local government to act to handle this case so that it does not continue to increase. However, the handling of this COVID-19 case needs intervention. Adequate Epidemiological Information is information that can provide an overview of the situation regarding COVID-19 in Makassar City, which includes variables of people, place, and time as well as risk factors that increase the occurrence of COVID-19. Therefore, the Makassar City Health Office conducted COVID-19 surveillance to obtain adequate epidemiological information. The implementation of COVID-

19 surveillance at the Makassar City Health Office is essential because it functions to evaluate programs and make recommendations so that the handling of COVID- 19 cases can be right on target.

**Overview of the Implementation of the COVID-19 Surveillance System at the Makassar City Health Office**

**Input**

The input components in the COVID-19 surveillance system include:

a. Human Resources (HR)

Human resources in COVID-19 surveillance at the Makassar City Health Office consist of 8 people from the disease prevention and control, including one program coordinator, namely the Head of the Surveillance and Immunization Section, assisted by several staff and contract workers. The latest educational background includes D3 (Nursing), S1 (Doctor and Bachelor of Public Health, and Master of Public Health). Meanwhile, human resources for COVID-19 surveillance activities at the health facilities level are doctors, nurses, midwives, and public health.

b. Funding

The current source of funds for COVID-19 surveillance comes from the Makassar City APBD through the Unexpected Cost for COVID-19 Control and comes from the APBN.

c. Means and Types of Data

1. Source and Type of Data The source of data on COVID-19 surveillance activities comes from the results of laboratory examinations reported to the Makassar City Health Office using form 7 (Form PDP Covid-19 ODP COVID-19 Research and Development Center for Biomedical and Basic Health Technology, Health Research and Development Agency). The data collected included the identity of the specimen sender, patient identity, treatment history, signs and symptoms, date of onset, specimen collection, contact/exposure history, and comorbid diseases. In addition, the types of data collected are suspect case data, confirmation, close contact, death, PCR examination, serological surveillance (rapid test, rapid reactive test, RTPCR, and RTPCR +), isolation/quarantine. As well as confirmed, suspected, and probable cases.
2. Office Stationery, computer equipment, and internet network. Facilities and infrastructure for COVID-19 surveillance activities are adequate. The facilities and infrastructure for surveillance activities at the district/city level are insufficient because the availability of manual data collection forms is not yet fully complete, which is used only from form 7 (COVID-19 Examination Application Form using TCM/COVID Form 5). While form 3 (COVID-19 Case Finding Notification Report at Health Facilities), form 6 (COVID-19 Epidemiological Investigation Form) is not used correctly, form 4 (COVID-19 aggregate daily report) is filled in excel form but has not been consistent in filling it out. The office stationery is complete. There are several computer devices, but they also use personal laptops and printers to support the COVID-19 surveillance program.

d. Methods

The current COVID-19 surveillance activities are based on the COVID-19 prevention and control guidelines of the Ministry of Health of the Republic of Indonesia in July 2020.[24] All policies are available at the Makassar City Health Office starting with the revision guidelines I-V. Based on interviews, the guidelines for the prevention and control of COVID-19 are revised too often, so there are obstacles in the revised guideline 5 because there is no mention of swab control for those who have confirmed COVID-19. At the same

time, many people want swab control to ensure there is no virus in the body.[25]

Improving the quality of recording and reporting of COVID-19 data must follow the form or attachment in the revision 5 guideline, but based on direct observation during Field Work Practice at the Makassar City Health Office still using the old form and not up to date based on the attachment of the latest form in the guide Guidelines for the prevention and control of COVID-19 revision 5.

e. Market (Information Dissemination)

Dissemination of information on the results of the COVID-19 surveillance implementation at the Makassar City Health Office is actively carried out to the Provincial Health Office. As a result, many agencies or fields require or request the results of COVID-19 surveillance, starting from the District Level, BPPA, BAPPEDA, BPBD, TNI/POLRI, and the media. The information needed or requested by the agency or field is data on patients confirmed to be COVID-19.

**Process**

a. Data Collection

The COVID-19 confirmed data collection activity came from the Health Service examination, sending specimens to the laboratory for analysis. A few days later, laboratory results from the Central Health Laboratory and the UNHAS Laboratory were submitted to the Health Office for further processing and presented to each Public Health Center for tracing and Epidemiological Investigation (EI). Based on interviews, data collection activities are carried out every day if there is a confirmed COVID-19, but it is not recorded using the attachment form 3 in accordance with the guidelines. And the EI Form was also not used because the officers were lazy to fill out the form, so there was less information about the patient's close contact, and the EI Form was taken over by the Provincial Health Office.

b. Data Compilation

Data compilation is done by using a computer/ laptop. Based on interviews and document studies, the data at the Makassar City Health Office has been grouped according to the variables of the person (gender, age), place and time, and daily data on COVID-19 cases.

c. Data Analysis

Data analysis is used to determine the success of controlling COVID-19 at the Regency/City/Provincial level following the indicators defined by the Ministry of Health.

The results of the analysis at the Makassar City Health Office as shown in Figure 2.

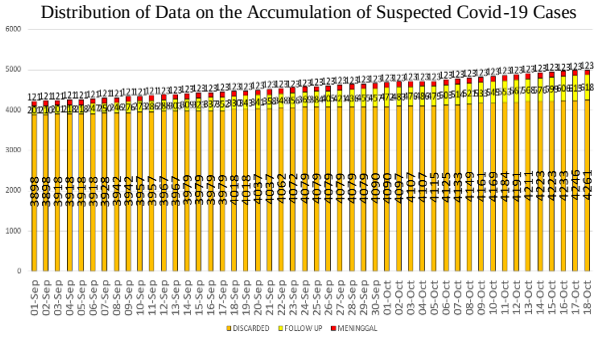


**Figure 2.** Distribution of Data on the Accumulation of Suspected Covid-19 Cases[9]

d. Interpretation

Based on the results of interviews, the COVID-19 surveillance officers at the Makassar City Health Service did not know how to interpret the data, the results and the presentation of the interpretation of the data (tables, graphs, diagrams) because everything was done by the Expert Team. However, based on the document study, the data analyzed in tables, graphs, and charts have not been equipped with data interpretation.

e. Information Dissemination

Data collected is disseminated by the coordinates of the COVID-19 surveillance program in the form of information on the epidemiology of COVID-19 in Makassar City to the public, media, local government, and other cross-sectors.

**Output**

The output is the result of the process of data collection, data analysis, and data interpretation. In information systems, the outcome can be in the form of information, suggestions, printed reports, etc.

The COVID-19 surveillance output is used as a basis for program improvement. Based on interviews with program managers, the work generated from analyzing and interpreting the data is the coverage obtained from program activities.

This coverage is compared with the indicators of the COVID-19 surveillance program as a measure of the progress or success of the program. The indicators used at the district/city level include the Epidemiological Criteria, the Health System Criteria, and the Public Health Surveillance Criteria as many as 24. However, this evaluation focuses on the Public Health Surveillance section, which consists of 10 Indicators covering surveillance systems, case investigations, and contact tracing. Then, from the data analysis results, epidemiological information about COVID-19 is made at the Makassar City Health Office and then reported to the Provincial Health Office.

The output from the COVID-19 surveillance data is not only used for monitoring and evaluation activities in measuring the achievement indicators of the City-scale COVID-19 control program but it is also used for the preparation of Makassar City Health Office reports such as Profile of the Makassar City Health Office; Daily Reports, Monthly and Annual Reports of Disease Control and Eradication Section; Makassar City Health Office Annual Report; Data for COVID-19 research purposes; Data on cross-sectoral requests from relevant Regional Apparatus Units; and Data for NGO and Community Organizations.

**Feedback**

Feedback from COVID-19 surveillance activities is used in decision-making for the program and is used as a means for program improvement.

The feedback from the Makassar City Health Office to the Health Facilities was not only related to the completeness, accuracy, and validity of the data but also to evaluating the achievement indicators of the COVID-19 program at the health facility level. For example, in terms of the achievement of new case discovery and equipped with a notification form of new case discovery.

Likewise, feedback from the Provincial Health Office to the City Health Office can also be through technical guidance on problems faced in COVID-19 surveillance activities.

**Identification of Problems in the Implementation of COVID-19 Surveillance Activities in Makassar City** *(Based on input, process, and output components)*

Problem identification was carried out using in-depth interviews with several sources to know the COVID-19 surveillance program at the Makassar City Health Office. The in-depth interview results are then recapitulated to determine the priority of the problem later.

The input components' problem is that all those on duty in COVID-19 surveillance activities have dual responsibilities, and there is an irregular job desk. And not using form attachment 3 (COVID-19 Case Finding Notification Report at Health Facilities), form attachment 4 (COVID-19 Aggregate Daily Report) is not used consistently, and there is no attachment form 6 (COVID-19 Epidemiological Investigation Form) from Fasyankes because it was taken over by the Provincial Health Office.

The problem with the process components

is the Health Facilities report only uses an excel format, but officers are also sometimes lazy to in and result in incomplete data, not reported every day, only monthly accumulation, and there is no EI report based on the EI form, and there is a The TC-19 All record information system existed in July 2020 but was not used at that time, began to be used in December 2020. Data analysis is assisted by a team of experts. However, data analysis is still incomplete, and the data that has COVID-19 aggregate daily report format based on attachment form 4 (Aggregate Daily Report) but it is not consistent in filling it out, only analyzing the release of COVID-19 cases; been analyzed has not been equipped with data interpretation.

The problem with the output component is the success rate of public health surveillance criteria has not been evaluated yet

**Priority Determination of COVID-19 Surveillance Problems at the Makassar City Health Office *(using the CARL Technique)***

Based on the results of calculations using the CARL technique, three priority problems are obtained as shown in Table 1.

**Table 1.** Priority Problem Based on CARL Method

| No | Problem | C | A | R | L | Value | Total | Rank |
|---|---|---|---|---|---|---|---|---|
| 1 | There is no EI report based on the EI form from the Health Facilities, and there is a COVID-19 Aggregate Daily Report format based on attachment form 4 (COVID-19 Aggregate Daily Report). Still, it has not been consistent in filling it out, only analyzing case releases. | 5 | 5 | 5 | 5 | 625 | 2371 | I |
| | | 5 | 5 | 5 | 5 | 625 | | |
| | | 5 | 3 | 4 | 4 | 240 | | |
| | | 4 | 4 | 4 | 4 | 256 | | |
| | | 5 | 5 | 5 | 5 | 625 | | |
| 2. | The Health Facilities report only uses an excel format, but officers are also sometimes lazy to fill in, resulting in incomplete data, not reported every day, only monthly accumulation. | 5 | 5 | 4 | 5 | 500 | 1232 | II |
| | | 3 | 5 | 5 | 5 | 375 | | |
| | | 2 | 2 | 4 | 3 | 48 | | |
| | | 4 | 4 | 4 | 4 | 256 | | |
| | | 3 | 3 | 4 | 4 | 144 | | |
| 3 | Do not use form attachment 3 (COVID-19 Case Finding Notification Report at Health Facilities), form attachment 4 (COVID-19 Aggregate Daily Report) is not used consistently, and there is no form attachment 6 (Covid-19 Epidemiological Investigation Form) from Health Facilities because taken over by the Provincial Health Office. | 5 | 5 | 4 | 5 | 500 | 1244 | III |
| | | 5 | 3 | 4 | 5 | 300 | | |
| | | 3 | 3 | 4 | 4 | 144 | | |
| | | 3 | 3 | 3 | 4 | 108 | | |
| | | 4 | 4 | 3 | 4 | 192 | | |

**Alternative Troubleshooting Plan**

The priority is on the Process component; namely, there is no Epidemiology Investigation (EI) report based on the EI form from the Health Facilities, and there is a COVID-19 Aggregate Daily Report format based on attachment form 4 (COVID-19 Aggregate Daily Report). Still, it is not consistent in filling it out, only analyzing the release coronavirus case. An alternative solution to this problem is developing a brief COVID-19 Epidemiological Investigation report through the Epiinfo application so that surveillance officers are willing and consistent in reporting COVID-19 Epidemiological Investigations. And the development of daily reports in the form of individual and aggregate data using a free application, namely google spreadsheet, to make it easier for users, in this case, the COVID-19 Surveillance Coordinator at the Makassar City Health Office. The individual and aggregate data obtained from the google spreadsheet application will be reported to the South Sulawesi Provincial Health Office easily, precisely, and quickly. South Sulawesi to the Makassar City Health Office.

The second priority is the Process component; the Health Service Report only uses an excel format. Still, officers are

sometimes lazy to fill in and result in incomplete data, not reported daily, only monthly accumulation. An alternative to solving this problem is the development of easy recording and reporting by developing the excel format based on a web application.

The third priority is the Input component, namely, not using form attachment 3 (COVID-19 Case Finding Notification Report at Health Facilities). Form attachment 4 (COVID-19 Aggregate Daily Report) is not used consistently. There is no form attachment 6 (Epidemiological Investigation Form COVID-19) from Health Facilities because it was taken over by the Provincial Health Office. An alternative solution to this problem is that the holder of the surveillance program at the Makassar City Health Office should require Health Facilities to fill out the notification report on the discovery of COVID-19 cases in Appendix 3 because this form is crucial for daily data recapitulation data. For the COVID-19 Aggregate Daily Report in Appendix 4, it is mandatory for one of the surveillance program officers at the Makassar City Health Office to fill in either manually or via excel consistently because the data contained in this form is crucial for data analysis.

## CONCLUSIONS

The description of the implementation of the COVID-19 surveillance system at the Makassar City Health Office is based on a system approach: input, process, output, and feedback. The results of identifying problems in implementing COVID-19 surveillance based on in-depth interviews were also based on a system approach: input, process, and output. As for the priority of COVID-19 surveillance problems that were obtained 3. As well as alternative problem-solving plans, there are also three alternatives according to the problems in COVID-19 surveillance at the Makassar City Health Office.

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We would like to thank the Makassar City Health Office.

## CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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***Original Article***

# Association of IL – 23 R rs 7518660 Gene Polymorphism with Susceptibility and Disease Severity of Pulmonary Tuberculosis

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***ABSTRACT***

*Pulmonary Tuberculosis (TB) is a global health problem. Of all people infected with Mycobacterium tuberculosis only a small proportion develops into TB. IL 23 is the key cytokine in the pathogenesis of TB infection. This study aims to determine the association of IL-23 R rs 7518660 gene polymorphism with susceptibility and disease severity of Pulmonary TB. A case control study involved 105 people consisting of 31 drug sensitive pulmonary TB patients, 40 patients with drug-resistant pulmonary TB and 34 healthy subjects as a control. IL-23 R rs 7518660 gene polymorphism G allele increases susceptibility to both TB drug-sensitive and drug-resistant. G and A allele, AA and AG genotypes indicates (p value >0.05) in correlation with disease severity based on lesion in chest X-ray and high load of Mycobacterium tuberculosis in sputum. There was a significant relationship between allele A and susceptibility to pulmonary TB with an odds ratio of 0.231. It showed that patients with A alleles (AG and AA genotypes) were at risk of developing TB by 1/0.231 = 4.33 times lower than patients with GG genotypes. Meanwhile, the relationship of the G allele with susceptibility to pulmonary TB obtained (p value <0.05) and an odds ratio value of 0.127 indicating that patients with G alleles (GG and AG genotypes) were at risk of developing TB of 1/0.127 = 7.87 times higher than in patients with the AA genotype. Conclusion: We found significant correlation between IL-23 R rs 7518660 gene polymorphism G allele with susceptibility to pulmonary TB, but the result was not significant with disease severity.*

***Keywords:*** *disease severity; IL-23 R rs 7518660 gene; polymorphism; pulmonary TB; susceptibility,*

***ABSTRAK***

*Tuberkulosis (TB) Paru merupakan masalah kesehatan global. Dari semua orang yang terinfeksi Mycobacterium tuberculosis hanya sebagian kecil yang berkembang menjadi TB. IL23 adalah sitokin kunci dalam patogenesis infeksi TB. Penelitian ini bertujuan untuk mengetahui hubungan polimorfisme gen IL-23 R rs 7518660 dengan kerentanan dan keparahan penyakit TB Paru. Studi kasus kontrol melibatkan 105 orang yang terdiri dari 31 pasien TB paru sensitif obat, 40 pasien TB paru resisten obat dan 34 subjek sehat sebagai kontrol. Polimorfisme gen IL-2.3 R rs 7518660 alel G meningkatkan kerentanan terhadap TB sensitif obat dan resisten obat. Alel G dan A, genotipe AA dan AG menunjukkan (p value >0.05) berkorelasi dengan derajat keparahan penyakit berdasarkan lesi pada rontgen dada dan tingginya kadar Mycobacterium tuberculosis dalam sputum. Terdapat hubungan yang bermakna antara alel A dengan kerentanan terhadap TB paru dengan odds ratio sebesar 0,231. Hal ini menunjukkan bahwa pasien dengan alel A (genotipe AG dan AA) berisiko terkena TB sebesar 1/0.231 = 4.33 kali lebih rendah dibandingkan pasien dengan genotipe GG. Sedangkan uji hubungan alel G dengan kerentanan terhadap TB paru diperoleh (p<0.05) dan nilai Odd ratio 0.27 yang menunjukkan bahwa pasien dengan alel G (genotipe GG dan AG) berisiko mengalami TB 1/0,127 = 7.87 kali lebih tinggi*

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*dibandingkan pada pasien dengan genotipe AA. Terdapat korelasi yang signifikan antara polimorfisme gen IL-23 R rs 7518660 alel G dengan kerentanan terhadap TB paru, tetapi tidak signifikan dengan keparahan penyakit.*

***Kata kunci:*** *gen IL-23 R rs 7518660; kerentanan; keparahan penyakit; polimorfisme; TB paru*

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## INTRODUCTION

Tuberculosis (TB) is an infectious disease that is currently the main cause of health problems. About a quarter of the world's population are infected with *Mycobacterium tuberculosis*. The biggest contributors to the global increase in TB worldwide are from India and Indonesia. In India, people newly diagnosed with TB increased by 1.2 million to 2.2 million between 2013 and 2019 (74%). In Indonesia, the number increased from 331,703 in 2015 to 562,049 in 2019 (69%). The target of the 2030 Sustainable Development Goals (SDGs) is to reduce TB mortality by 90% and reduce TB incidence by 80%.[1]

Of all people infected with *Mycobacterium tuberculosis*, only about 5-10% become sick; this is related to the body's immune response at the beginning of *Mycobacterium tuberculosis* infection[4]. A person's susceptibility to TB is determined by genetic factors encoded in genes in Deoxyribose Nucleic Acid (DNA) molecular strand, in which the distribution is different for each population and race. The role of gene polymorphism will change the structure of the protein produced so that it will affect individual phenotypes, including susceptibility to disease.[3, 5]

Drug-sensitive TB is a form of TB that is still sensitive to first line Anti Tuberculosis Drugs. This condition requires fast, precise, and directed treatment and action thus TB patients do not develop to the-drug resistance stage. As many as 96% of cases of resistance to Rifampicin are caused by mutations in the 'hot-spot region' by 81 bp spanning codons 507-533 in the rpoB gene.[6] According to the World Health Organization (WHO) in 2017, incidence of Multi Drug Resistance (MDR) TB cases amounted to around 3.3% of all new cases, and overall patients had received Anti Tuberculosis Drugs therapy previously (20%). Data obtained from dr. Saiful Anwar Hospital Malang reached 21 new patients every month.[7]

Several pro-inflammatory cytokine variants are associated with the possibility of pulmonary TB, one of them is the IL-23 R rs 7518660 gene polymorphism. IL-23 plays a role in the regulation of the immune system in the TB infection process[15]. Based on the data above, this study analyzes the presence of the IL-23 R rs 7518660 gene polymorphism which is associated with the susceptibility and severity of pulmonary TB in patients.[9,11]

## MATERIALS AND METHODS

### Research Design

This research used a Case-Control Study design. The aim of this study was to determine IL-23 R rs 7518660 gene polymorphism with pulmonary TB by comparing the case and the control group based on their exposure status.

### Research Subjects and Sample Size

The sample population were patients with pulmonary TB who seek treatment at the outpatient clinic of dr. Saiful Anwar Hospital Malang. All ethnic groups who seek treatment at the Pulmonary Clinic or being hospitalized at dr. Saiful Anwar Hospital Malang were included in the study and recorded.

Case group: Patients with drug-sensitive and drug-resistant pulmonary TB.

Control group: Healthy subjects.

**Inclusion and Exclusion Criteria**

Inclusion Criteria:

a. Patients diagnosed with drug-sensitive or drug-resistant pulmonary TB
b. Age between 18 – 65 years old
c. Willing to participate in research and sign the "informed consent"

Exclusion Criteria:

a. Patients with HIV-AIDS
b. Patients with autoimmune disease
c. Pregnant women

Note: Patients with Diabetes Mellitus, Chronic Kidney Disease, malnutrition, and smoking were not excluded in this research, but they were still given notes for data analysis (information is listed in Table 1)

**Research Variables**

Independent Variable:

a. IL-23 R rs 7518660 gene polymorphism

Dependent Variables:

a. Susceptibility to drug-sensitive and drug-resistant pulmonary TB
b. The severity of pulmonary TB, based on chest X-ray lesion and the number of *Mycobacterium tuberculosis* detected on GeneXpert sputum.

From chest X-ray lesion, the patients with minimal and moderate lesion added categorized as mild criteria, whereas the far advanced lesion added into severe criteria. From the data of GeneXpert sputum, we divided into two categories regarding to the number of thresholds based on repeat cycles of *Mycobacterium tuberculosis* DNA amplification. Very low and low added were categorized as mild criteria, whereas medium and high added into severe criteria.

**Data Collection**

Samples were obtained by consecutive sampling method in patients who met the inclusion and exclusion criteria in the outpatient and hospitalized patients at dr. Saiful Anwar Hospital Malang.

**IL-23 R rs 7518660 Gene Polymorphism Examination Procedure**

Identification of the allele position where the polymorphism occurred was performed by incubating the Polymerase Chain Reaction product at 94ºC for 30 seconds to denature the DNA genome, followed by primer annealing at 68ºC for 20 seconds and extension at 72ºC for 20 seconds.[10,14] Polymerase Chain Reaction was performed for 35 cycles, followed by a final extension at 72ºC for three minutes. Each sample is grouped according to the results of 2% agarose gel electrophoresis, while the visualization of the gel electrophoresis results were performed using a UV-transilluminator and a polaroid camera.[9,10,14]

**Data Processing and Analysis Techniques**

Processing and data analysis were performed with IBM SPSS software version 26.0. The relationship between polymorphism with susceptibility and severity of pulmonary TB was analyzed using the Chi-square test using a 95% confidence level, significant if $p<0.05$. Meanwhile, to determine the magnitude of the risk factor, it was calculated using the odds ratio (OR).

## RESULTS AND DISCUSSION

**Sociodemographic Characteristics of Research Subjects**

This research was conducted on 105 samples which were divided into three groups. The healthy control group consisted of 34 samples and the TB case group consisted of 71 samples. TB cases were composed of 31 samples of drug-sensitive TB and 40 samples of drug-resistant TB. The sociodemographic characteristics of the research subjects can be seen in Table 1.

**Table 1.** Sociodemographic Characteristics of Research Subjects

| Characteristics | | Healthy control (n=34) | TB Cases | | p-value |
|---|---|---|---|---|---|
| | | | Drug sensitive (n=31) | Drug resistant (n=40) | |
| **Age** | Minimum | 29 | 19 | 18 | 0.001[a] |
| | Maximum | 58 | 69 | 69 | |
| | Mean ± SD | 33.79 ± 4.98 | 40.42 ± 14.09 | 45.5 ± 13.06 | |
| **Gender** | Male | 20 (58.8%) | 15 (48.4%) | 24 (60%) | 0.577[b] |
| | Female | 14 (41.2%) | 16 (51.6%) | 16 (40%) | |
| **Body Mass Index (BMI)** | Minimum | 19.3 | 13.8 | 12.1 | 0.000[a] |
| | Maximum | 31.1 | 29.9 | 26.1 | |
| | Mean ± SD | 22.86 ± 2.86 | 18.55 ± 3.89 | 18.5 ± 3.04 | |
| **Smoking status** | Yes | 1 (2.9%) | 4 (12.9%) | 4 (10%) | 0.329[b] |
| | No | 33 (97.1%) | 27 (87.1%) | 36 (90%) | |
| **Diabetes Mellitus (DM)** | Yes | - | 8 (25.8%) | 13 (32.5%) | 0.540[b] |
| | No | - | 23 (74.2%) | 27 (67.5%) | |
| **Chronic Kidney Disease (CKD)** | Yes | - | 2 (6.5%) | 1 (2.5%) | 0.412[b] |
| | No | - | 29 (93.5%) | 39 (97.5%) | |
| **Malnutrition** | Yes | - | 21 (67.7%) | 21 (52.5%) | 0.195[b] |
| | No | - | 10 (32.3%) | 19 (47.5%) | |

a: Kruskal Wallis test
b: Chi-square test
SD: Standard Deviation

(Source: Primary Research Data Processed)

Based on the characteristics of the research subjects, the average age of the healthy control group was 33.79 ± 4.98 years old, the drug-sensitive TB group was 40.42 ± 14.09 years old, and the drug-resistant TB group was 45.5 ± 13.06 years old. For the age variable, a normality test was performed using the Shapiro-Wilk test. The research variable was normal if the p-value > 0.05. The result of the normality test for the age variable was p-value=0.000, which showed that the normality of the data was not met for this variable. Furthermore, the Kruskal Wallis test was performed and obtained a p-value of 0.001 ($p<0.05$) which proved that there was a significant difference in age characteristics in the three groups, where the healthy control group had a lower average age than the TB case group.

In terms of gender characteristics, the Chi-square test was performed and obtained a p-value of 0.577 ($p>0.05$) which proved that there was no gender difference between the three groups.

In terms of Body Mass Index (BMI) characteristics, the average BMI of healthy control group was 22.86 ± 2.86, the TB SO group was 18.55 ± 3.89 and the TB RO group was 18.5 ± 3.04. By using the Kruskal-Wallis test, a p-value of 0.000 ($p<0.05$) was obtained which proved that there was a significant difference in the characteristics of BMI in the three groups, where the TB group, both drug-sensitive and drug-resistant, had a lower average BMI compared to the healthy control group.

Based on the smoking status and the comorbid characteristics of TB patients, such as Diabetes Mellitus, Chronic Kidney Disease and malnutrition, p-value more than 0.05 ($p>0.05$) was obtained. From this test, it showed that there were no significant differences in smoking status and the comorbid characteristics of TB patients.

**Clinical Characteristics of Research Subjects**

Based on the imaging of the chest X-ray lesion in Figure 1, it showed that the most common lesion in the TB case group, both in the drug-sensitive and drug-resistant TB groups, were more (far) advanced lesion as much as 81.69%. The minimal lesion was the least chest X-ray imaging (1.41%). The following charts describe the chest X-ray lesion in each case groups.

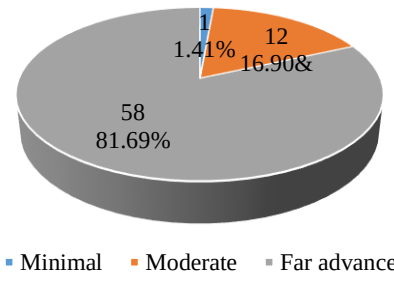


**Figure 1.** Description of Chest X-ray Lesion in Each Case Group

The imaging of chest X-ray lesion in each group of TB cases is presented in Table 2. Based on Table 2, it shows that, in the drug-sensitive TB group, the most extensive or far advanced lesion description was 87.1%. Likewise, in the drug- resistant TB group, the most extensive lesion description was 77.5%. By using the Chi-square test, a p-value of 0.474 (p>0.05) was obtained. From this test, it showed that there was no significant difference in chest X-ray images between the drug-sensitive TB and drug-resistant TB groups.

**Table 2.** The Imaging of the Chest X-ray Lesion in the Case Group

| The Imaging of Chest X-ray Lesion | Groups | | p-value |
|---|---|---|---|
| | Drug-sensitive TB | Drug-resistant TB | |
| Minimal | 0 (0%) | 1 (2.5%) | |
| Moderate | 4 (12.9%) | 8 (20%) | 0.474 |
| Far advanced | 27 (87.1%) | 31 (77.5%) | |

(Source: Primary Research Data Processed)

Based on the number of *Mycobacterium tuberculosis* detected in sputum, Figure 2 shows that the number of *Mycobacterium tuberculosis* in the GeneXpert sputum was mostly in TB case group, both in the drug-sensitive and drug-resistant TB groups were at a medium level of 42.25%. The very low level was a picture of the least number of GeneXpert sputum examination, which was 7.04%. The following chart describes the number of *Mycobacterium tuberculosis* detected on sputum examination in each case group.

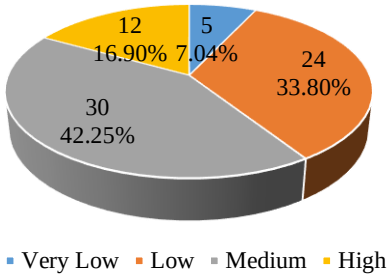


**Figure 2.** Overview of the GeneXpert Sputum of the *Mycobacterium tuberculosis* Case Group

Based on the number of *Mycobacterium tuberculosis* detected in sputum, Figure 2 shows that the number of *Mycobacterium tuberculosis* in the GeneXpert sputum was mostly in TB case group, both in the drug-sensitive and drug-resistant TB groups were at a medium level of 42.25%. The very low level was a picture of the least number of GeneXpert sputum examination, which was 7.04%. The following chart describes the number of *Mycobacterium tuberculosis* detected on sputum examination in each case group.

The description results of the number of *Mycobacterium tuberculosis* detected in the GeneXpert sputum is presented in Table 3. Based on Table 3 shown in the drug-sensitive TB group, the number of *Mycobacterium tuberculosis* detected in the GeneXpert sputum was mostly in the low category, which was 58.1%. Meanwhile, in the drug-resistant TB group, the GeneXpert sputum description was mostly in the medium category, which was 50%. By using the Chi-square test, a p-value of 0.001 (p<0.05) was obtained. From this test, it showed that there were significant differences in the results of the GeneXpert sputum between the drug-sensitive TB and drug-resistant TB groups.

**Table 3.** Overview of the Number of *Mycobacterium tuberculosis* Detected on GeneXpert Sputum in Research Subjects

| Number of Mycobacterium Tuberculosis Detected on GeneXpert Sputum | Groups | | p-value |
|---|---|---|---|
| | Drug-sensitive TB | Drug-resistant TB | |
| Very Low | 1 (3.2%) | 4 (10%) | 0.001 |
| Low | 18 (58.1%) | 6 (15%) | |
| Medium | 10 (32.3%) | 20 (50%) | |
| High | 2 (6.5%) | 10 (25%) | |

(Source: Primary Research Data Processed

The distribution of patient types is described in Figure 3 which shows that the most drug-resistant TB patient types were relapse and new cases, each group consisted of 14 people (35%). The lowest type of TB drug-resistant patient was K1 failure.

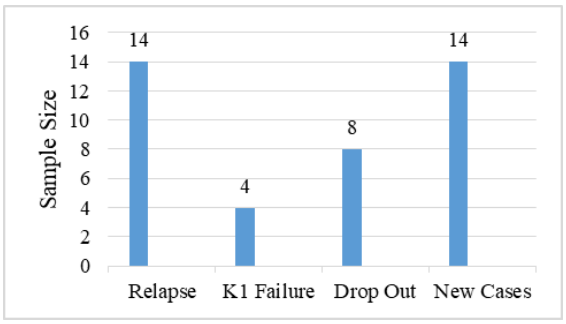


**Figure 3.** Description of the Distribution of the Type of TB Patients RO

The allele frequencies and genotypes of the IL-23 R rs 7518660 gene polymorphism in the healthy and TB control groups, on both drug-sensitive and drug-resistant TB are presented in Table 4.

Based on Table 4, it is shown that the frequency of the G allele in the control group was 17 (50%), the drug-sensitive TB group was 30 (96.8%) and the drug-resistant TB group was 33 (82.5%). The frequency of the G allele was more in the TB case group than in the control group. From the Chi-square test results obtained p-values of 0.000 (K vs drug-sensitive TB) and 0.003 (K vs drug-resistant TB).

From this test, it was proven that there was significant difference in the frequency of the G allele between the TB group and the control group. Meanwhile, the comparison of the G allele frequency between the drug-sensitive TB and drug-resistant TB groups obtained a p-value of 0.059 (p>0.05), which showed that there was no significant difference in the frequency of the G allele.

**Table 4.** Comparison of the Allele Frequencies and Genotypes of IL-23 R rs 7518660 Gene Polymorphism in TB and Healthy Controls

| Variables | Healthy control (K) (n=34) | TB Cases | | p-value | | |
|---|---|---|---|---|---|---|
| | | Drug-sensitive TB (n=31) | Drug-resistant TB (n=40) | K vs drug-sensitive TB | K vs Drug-resistant TB | Drug- sensitive vs Drug- resistant TB |
| GG | 4 (11.8%) | 9 (29%) | 17 (42.5%) | 0.082$^{ns}$ | 0.003 | 0.243$^{ns}$ |
| AG | 13 (38.2%) | 21 (67.7%) | 16 (40%) | 0.017 | 0.877$^{ns}$ | 0.020 |
| AA | 17 (50%) | 1 (3.2%) | 7 (17.5%) | 0.000 | 0.003 | 0.059$^{ns}$ |
| Alel G | 17 (50%) | 30 (96.8%) | 33 (82.5%) | 0.000 | 0.003 | 0.059$^{ns}$ |
| Alel A | 30 (88.2%) | 22 (71%) | 23 (57.5%) | 0.082$^{ns}$ | 0.003 | 0.243$^{ns}$ |

ns: Not Significant (Source: Primary Research Data Processed)

Table 5 below describes the results of analysis of the relationship between the IL-23 R rs 7518660 gene polymorphism with susceptibility of pulmonary TB. GG genotype was used as a comparison.

**Table 5.** Analysis of the Relationship Between the IL-23 R rs 7518660 Gene Polymorphism with the Susceptibility of Pulmonary TB

| Variables | | Healthy Control | Drug-sensitive and Drug-resistant TB | p-value | OR | 95% CI |
|---|---|---|---|---|---|---|
| Genotype | GG | 4 (11.8%) | 26 (36.6%) | | (Reff) | |
| | AG | 13 (38.2%) | 37 (52.1%) | 0.180$^{ns}$ | 0.438 | 0.128 - 1.495 |
| | AA | 17 (50%) | 8 (11.3%) | 0.000* | 0.072 | 0.019 - 0.278 |
| Allele G | | 17 (50%) | 63 (88.7%) | 0.000* | 0.127 | 0.047 - 0.344 |
| Allele A | | 30 (88.2%) | 45 (63.4%) | 0.008* | 0.231 | 0.073 - 0.729 |

ns: Not Significant (Source: Primary Research Data Processed)
*: Significant

The relationship between the AG genotype and susceptibility to pulmonary TB obtained a p-value of 0.180 which proves that there was no significant relationship between the AG genotype and susceptibility to pulmonary TB (OR = 0.438 (0.128 - 1.495)). While the AA genotype obtained a p-value of 0.000 which proves that there was a significant relationship between the AA genotype and susceptibility to pulmonary TB. The odds ratio of 0.072 (0.019 - 0.278) indicates that patients with the GG genotype are at risk of developing TB by 1/0.072 = 13.81 times higher than patients with the AA genotype.

**Table 6.** Analysis of the Relationship Between the IL-23 R rs 7518660 Gene Polymorphism with the Severity of Pulmonary TB Based on Chest X-ray Lesion

| Variables | | Minimal and Moderate Lesion | Far Advanced Lesion | p-value | OR | 95% CI |
|---|---|---|---|---|---|---|
| Genotype | GG | 4 (30.8%) | 22 (37.9%) | | (Reff) | |
| | AG | 6 (46.2%) | 31 (53.4%) | 0.929 | 0.939 | 0.237 - 3.727 |
| | AA | 3 (23.1%) | 5 (8.6%) | 0.176 | 0.303 | 0.051 - 1.805 |
| Allele G | | 10 (76.9%) | 53 (91.4%) | 0.136 | 0.314 | 0.065 - 1.531 |
| Allele A | | 9 (69.2%) | 36 (62.1%) | 0.628 | 0.727 | 0.200 - 2.647 |

(Source: Primary Research Data Processed)

Table 6 describes the results of the relationship analysis between IL-23R rs 7518660 gene polymorphism and the severity of pulmonary TB based on Chest X-ray lesion where the GG genotype was used as a comparison. The relationship between the AG genotype and the severity of pulmonary TB obtained a p-value of 0.929, which proves that there was no significant relationship between the AG genotype and the severity of pulmonary TB (OR = 0.939 (0.237 - 3.727). Likewise, the AA genotype showed no significant relationship between the AA genotype and the severity of pulmonary TB (p>0.05).

**Table 7.** Analysis of the relationship between the IL-23R rs 7518660 gene polymorphism with the severity of pulmonary TB based on the number of *Mycobacterium tuberculosis* detected on GeneXpert sputum

| Variables | | Very Low and Low | Medium and High | p-value | OR | 95% CI |
|---|---|---|---|---|---|---|
| Genotype | GG | 4 (30.8%) | 22 (37.9%) | | (Reff) | |
| | AG | 6 (46.2%) | 31 (53.4%) | 0.337 | 1.643 | 0.595 - 4.538 |
| | AA | 3 (23.1%) | 5 (8.6%) | 0.213 | 3.000 | 0.508 - 17.708 |
| Allele G | | 27 (93.1%) | 36 (85.7%) | 0.333 | 2.250 | 0.421 - 12.028 |
| Allele A | | 16 (55.2%) | 29 (69%) | 0.233 | 1.813 | 0.679 - 4.837 |

(Source: Primary Research Data Processed)

Table 7 describes the results of relationship analysis between the IL-23 R rs 7518660 gene polymorphism and the severity of pulmonary TB based on the number of *Mycobacterium tuberculosis* detected in GeneXpert sputum where the GG genotype was used as a comparison. The relationship between the AG genotype and the severity of pulmonary TB obtained a p-value of 0.337, which proves that there was no significant relationship between the AG genotype and the severity of pulmonary TB (OR = 1.643 (0.595 - 4.538)). Likewise, the AA genotype showed no significant relationship between the AA genotype and the severity of pulmonary TB ($p>0.05$).

In the results of relationship analysis between the G allele and the severity of pulmonary TB based on the number of *Mycobacterium tuberculosis* detected in GeneXpert sputum, a p-value of 0.333 ($p>0.05$) was obtained, which proves that there was no significant relationship between the G allele and the severity of pulmonary TB (OR = 2.250 (0.421 - 12.028)). Likewise, the results of testing the relationship between the A allele and the severity of pulmonary TB showed that there was no significant relationship between the A allele and the severity of pulmonary TB ($p>0.05$).

For age characteristics, a p-value of 0.001 ($p<0.05$) was obtained which proves that there was a significant difference in age characteristics in the healthy control group, drug-sensitive TB and drug-resistant TB, where the healthy control group has a lower average age than the TB case group.[17] In this study, the average age in the drug-sensitive and drug-resistant TB groups was the productive adult age group, but the drug-sensitive TB group was slightly younger than the drug-resistant TB group[13]. Based on data from the WHO in 2015 and Permenkes 2016, it was stated that the incidence of pulmonary TB was highest in the productive adult age group. Research from Dodd et al. stated that the incidence of pulmonary TB in adults was 1.5-6 times higher than in children and adolescents. This is due to the tendency of greater social interaction in adulthood. [22]

The clinical characteristics of the subjects of this study used the parameters of the lesion area on the chest X-ray and the number of *Mycobacterium tuberculosis* detected in the GeneXpert examination to be assessed based on the severity of pulmonary TB. The results showed that, in the drug-sensitive TB group and drug-resistant TB group, the most extensive or far advanced lesion were 87.1% and 77.5%, respectively. Based on the correlation test of the X-ray lesion area parameters, it showed that there was no difference in the imaging of the chest X-ray lesion between the drug-sensitive TB and drug-resistant TB groups. Icksan et al.[23] stated that the most common lesion on the chest X-ray was extensive lesion consisting of cavities, consolidation, fibrosis with atelectasis, bullae, and calcifications where the degree of damage was more extensive in the drug-resistant TB group.[23]

Based on the results of the number of *Mycobacterium tuberculosis* detected in the GeneXpert sputum examination, it was

shown that there were differences in the GeneXpert sputum examination between the drug-sensitive TB and drug-resistant TB groups. In the drug-sensitive TB group, the most *Mycobacterium tuberculosis* detected was in low level (58.1%), while in the drug-resistant TB group, *Mycobacterium tuberculosis* detected was in medium level (50%). GeneXpert examination in the drug-resistant TB group showed more *Mycobacterium tuberculosis* than the drug-sensitive TB group. The number of *Mycobacterium tuberculosis* detected on the GeneXpert examination was directly proportional to the viscosity of the sputum examined. Our study used the GeneXpert sputum examination which has a more sensitive result than the Acid Fast Bacillus (AFB) examination[8]. The analysis of sputum samples used the Polymerase Chain Reaction method which calculates the number of thresholds based on repeat cycles of *Mycobacterium tuberculosis* DNA amplification. The GeneXpert method is semi-quantitative, while the high level is stated if there is 16 *Mycobacterium tuberculosis* Ct, medium if there is 16-22 *Mycobacterium tuberculosis* Ct, low if there is 22-28 *Mycobacterium tuberculosis* Ct, and very low if there is 28-38 *Mycobacterium tuberculosis* Ct. Therefore, the lower the *Mycobacterium tuberculosis* Ct number, the higher *Mycobacterium tuberculosis* number that will be detected.[23,24,26]

In this study, the frequency of IL-23 R rs 7518660 G allele polymorphism and the AG genotype were higher in the pulmonary TB group than in healthy controls and it was statistically significant. This was on concordance with the results of previous research on the Chinese Uygurs ethnic group in 2015 which stated that the allele frequencies studied showed significant differences between the case group and healthy controls, where the G allele was more dominant in the TB case group compared to healthy controls. Jiang et al.'s[9] study for the AG genotype with an odds ratio of 2.99 had 0.34 times less chance of developing TB than the GG genotype. Based on statistical data analysis, the frequency of IL-23R rs 7518660 gene polymorphism genotype AA was higher in healthy controls. This indicates the protective effect of allele A against pulmonary TB. Research in Tunisia in 2012 found that the frequency of the A allele and the AA genotype increased the risk 2.79 times greater for the incidence of pulmonary TB.[9,18]

In this study, there was a significant relationship between allele A and susceptibility to pulmonary TB with an odds ratio of 0.231. This showed that patients with A alleles (AG and AA genotypes) were at risk of developing TB by 1/0.231 = 4.33 times lower than patients with GG genotypes. Meanwhile, the relationship test of the G allele with susceptibility to pulmonary TB obtained a p-value of 0.000 ($p<0.05$) and an odds ratio value of 0.127, indicating that patients with G alleles (GG and AG genotypes) were at risk of developing TB of 1/0.127 = 7.87 times higher than in patients with the AA genotype. This also in concordance with the research conducted on the Chinese Uygur ethnic group in 2015, which stated that a person with the G allele has a higher risk of developing pulmonary TB compared to the A allele with an odds ratio of 4.83.[9]

Colonization of *Mycobacterium tuberculosis* caused widespread organ damage and was at risk of mutation[12]. The results showed that there was no significant relationship between the A, G alleles and the AA, AG genotype with the severity of pulmonary TB based on the lesion on the chest X-ray ($p>0.05$). Previous studies on Chinese Uygurs also did not show significant results on the severity of lesion on chest radiographs. The same study examined the polymorphism of the IL-23 R SNP gene rs1884444 which showed a significant relationship to the severity of pulmonary TB based on chest X-ray lesion.[19]

In this study, we analyzed whether there was a relationship between the IL-23 R rs 7518660 gene polymorphism and the severity

of pulmonary TB based on the number of *Mycobacterium tuberculosis* detected in GeneXpert sputum. The results showed that there was no significant relationship between the A, G alleles and the AA, AG genotype with the severity of pulmonary TB based on the number of *Mycobacterium tuberculosis* detected in GeneXpert sputum ($p>0.05$). Shabbir et al. (2007) stated that one of the influencing factors was the limitation in checking the quality of sputum samples. It is known that the good sputum quality will result in a good sampling process, which that will determine the number of bacteria, which will subsequently determine the level of transmission and the severity of TB patients.[20,21]

The absence of a significant relationship between the IL-23 R rs 7518660 gene polymorphism in terms of both alleles and genotypes on the severity of TB based on the number of *Mycobacterium tuberculosis* detected on sputum examination was also shown by a study conducted in the Uygurs of China in 2015.[9,16,25]

## CONCLUSIONS

The frequency of IL-23 R rs 7518660 gene polymorphism G allele and AG genotype was shown to be higher in the pulmonary TB group than in healthy control subjects. While the frequency of IL-23R rs 7518660 gene polymorphism allele A was higher in healthy controls and there was a significant relationship between IL-23 R rs 7518660 gene polymorphism and susceptibility to pulmonary TB, where the higher frequency of IL-23 R rs 7518660 gene polymorphism allele A and G results in the higher risk of developing pulmonary TB in both drug-sensitive and drug-resistant TB.

The result of this study has meaningful information about the relationship between IL-23 R rs 7518660 gene polymorphism with susceptibility of pulmonary TB, but it was not significant with disease severity. For researchers, the results of this study could be reference for further research using different research methods or other markers of the IL-23 R gene polymorphism. In future studies, risk factors should be considered in sample selection, thus the other risk factors are more homogeneous. Susceptibility to pulmonary TB is polygenic, so it is necessary to examine a wider gene polymorphism with more sensitive examination methods such as Restriction Fragment Length Polymorphism (RFLP) and DNA sequencing; therefore, it can explain more about the influence of certain genes on pulmonary TB and even its effect on the severity of the disease caused by those genes.

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## CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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***Original Article***

# The Activities on Prevention of Malaria and Filariasis Vector Bites among Indonesian Society: A Nationwide Disease Prevention Survey

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***ABSTRACT***

*Vector Borne Diseases are diseases that cause many problems. These diseases are spread by mosquitoes as the vectors. They transmit parasites to humans through their bites. The people who live in Indonesia have several characteristics that make them vulnerable to these diseases. Therefore, it is necessary to explore these characteristics in order to gain better prevention promotional targeting strategy. This study aims to determine the factors that can influence mosquito bite prevention behaviour in Indonesian society. The data from a nationwide survey research were used with a cross sectional design conducted once in every five years. The Riskesdas was conducted from April to May 2018 in all districts in Indonesia. The influencing factors observed were including experience of exposure to vector borne diseases (malaria or filariasis), gender, age group, education level and area of residence. This study conducted a multivariate test using logistic regression analysis to determine the factors that influence mosquito bite prevention behaviour. The results demonstrated that the factors of experience of exposure to vector borne diseases, gender, age group, education level and area of residence could determine the mosquitoes bite prevention behaviour in Indonesian society. Respondents who have experience of being exposed to malaria or filaria, under 60 years old, women, college graduates, and rural communities are more likely to prevent mosquito bites, therefore they could be empowered in promoting public awareness towards mosquito bites prevention.*

**Keywords:** *filaria; malaria; mosquitoe; prevention; sociodemographic*

***ABSTRAK***

*Penyakit Tular Vektor merupakan penyakit yang menimbulkan banyak masalah. Penyakit ini disebarkan oleh nyamuk sebagai vektornya. Ini menularkan parasit ke manusia melalui gigitannya. Masyarakat yang tinggal di Indonesia memiliki beberapa karakteristik yang membuat mereka rentan terhadap penyakit tersebut. Oleh karena itu, perlu dijajaki ciri-ciri tersebut guna mendapatkan strategi penargetan promosi pencegahan yang lebih baik. Penelitian ini bertujuan untuk mengetahui faktor-faktor yang dapat mempengaruhi perilaku pencegahan gigitan nyamuk pada masyarakat Indonesia. Penelitian ini menggunakan data dari penelitian survei nasional dengan desain cross sectional yang dilakukan setiap lima tahun sekali. Penelitian ini menggunakan data penelitian kesehatan dasar yang dilakukan pada bulan April hingga Mei 2018 di seluruh kabupaten di Indonesia. Faktor-faktor yang digunakan dalam penelitian ini meliputi pengalaman pajanan penyakit tular vektor (malaria atau filariasis), jenis kelamin, kelompok umur, tingkat pendidikan dan daerah tempat tinggal. Penelitian ini melakukan uji multivariat dengan menggunakan analisis regresi logistik untuk mengetahui faktor-faktor yang mempengaruhi perilaku pencegahan gigitan nyamuk. Hasil penelitian menunjukkan bahwa pengalaman pajanan penyakit tular vektor, jenis kelamin, kelompok umur, tingkat pendidikan dan daerah tempat tinggal merupakan faktor yang dapat menentukan perilaku pencegahan gigitan nyamuk pada masyarakat Indonesia.*

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*Responden yang memiliki pengalaman terkena malaria atau filaria, di bawah 60 tahun, perempuan, lulusan perguruan tinggi, dan masyarakat pedesaan lebih mungkin untuk mencegah gigitan nyamuk, sehingga mereka dapat diberdayakan dalam meningkatkan kesadaran masyarakat terhadap pencegahan gigitan nyamuk.*

***Kata kunci:*** *filaria; malaria; nyamuk; pencegahan; sosiodemografi*

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## INTRODUCTION

Vector Borne Diseases are diseases that cause many problems in the world. Malaria in 2018 has caused 405,000 deaths globally.[1] Lymphatic filariasis is also a health problem globally, especially in many tropical and subtropical countries. Untreated lymphatic filariasis can lead to elephantiasis and hydrocele that cause significant social and economic burdens in a person's life.[1,2] Indonesia is declared as one of the malaria and filariasis endemic countries.[3,4] Indonesian society have several characteristics that vulnerable to diseases like malaria and filariasis. The characteristics are including tropical climate, population size, high migration rate, socio-economic imbalance, and regional government autonomy.[2,5]

Diseases such as malaria and filariasis are spread by mosquitoes vectors. Mosquitoes transmit parasites Plasmodium or micro-filariae to humans through their bites. Therefore, it is important for the community to make efforts to prevent mosquito bites. Several studies have shown that action to prevent mosquito bites by individuals were including the use of mosquito nets, repellents, mosquito coils, electric racquets, and electric repellents. Repellents and mosquito coils work by hiding human odors from mosquitoes. Electric racquets and mosquito nets are used for preventing mosquitoes from landing on humans. These efforts have proven useful in reducing mosquito bites.[6,7]

Indonesian people's behaviour is still not reliable enough to prevent bites from infectious disease vectors. Despite the fact that eradicating mosquito nests is the main effort that can be done to prevent the infection of diseases such as dengue haemorrhagic fever, a disease that is one of the highlights in Indonesia, the results of Riskesdas' report that Indonesians are not very active in eradicating mosquito nests in their environment.[4]

Nevertheless, research on the relationship between various factors and efforts to prevent mosquito bites in Indonesia is still limited. Research on the behaviour of mosquito are lacked. A research related to malaria trans-mission prevention efforts was found carried out only in the eastern part of Indonesia.[8] No article that focused on the specific factors that can influence the overall mosquito bite prevention behaviour of the overall Indonesian people was found. Therefore, a study on the influencing factors in preventing mosquito bite among Indonesian society has been conducted that may contribute to build a recommendation policy to decrease the spread of mosquitoes-transmitted diseases, such as malaria and filariasis.

## MATERIALS AND METHODS

### Location of the Study

This is a national study conducted at all city/village in 34 provinces in Indonesia.

### Data and Analysis

The data used in this study was the secondary data of basic health research (Riset Kesehatan Dasar or Riskesdas) a survey research that has been conducted and developed since 2007, and was continued in 2010, 2013, and 2018.[9–12] The questionnaire used was little different in each year. This includes the development of questions from 2013 to 2018. This research aims to describe

the indicators of Indonesian public health situations that are used as the basis for policymaking at the national, provincial and district levels. These indicators include access to health services, environmental health, housing conditions, economy, infectious and non-infectious diseases, financial health, maternal and child health, and immunization. This research aims to describe the basic health status of the Indonesian population, therefore the sample is taken from the population, which means that all Indonesian citizens (265 million people) were taken into account (bps 2018)

**Inform Consent**

The survey was conducted by the Health Research and Development Institute of the Indonesian Ministry of Health (Badan Litbangkes Kemenkes). The survey was conducted by trained enumerators. Each enumerator was trained to use the questionnaire and communicate with the respondent. Enumerators are also trained to convey respondents' rights and obtain permission to collect data from respondents. Each enumerator visited each selected household, accompanied by the village head and local health workers.

Each household, spouse or their elder person was asked to sign the inform consent to participate in this survey before starting the interview. Children under 15 years old were interviewed accompanied by their parents/guardians. Each respondent was informed about the research, and their option to stop the interview at any time without coercion. Respondents who refused, gave up, decided to stop being interviewed and were not willing to be re-interviewed were excluded from the sample of this study. Data related to individual identities were removed from the data subset for further analysis. Areas with difficult access, natural disasters and conflicts were excluded in this survey.

**Samples and Variables**

The sample frame used in Riskesdas 2018 was the 2018 socio-economic survey (Susenas) samples of 300,000 households from 30,000 Census Blocks (BS). Census blocks were selected using the Probability proportional to size (PPS) method with systematic random sampling in each city/village per district/city.[4] Riskesdas 2018 conducted a survey to a total sample of 295,720 households with a total of 1,091,528 household members (individuals) in 34 provinces of Indonesia. Data collection used a paper-based structured questionnaire which was asked to all household members. The Riskesdas 2018 questionnaire consisted of a household questionnaire and an individual questionnaire. Specifically for this study, the questionnaire data used were individual data only.

The data used in this study was only the 2018 Riskesdas data in the prevention of disease transmission due to mosquito bites (Ministry of Health Research and Development Agency 2019). The independent variables studied included experience of exposure to malaria or filaria, age group, gender, recent education level, and area of residence. The dependent variable was including the use of repellents/materials to prevent mosquito bites, mosquito nets, and electric mosquito repellent device (example: electric mosquito racket) or not. The data were categorized into 2 categories, "Yes" for respondents who prevented mosquito bites and "No" for respondents who did not use mosquito bite prevention at all.

The first independent variable was the variable related to the experience of being exposed to malaria or filariasis, respondents who have been positive for malaria/have been tested for malaria/ have been given filarial medicine/have been positive for filaria were classified as having been exposed to vector-borne disease information. The second independent variable is the age group variable. This variable is categorized into 4 categories ranging from the age group 0-20 years old, 21-40 years old, 41-60 years old to older than 60 years old. Gender variables include men and women, and the last variable, the area of residence which consisted of urban and rural areas. Another

independent variable was the level of education which was divided into 7 categories including never attended school, did not graduate from elementary school, graduated from elementary school, graduated from middle school, graduated from high school, graduated from diploma degree and graduated from college.

**Data Analysis**

This study conducted a multivariate test using logistic regression analysis to determine the factors that influence the behaviour in preventing mosquito bites. Multivariate analysis was performed using logistic regression with a backward Wald method to determine the relationship of the response variable (mosquito bite prevention behaviour) and each explanatory variable (exposure experience, age group, education level, gender, and regional characteristics). The relationship between variables was described by the value of the Odd ratio (OR) along with the value of the confidence interval (95% CI). The analysis was carried out to find the most optimal equation model. The difference in OR was >10% between the previous model and the model after the variable was removed then used to determine whether the variable can be included in the final model or not. All data were analysed using SPSS version 15 (IBM Inc., Chicago, IL.USA).

**Ethic Statement**

Riskesdas 2018 has received ethical approval from the National Ethics Commission (Ethics Commission of the Ministry of Health Research and Development Agency) number LB.02.01/2/ KE.024/2018.

## RESULTS AND DISCUSSION

This research was conducted to measure people's behaviour in preventing mosquito bites by several factors among Indonesian society. The data of various factors was significantly associated with the mosquito bite prevention behaviour as p-values were <0.05 as shown in Table 1.

**The Experience of Exposure**

The experience of exposure to vector borne disease was the factor that significantly influenced prevention efforts. Respondents who had never been exposed to malaria or filaria were less likely to make an effort in preventing mosquito bites compared to respondents who had been exposed (0.609 times) (CI = 0.601-0.616; p <0.001).

**Age**

The age group factors influenced prevention efforts. Respondents below 20 years old were more likely to undertaken a bite prevention effort compared to those over 60 years old (1,261 times) (CI = 1,240-1,283; p <0.001). Respondents between 21-40 years old also have a higher probability in taking mosquito bite prevention than respondents over 60 years old (1,385 times) (CI = 1,361-1,411; p <0.001). In the 40-61 years old age group, more people did bite prevention compared to the respondents who were over 60 years old (1,037 times) (CI = 1,000-1,076; p <0.001).

**Gender**

Apart from experience of exposure to disease and age group, gender also has a significant role in influencing prevention efforts. Male respondents were less likely to take prevention compared to female respondents (0.906 times) (CI = 0.897-0.915; p <0.001).

**Education**

Education was also a factor influencing prevention efforts. Respondents with education level of ‘never attended school' were more likely to take precautions than respondents who graduated from college education level (1,164 times) (CI = 1,132-1,196; p <0.001). Respondents who did not complete elementary school were also more likely to take precautions than respondents who graduated

from college (1,303 times) (CI = 1,271-1,336; p <0.001). Respondents with elementary education level were more likely to take precautions than respondents who graduated from college (1,221 times) (CI=1,192-1,250; p <0.001). Respondents who graduated from middle school also showed a tendency to take precautions compared to respondents who graduated from college (1,137 times) (CI = 1,110-1,165; p <0.001). Respondents with a high school education level also showed a tendency to take precautions compared to respondents who graduated from college (1,066 times) (CI = 1,042-1,091; p <0.001) based on table 1 it can also be seen that respondents who graduated from diploma education were more likely to do prevention compared to respondents who graduated from college (1,037 times) (CI= 1,000-1,076; p= 0.053).

## Regional

The regional factors in Table 1 shows that respondents in urban areas were less likely to take bite prevention efforts compared to respondents from rural areas (0.607 times) (CI = 0.601-0.613; p <0.001).

## The Findings

This study's findings show that the percentage of respondents who did not do bite prevention was higher than who did it. These findings are in line with studies elsewhere.[16] Several studies in Indonesia stated that inconvenience in practicing mosquito bite prevention is the main reason why many Indonesians do not make efforts to prevent mosquito bites. For example, mosquito nets were reported to cause people to feel stiflingly hot.[13] The reason for the inconvenient feeling was also reported by research related to mosquito repellent.[14,15]

Besides the feeling of inconvenient there were other factors that might affect bite prevention practice. This current study revealed that experience of exposure to vector borne diseases (malaria or filariasis), gender, age group, education level, and area of residence were associated with mosquito bite prevention behaviour in Indonesian society.

Experience of exposure to disease can affect a person's belief and knowledge of a disease. The experience of each individual's exposure to disease is closely linked to the public and private sectors. Cooperation and participation or community involvement between the public (government) and private sectors are very important in order to create continual promotional messages related to bite prevention.[16]

**Table 1**. The Estimated Association Between Mosquito Bite Prevention Behaviour with Various Factors by Logistic Regression.

| Factors | Prevention Behaviour | | OR | 95%CI | p-value |
|---|---|---|---|---|---|
| | Yes (%) | No (%) | | | |
| **Vector diseases experience** | | | | | |
| No | 20.2 | 54.2 | 0.609 | 0.601-0.616 | <0.001 |
| Yes | 4.4 | 21.1 | 1 | | |
| **Age Group** | | | | | |
| 0-20 years old | 9.2 | 30,1 | 1.261 | 1.240-1.283 | <0.001 |
| 21-40 years old | 6.7 | 20.7 | 1.385 | 1.361-1.411 | <0.001 |
| 41-60 years old | 6.2 | 18.4 | 1.296 | 1.273-1.319 | <0.001 |
| >60 years old | 2.6 | 6.1 | 1 | | |

| | | | | | |
|---|---|---|---|---|---|
| **Gender** | | | | | |
| Men | 12.5 | 36.5 | 0.906 | 0.897-0.915 | <0.001 |
| Women | 12.2 | 38.9 | 1 | | |
| **Level of Education** | | | | | |
| Never attended school | 2.1 | 6.3 | 1.164 | 1.132-1.196 | <0.001 |
| Did not finish elementary school | 5.1 | 17.4 | 1.303 | 1.271-1.336 | <0.001 |
| Elementary school Graduate | 5.7 | 18.7 | 1.221 | 1.192-1.250 | <0.001 |
| Middle school Graduate | 4.2 | 12.6 | 1.137 | 1.110-1.165 | <0.001 |
| High school graduate | 5.8 | 14.9 | 1.066 | 1.042-1.091 | <0.001 |
| Diploma Graduate | 0.7 | 1.7 | 1.037 | 1.000-1.076 | 0.053 |
| College graduate | 1.4 | 3.3 | 1 | | |
| **Area** | | | | | |
| Urban | 13.2 | 29.1 | 0.607 | 0.601-0.613 | <0.001 |
| Rural | 11.5 | 46.3 | 1 | | |

In this study, people with exposure experience were the people who had their blood drawn to be tested for malaria/people who were positive for malaria/people who were given filariasis prevention drugs/ people diagnosed with filariasis by health workers. Therefore, the delivery of health promotion presented by health workers when they were taking blood for malaria test or administering filariasis drugs is very important to encourage these individuals to take efforts in mosquito bites prevention.

For respondents who have been exposed to vector-borne diseases, suffering from the disease is likely lead to behavioural changes in preventive measures to avoid the same infection. Action theory states that the individual takes an action based on the experience, perception, understanding or emerges from certain situations, as well as the existence of a stimulus object.[16] individuals' behaviour could also be influenced by their experience, acceptance/understanding of information, existing traditions and religion.[17] The results of the study in table 1 show that the frequency of mosquito bites prevention is higher in respondents who have been exposed to vector-borne diseases than respondents who have never been exposed to it. The positive effect of the suffering experience has also been reported respondents who have been infected with malaria gave them a strong urge to recover.[18]

The results of this study indicate that women are more likely to make efforts to prevent mosquito bites than men. This in line with the health belief model theory that behaviour can be influenced by one's gender.[19] This is probably because the Indonesian women are commonly doing household chores, such as cleaning the house and therefore, mosquito control at home mostly done by housewife. Better practice scores among women might be affected by their role and their sense of responsibility in taking care of their family and household needs.[20]

The same results were also reported bby Vannayong [21] that female respondents were more willing to carry out activities to prevent mosquito bites, such as cleaning water reservoirs. The result of this study is also consistent with a study in Ecuador, which reported that Ecuadorian women had better

knowledge and doing better measures in disease prevention than men.[22]

A person's educational background might affect their job. People with college graduate backgrounds are more likely to have active jobs. A person's job status can inhibit or encourage a person's actions to live healthy, therefore a job status is defined as a predisposing factor.[23] Another possibility is that people at this level are reluctant to do the bite prevention since they feel that they do not have time to do it. A high level of activity makes someone who has malaria symptoms reluctant to take prevention action because of their busy schedule[18]. The results of analysis are similar to the results of Wong's research [24] that dengue prevention behaviour is mostly carried out by respondents who do not work or workers who do not need skills (unskilled workers).

Unusual finding showed that the respondents from urban areas had significantly lower probability in doing bite prevention than those who live in rural areas. The high availability of vector's habitat in rural areas might cause this finding. The malaria and filaria vector mosquitoes prefer the outdoor areas. Water is an important factor in the life cycle of these mosquitoes, mosquitoes leave their larvae which then develop into adult mosquitoes. The Anopheles mosquito, which acts as a vector for malaria, is commonly found in rice fields, brackish water, swamps, and mountainous areas. Mosquitoes can live in clear water and come into direct contact with the ground. Meanwhile, the Culex mosquito, which is the vector for filariasis, can be found living in polluted water, such as ditches, rivers full of garbage, and standing water, but can also be found living in clear water.[25]

Rural communities are more likely to have larger yards than urban communities. The size of the yards can sometimes cause rural communities to be more active in controlling the mosquito breeding places. When the rainy season comes, the leaves will filled with water and become a mosquitoes breeding place. The lush plants also affects the mosquito population because mosquitoes prefer to perch.[25] Plants will block sunlight and make the place even more humid and suitable for resting place.[26] This increases the risk of being bitten by mosquitoes, which may make the village community more active in carrying out mosquito bite prevention activities.

**Limitations of the Study**

In practice, this study was inseparable from several limitations. The education variable in this study did not have an even number of respondents at each level, the higher education variable tended to be less than the other respondents. Therefore, interpretation must be carried out with caution. In addition, this study did not include occupational factors as one of the explanatory factors, therefore further studies are needed to show a direct association between work and mosquito bite prevention practices.

We conceptualized the general picture by taking into account urban and rural disparities based on a study conducted by Wilson [27] and Asingizwe.[28] Communities living in less developed areas or rural areas might have a lack of access to improved housing, essential health services, effective and timely diagnosis and treatment that might contribute to the higher risk of the transmission of malaria. Studies also have shown that financial problems have been a significant challenge in delivering malaria prevention and treatment program in rural communities. Other disparities from Riskesdas can be seen in other publications.[29]

## CONCLUSIONS

Respondents who have experience of being exposed to malaria or filaria, under 60 years old, women, college graduates, and rural communities are more likely to perform mosquito bites prevention, therefore they could be empowered in promoting public

awareness towards mosquito bites prevention. The results of this study suggest the need for future research regarding Information, education and communication strategies along with current implemented intervention efforts evaluation.

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## CONFLICT OF INTEREST

All authors declared that they do not have any conflict of interest in both the research and also in the article writing process.

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***Original Article***

# Proportion of Extrapulmonary MDR-TB Confirmed by GeneXpert® in Dr. Hasan Sadikin General Hospital, West Java, Indonesia Year 2012–2021

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***ABSTRACT***

*As the third-highest country with tuberculosis (TB) incidence worldwide in 2020, Indonesia has increasing TB cases resistant to various anti-TB therapy or multidrug-resistant (MDR)-TB, and ranked fifth for its high incidence reported in Global Tuberculosis Report 2020. Moreover, extrapulmonary TB (EPTB) is rising, and data studies on EPTB with MDR-TB in Indonesia are scarce. This study aimed to explore the proportion of extrapulmonary MDR-TB among TB cases in Dr. Hasan Sadikin General Hospital Bandung, West Java, Indonesia. A descriptive retrospective and cross-sectional study design were conducted, retrieving medical records from all suspect MDR-TB adult patients examined by GeneXpert®, at Dr. Hasan Sadikin General Hospital Bandung, West Java period 2012–2021. Those with EPTB were further analyzed, and the demographic data was collected as well as clinical history, behavioral history, sites of extrapulmonary MDR-TB, and drug resistance. Of a total 7,013 TB cases, 1,900 (27.1%) were MDR-TB cases, of whom 0.08% (n6) were extrapulmonary MDR-TB cases and 0.16% (n11) were combined with PTB. The main characteristics of cases with extrapulmonary MDR-TB were median age 27-year-old (range 25–34), male gender (64.7%), underweight BMI (84.6%), and predominantly were primary cases (35.3%). The anti-TB drug resistance in MDR-TB were pre-XDR-TB (11.7%), XDR-TB (5.6%), MDR-TB (42%), and RR-TB (40.7%). Although the proportion of extrapulmonary MDR-TB among all TB cases is small (0.2%), this disease can't be ignored and has a great potential to be explored. Most of them are rifampicin-resistant. Further studies need to include a larger population to have more overview of MDR-TB with EPTB.*

***Keywords:*** *extrapulmonary; Indonesia; multidrug-resistant; rifampicin; tuberculosis;*

***ABSTRAK***

*Sebagai negara ke-3 dengan kejadian tuberkulosis (TB) terbanyak di seluruh dunia pada tahun 2020, Indonesia juga mempunyai angka kejadian TB resisten obat ganda (MDR) yang meningkat, dan diketahui sebagai negara ke-5 terbanyak untuk kejadian MDR-TB di dunia berdasarkan Global Tuberculosis Report 2020. Ditambah dengan adanya kejadian TB ekstra paru yang meningkat, namun penelitian terkait MDR-TB ekstra paru di Indonesia masih sangat jarang. Penelitian ini bertujuan untuk mencari proporsi kasus MDR-TB ekstra paru dibandingkan dengan keseluruhan kasus di RSUP Dr. Hasan Sadikin Bandung, Jawa Barat. Deskriptif retrospektif dan desain potong lintang, dengan pengambilan data rekam medis pasien dewasa yang merupakan suspek MDR-TB dan diperiksa dengan TCM GeneXpert® di RSUP Dr. Hasan Sadikin Bandung, Jawa Barat pada tahun 2012 sampai tahun 2021. Proporsi MDR-TB ekstraparu kemudian dianalisis lebih lanjut, berserta dengan data demografi dan riwayat klinis, kebiasaan perilaku, lokasi infeksi MDR-TB ekstra*

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*paru, dan pola resistan pada MDR-TB. Dari 7,013 kasus TB, terdapat 1,900 kasus (27.1%) MDR-TB, yang terdiri dari 0.08% (n6) MDR-TB ekstra paru dan 0.16% (n11) MDR-TB kombinasi paru dan ekstra paru. Proporsi karakteristik yang terbesar pada penelitian ini ditandai dengan median pada umur 27 tahun, dengan kelompok umur 25 – 34 tahun, jenis kelamin laki-laki (64.7%), IMT <18.5kg/m2 (84.6%), dan kasus primer (35.3%). Proporsi pola resisten obat terbanyak yang ditemukan adalah pre-XDR-TB (11.7%), XDR-TB (5.6%), MDR-TB (42%), dan RR-TB (40.7%). Meskipun proporsi MDR-TB ekstra paru pada seluruh kasus TB hanya sedikit (0.2%), penyakit ini tidak bisa diabaikan dan masih mempunyai potensi yang besar untuk diteliti. Proporsi terbesar merupakan resistan terhadap rifampicin. Studi lebih lanjut memerlukan populasi yang lebih besar untuk mengetahui secara keseluruhan mengenai MDR-TB ekstra paru.*

***Kata kunci:*** *ekstra paru; Indonesia; resisten obat ganda; rifampicin; tuberkulosis*

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## INTRODUCTION

Tuberculosis (TB) is well-known for its highly contagious transmission of *Mycobacterium tuberculosis (Mtb)* by airborne through coughing, sneezing, talking, or doing other things.[1] Although it has been identified for many years, the incidence of TB is still thriving from time to time.[2] Comparing the incidences between the year 2015 and 2019 in Indonesia, there were rises around 69%, which caused Indonesia to become the third country, coming up after India, with the highest TB incidences in the world in 2020.[3]

Inappropriate anti-TB drugs administration would lead to failed eradication of *Mtb* and risk leading to *Mtb* mutation, resulting in resistance to 1st category of anti-TB drugs, which could be confirmed as multidrug-resistant TB (MDR-TB) with GeneXpert®.[4] In Global Tuberculosis Report 2020, Indonesia was the fifth country with the highest MDR-TB incidence globally.[5] The MDR-TB incidence in Indonesia reached 8.8 cases in 100,000 populations, with 2.4% primary cases and 13% have treated with anti-TB drugs in 2019, which unknown for its incidence in 2020 although Indonesia was in the 30 high MDR-TB burden countries.[3,5] From inappropriate anti-TB drugs administrations, there are several risk categories defined in the National Guideline for Tuberculosis by the Ministry of Health Republic of Indonesia.[6–9]

Confirmed MDR-TB patients are those whose samples have been examined and proved that there were anti-TB drug-resistant *Mtb*, especially against isoniazid and rifampicin, can be together with or without other anti-TB drugs. MDR-TB could be grouped by its sites of infection, such as exclusively pulmonary TB (PTB), extrapulmonary TB (EPTB), and EPTB with PTB.[10] The extrapulmonary MDR-TB proportion in China is 2.5% among all TB patients and 9.3% among MDR-TB patients in 2008 – 2017; and 5.1% among all TB patients and 12.6% among MDR-TB patients in India period 2012 – 2014.[11,12]

The location of extrapulmonary TB could differ in every patient, mainly manifested in lymph nodes and pleura, consecutively causing TB lymphadenitis and TB pleurisy due to their sites being the nearest from the lungs.[13] Apart from them, TB infections may take place in the skeletal, abdomen, pericardium, central nervous system, and other locations.[11]

Although extrapulmonary MDR-TB cases are not rare, there have not been many studies reported, especially in Indonesia. Therefore, this study aimed to measure the proportion of extrapulmonary MDR-TB among TB cases and explore characteristics related to the MDR-TB cases at Dr. Hasan Sadikin General Hospital Bandung, West Java, Indonesia in 2012-2021.

## MATERIALS AND METHODS

### Study Site and Period

This study used a retrospective cross-sectional study design. Secondary data were collected using total sampling method, retrieved from the medical record in MDR clinic Dr. Hasan Sadikin General Hospital Bandung, cross-checked with data from e-TB manager, SITB (*Sistem Informasi Tuberkulosis*), and Lab TB 04 at Dr. Hasan Sadikin General Hospital Bandung, West Java, Indonesia, in the period between April 2012 – August 2021.

### Samples and Data Collection

The inclusion criteria were all data of adult MDR-TB and TB patients (≥18 years) registered in SITB and e-TB Manager as TB03 and TB06, and GeneXpert® Lab as TB04 in Dr. Hasan Sadikin General Hospital Bandung (Figure 1). The incomplete data, which were completely missing from the medical record, were excluded from this study.

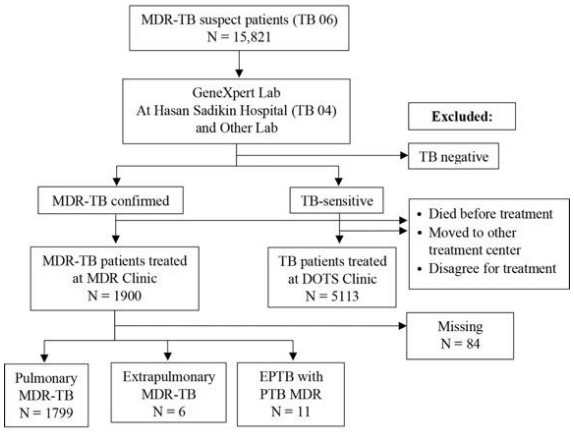


**Figure 1.** Flowchart of MDR-TB Suspect Cases at Dr. Hasan Sadikin General Hospital Bandung, West Java

The total number of cases of MDR-TB and TB sensitive were collected. The site location of MDR-TB, drugs resistances, and the extrapulmonary sites in MDR-TB was also collected and analyzed for their distribution proportion, along with the following data from the medical records, such as age, gender, body mass index, comorbid diseases (Diabetes Mellitus, HIV Status, Systemic Lupus Erythematosus, and others), smoking history, alcohol consumption history, and risk category for MDR-TB, were also analyzed for their proportions.

The gold standard for extrapulmonary MDR-TB diagnostics in Dr. Hasan Sadikin General Hospital Bandung preceded by rapid molecular test using GeneXpert®. The samples or tissue samples are collected from the suspected extrapulmonary TB locations. If the result appeared resistant, certified culture methods and drug susceptibility test (DST) would be performed with another collected tissue samples from the previous location. However, if the location of the samples is considered hard to reach, rapid molecular test is enough to diagnose extrapulmonary MDR-TB.

### Data Definition and Analysis

The risk category for MDR-TB patients according to the national guideline for TB consisted of 12 categories, which number 10 – 12 were applied since 2020:[6–8]

1. Chronic TB patients, who are still sputum smear-positive at the end of the first line TB re-treatment (Category 2);
2. TB patients with 2nd category treatment which not converted in 3 months of treatment;
3. TB patients who have a non-standard TB treatment history using quinolone and 2nd line anti-TB drug injection for at least 1 month, who received any TB treatments outside of the national program, for example, non-DOTS and private clinic;
4. TB patients who failed 1st category treatment;
5. TB patients with 1st category treatment who remain positive after 3 months of treatment; Relapse TB patients, categories 1 and 2, whose most recent treatment outcome was ‘cured’ or ‘treatment completed’ yet return with TB symptoms;
6. Returning TB patients after loss to follow-up (negligent treatment/default), who

interrupted any TB treatments for two or more consecutive months and returned with TB symptoms;
7. Suspected TB patients with a history of close contact with MDR-TB patients, who live in the same household or spending many hours a day in the same indoor living space with an MDR-TB patient and show TB symptoms;
8. TB-HIV co-infection patients who do not respond to anti-TB drug administration;
9. MDR-TB patients who failed treatment;
10. Relapse MDR-TB patients;
11. Returning MDR-TB patients after loss to follow-up (negligent treatment/default).

Patients who don't belong to these categories and tested positive for resistance to at least rifampicin and isoniazid without any history of consuming 1st line TB treatment are considered to be primary MDR-TB.[9]

This study still used the old definitions of pre-XDR-TB is MDR-TB with resistance to any fluoroquinolone or at least one of three second-line injectable drugs (capreomycin, kanamycin, and amikacin), and XDR-TB is TB that is resistant to any fluoroquinolone and at least one of three second-line injectable drugs (capreomycin, kanamycin, and amikacin). However, there are new definitions by WHO in 2021 because this study used the data from the year 2012-2021, which used the old definitions for patients grouping.[14]

Data retrieved was further presented in the proportion of MDR-TB, characteristics, EPTB sites, and anti-TB drug resistance, using a descriptive method with SPSS IBM® SPSS® ver. 22.

### Ethical Issues

Ethical permission for this study had been granted from the Ethics Committee of Universitas Padjadjaran with number 494/UN6.KEP/EC/2021 and the Research Permit were given from the Health Research Ethics Committee of Dr. Hasan Sadikin General Hospital Bandung with number LB.02.01/X.2.2.1/16836/2021.

## RESULTS AND DISCUSSION

The data we collected was 7013 TB cases, consisting of 1900 MDR-TB cases (27.1%) and 5113 TB sensitive cases (72.9%). As we collected the data from 1900 registered MDR-TB patients, we found 97 patients that came repetitively, hence re-registered into the database, of whom came five times (n1), thrice (n6), and twice (n90), thus resulting in the same name counted as different cases in this study. Nevertheless, this study still included all of these data because the cases were considered different from those who lost to follow-up, relapsed, and failed conversion after treatment.

Of a total of 1900 adults, 1799 had pulmonary TB (PTB), 6 had extrapulmonary TB (EPTB), 11 combined had EPTB with PTB, and 84 with no data found, which excluded in other variables analyzed in Table 1–3. Table 1 shows the proportion of MDR-TB characteristics and exclusively shows the proportion of PTB MDR, EPTB MDR, and their combination. Most of the MDR-TB patients were in the age group 35 – 44 years old and 25 – 34 years old among EPTB MDR patients. The majority of the MDR-TB patients were male (58%). Underweight was found the most in MDR-TB patients (46.3%), pulmonary MDR-TB patients (61.2%), and extrapulmonary MDR-TB patients (84.6%).

There were 275 pulmonary MDR-TB patients with diabetes mellitus as their comorbid disease and 80 MDR-TB patients with hypertension. Interestingly, there were two MDR-TB patients with systemic lupus erythematosus (SLE) and 25 MDR-TB patients with HIV co-infection, consisting of 17 pulmonary MDR-TB patients, one combined EPTB with PTB MDR patient, and the rest were unknown. There were 43% of MDR-TB patients who had never smoked and 74.2% of MDR-TB patients who had never consumed alcohol. Category 6 from the risk category of MDR-TB, defined as relapse TB patients (category 1 and 2), was the most frequent in this study (36.8%) and among extrapulmonary MDR-TB was primary MDR-TB (35.3%), defined as acquired MDR-TB patients who don't belong to the 12 categories.

**Table 1.** Characteristics Proportion in MDR PTB, EPTB, and EPTB with PTB

| Characteristic | | MDR-TB Total | MDR-TB Locations | | |
|---|---|---|---|---|---|
| | | | PTB | EPTB | EPTB with PTB |
| | | n (%) | n (%) | n | n |
| | | **1816** | **1799** | **6** | **11** |
| **Gender** | Male | 1058 (58.3) | 1047 (58) | 4 | 7 |
| | Female | 758 (41.7) | 752 (42) | 2 | 4 |
| **Age (years) – Median (IQR)** | | 38 (35–44) | 38 (35–44) | 28 (25–34) | 27 (25–34) |
| **Clinical History** | | | | | |
| **BMI (kg/m$^2$)*** | | **1432** | **1419** | **6** | **7** |
| | <18.5 | 879 (46.3) | 868 (61.2) | 5 | 6 |
| | 18.5-22.9 | 426 (22.4) | 424 (29.9) | 1 | 1 |
| | 23-24.9 | 62 (3.3) | 62 (4.4) | - | - |
| | ≥25 | 65 (3.4) | 65 (4.6) | - | - |
| **Comorbid Diseases** | Diabetes Mellitus | 275 (15.1) | 275 (15.3) | - | - |
| | HIV/AIDS | 25 (1.4) | 18 (1) | - | 1 |
| | Hypertension | 80 (4.4) | 80 (4.5) | - | - |
| | SLE | 2 (0.1) | 2 (0.1) | - | - |
| **Behavioral History** | | | | | |
| **Smoking** | | **1734** | **1722** | **5** | **7** |
| | Yes | 101 (5.8) | 99 (5.7) | 1 | 1 |
| | Ex-smoker | 815 (47) | 812 (47.2) | 2 | 1 |
| | Non-smoker | 818 (47.1) | 811 (47.1) | 2 | 5 |
| **Consuming Alcohol** | | **1733** | **1721** | **5** | **7** |
| | Yes | 8 (0.5) | 8 (0.5) | - | - |
| | Ex-drinker | 315 (18.2) | 314 (18.2) | 1 | - |
| | Non-drinker | 1410 (81.4) | 1399 (81.3) | 4 | 7 |
| **Risk Category for MDR-TB†** | | **1814** | **1797** | **6** | **11** |
| | 1. Chronic TB patients | 184 (10.2) | 183 (10.2) | - | 1 |
| | 2. TB patient with 2$^{nd}$ category treatment which not converted in 3 months of treatment | 80 (4.3) | 80 (4.5) | - | - |
| | 3. TB patient who have a non-standard TB treatment history using quinolone and 2nd line anti-TB drug injection for at least 1 month | 104 (6.1) | 103 (5.7) | - | 1 |
| | 4. TB patients who failed 1st category treatment | 214 (11.7) | 213 (11.9) | - | 1 |
| | 5. TB patients with 1st category treatment who remain positive after 3 months of treatment | 76 (4.2) | 74 (4.1) | - | 2 |
| | 6. Relapse TB patient, categories 1 and 2 | 672 (36.8) | 667 (37.1) | 3 | 2 |

| | | | | |
|---|---|---|---|---|
| 7. Returning TB patients after loss to follow-up | 201 (11.3) | 201 (11.2) | - | - |
| 8. Suspected TB patients with a history of close contact with MDR-TB patients | 54 (2.9) | 54 (3) | - | - |
| 9. TB-HIV co-infection patients who do not respond to anti-TB drug administration | 4 (0.3) | 4 (0.2) | - | - |
| 10. MDR-TB patients who failed treatment | 6 (0.3) | 6 (0.3) | - | - |
| 11. Relapse MDR-TB patients | 13 (0.7) | 12 (0.7) | - | 1 |
| 12. Returning MDR-TB patients after loss to follow-up | 3 (0.2) | 3 (0.2) | - | - |
| Primary MDR | 208 (11) | 197 (11) | 3 | 3 |

Note: There were samples that weren't listed. *BMI classification based on Asia-Pacific guidelines; Underweight: <18.5 kg/m2. Normal: 18-22.9 kg/m2. Overweight: 23-24.9 kg/m2. Obese: >25 kg/m2
†Risk category number 10 – 12 applied since the year 2020. MDR: Multi drug Resistant, PTB: Pulmonary TB, EPTB: Extrapulmonary TB

Table 2 shows the site of infection in extrapulmonary MDR-TB, the most frequent was in the bone. The proportion of drug resistance was described in Table 3, which shows the most frequent resistance from this study was the MDR-TB (41.4%) and rifampicin-resistant TB (RR-TB) in extrapulmonary MDR-TB (76.8%).

**Table 2.** Distribution Proportion of EPTB by Site in MDR-TB Patients

| Extrapulmonary MDR-TB Location | n (%) | EPTB, n (%) | EPTB with PTB, n (%) |
|---|---|---|---|
| TB Lymphadenitis | 4 (23.5) | 1 | 3 |
| TB Meningits | 3 | 1 | 2 (66.7) |
| Bone or Joint TB | 6 (35.3) | 3 (50) | 3 |
| TB Spondylitis | 5 (29.4) | 2 (40) | 3 |
| TB Colitis | 3 | 1 (33.3) | 2 (66.7) |
| TB Pleurisy | 1 | - | 1 (100) |
| **Total (n)** | 17 | 6 | 11 |

MDR: Multidrug-resistant, PTB: Pulmonary TB, EPTB: Extrapulmonary TB

**Table 3.** Anti-TB Drug Resistance Proportion in MDR-TB Patients

| Drug Resistance | n (%) | n = 1816 | | |
|---|---|---|---|---|
| | | PTB, n (%) | EPTB, n | PTB + EPTB, n |
| Pre-XDR-TB | 212 (11.7) | 211 (11.7) | - | 1 |
| XDR-TB | 102 (5.6) | 101 (5.6) | - | 1 |
| **MDR-TB, n** | **757 (41.7)** | **755 (42)** | **1** | **1** |
| Rifampicin-isoniazid | 350 (19.3) | 349 (19.4) | - | 1 |
| Rifampicin-isoniazid-ethambutol | 141 (7.8) | 140 (7.8) | 1 | - |
| Rifampicin-isoniazid-streptomycin | 98 (5.4) | 98 (5.4) | - | - |
| Rifampicin-isoniazid-ethambutol-streptomycin | 167 (9.2) | 167 (9.3) | - | - |
| Rifampicin-isoniazid-ethambutol-streptomycin-pyrazinamide | 1 (0.1) | 1 (0.1) | - | - |
| Rifampicin-resistant Based | 745 (41) | 732 (40.7) | 5 | 8 |
| **Total (n)** | **1816** | **1799** | **6** | **11** |

Pre-XDR: Pre-extensively drug resistant, XDR: Extensively drug resistant, MDR: Multidrug-resistant, PTB: Pulmonary TB, EPTB: Extrapulmonary TB.

This study has explored the characteristics proportion, location, infection site in extrapulmonary and anti-TB drugs resistance of MDR-TB. With the GeneXpert®, MDR TB suspects have been examined since 2012. In total, 15821 adults examined, MDR TB confirmed were 1900 adults, of whom 1799 pulmonary TB (PTB), including one miliary TB case, 6 exclusively extrapulmonary TB (EPTB), 11 combined EPTB with PTB, and 84 unknown data locations. The total extrapulmonary MDR-TB cases were 17 cases, 0.24% of total TB cases, and 0.9% of MDR-TB cases. These results show differences with the studies in China, which were 2.5% of total TB patients and 9.3% of MDR-TB patients, and in India, were 5.1% of total TB cases and 12.6% of MDR-TB cases.[11,12] However, in MDR cases, extrapulmonary TB always has shown less frequent than pulmonary TB, which suggested by Raveendran *et al*., that could be caused by fewer number of extrapulmonary TB that has been treated before.[15]

In this study, the median age of MDR-TB patients was 38-year-old in the age group 35 – 44 years old and in extrapulmonary was 27-year-old in the age group 25 – 34 years old, which is similar to previous studies where most patients belonged to the productive age group of 21 – 45 years old.[12,16,17] Most productive age people spend most of their time outside their home, meeting or passing by many people frequently, which increases the risk of TB or MDR-TB exposure, well-known for its high incidence in Indonesia.[5,12]

Among MDR-TB and EPTB MDR patients, males were found more commonly (58.3% and 64.7%), similar to previous studies in India and China, consecutively 59.5% and 69.1%.[12,17] This finding is probably due to the patriarchal culture in the related country, causing females to become more passive to independently go to healthcare to check themselves up, resulting in female patients being found less than male patients.[12,17,18] A different result showed from a study in Peru, with a more female proportion (60.6%).[19] This difference was presumptively caused by the ratio of male-to-female that defers in each country. In 2012 – 2020, the male population outnumbered the female population in Indonesia, with an average of 50.4%.[20]

Almost half of the MDR-TB patients (46.3%) in this study had a body mass index (BMI) <18.5 kg/m$^2$, which is categorized as underweight. PTB MDR patients (61.2%), EPTB MDR patients (67%), and combined EPTB with PTB patients showed a similar result. A higher underweight population in MDR-TB patients was probably resulting from a decreased immune system that existed in underweight, leading to an increased risk of getting community-acquired infection.[21]

This study shows 275 MDR-TB patients (15.1%)—all belonged to pulmonary MDR-TB, had diabetes mellitus (DM), as the similar results found in a study in Sudan (15.8%).[22] This is probably related to decreasing the immune system in patients with DM, increasing the infection risk, and decreasing anti-TB drugs effectivity, resulting in delayed conversion in TB patients, leading to the risk of *Mtb* strains resistance.[23,24] Unfortunately, Indonesia is TB and DM high burden country, so doctors and government should pay more attention to these diseases.[25] The following comorbid disease is hypertension (4.4%). Its reasons are still unknown, and some studies showed no evidence between hypertension and TB.[26] Still, presumably, it is related to high hypertension prevalence in Indonesia, resulting in its pretty high proportion in MDR-TB.[28] There were also 25 patients (1.4%) with HIV co-infection, which its cause was similar with patients with DM, people living with HIV/AIDS (PLWHA) also had a decreased immune system, which could increase the risk of getting infection and malabsorption of anti-TB drugs, especially isoniazid and rifampicin, resulting in a higher risk of getting MDR-TB.[28] This study showed two patients with SLE, with probable mechanism, were the administration of

corticosteroid as SLE therapy, which lower the patient's immune system, resulting in an increased risk of getting any infection.[29]

In this study, 101 MDR-TB patients (5.8%) smoked, which had a considerable far gap than studies in India and Sudan, consecutively 65.8% and 59.2%.[12,22] However, in this study, there were also found 815 patients (47%) who had a smoking history but had stopped. Eight patients (0.5%) also consumed alcohol, which had a considerable gap with other studies in India and Sudan, with 42.1% and 47.4%, consecutively.[12,22] Different results in Indonesia might result from their majority religion, Muslim, which alcohol is considered *haraam* or forbidden so that most of them choose not to drink alcohol.[30]

According to the risk category of MDR-TB, most patients came after a TB relapse, meaning that the patient had been treated with anti-TB drugs, which correspond with the study in India (56.2%).[12] Previous anti-TB drugs exposure might increase MDR-TB incidence globally by 18% and in Indonesia 13% from an MDR-TB incidence. Those numbers might differ from other studies in other countries.[5,31] Primary MDR-TB patients took over 11% of MDR-TB patients and were found in six out of 17 extrapulmonary MDR-TB patients, similar to the result in a study done in India (7.9%).[32] Yet, Indonesia and India also had similar estimated percentages in primary MDR-TB incidence, consecutively 2.4% and 2.8%.[5]

Among 17 cases of extrapulmonary infection, the most frequent sites were bone (35.3%) and lymph (23.5%), with a similar percentage compared to extrapulmonary MDR-TB and combined EPTB with PTB MDR. A study in China about extrapulmonary TB also shows skeletal TB as its predominant site (41.4%), but it doesn't exclusively show the results of extrapulmonary MDR-TB.[11] Meanwhile, a study in India showed that 51.3% of sites involved in extrapulmonary MDR-TB were in lymph nodes, which is reasonable due to TB pathogenesis resulting in *Mtb* travel to lymph nodes for antigen-presenting, shuttled to other lymph nodes, or continue to travel via lymph fluid.[32] This study found that the most frequent anti-TB drug resistance was rifampicin (41%), followed by RIF+INH-resistant (19.3%). Nevertheless, more resistances towards INH+RIF+EMB+SM (31.1%) were found in India, which shows different results against this study.[12]

## CONCLUSIONS

The retrospective method limits this study to explore the proportion of extrapulmonary MDR-TB and its characteristics proportion due to missing and incomplete data. This study was conducted in a referral hospital resulting in more frequent MDR-TB cases. The extrapulmonary MDR-TB cases are scarce, not portraying the actual proportion, unlike the MDR-TB cases. Future studies are needed to include more cases in other centers to have more overview of MDR-TB with EPTB.

To conclude, the total extrapulmonary MDR-TB cases in Dr. Hasan Sadikin General Hospital Bandung period 2012 – 2021 take over 0.24% from all of TB cases and 0.9% from all MDR-TB cases, predominated by age group 25 – 34 years old with age median 27-year-old, male gender, underweight BMI, non-smoking behavior, non-alcohol consuming behavior, and previous history of TB. Most extrapulmonary MDR-TB cases are rifampicin-resistant, and the site of infection is located in bone.

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## CONFLICT OF INTEREST

The author(s) declared no potential conflicts of interest concerning this article's research, authorship, and/or publication.

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***Original Article***

# Bacterial Profile and Antibiotic Resistance Pattern among Children with Urinary Tract Infections in Dr. Soetomo Hospital, Surabaya, Indonesia

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***ABSTRACT***

*Urinary tract infections (UTIs) are the most common infections in pediatric patients characterized by the growth of bacteria in the urine in significant numbers. Antibiotics remain the primary treatment of UTI in children. However, there has been an increase in antibiotic resistance to uropathogens worldwide due to their inappropriate and extensive uses. There is considerable geographical variation in the distribution of bacteria and antibiotic resistance pattern. Thus, to prevent further resistance and provide empirical antibiotic options, this study aims to determine the profile of bacteria and antibiotics resistance pattern among UTI pediatric patients in Dr. Soetomo Hospital. This study was performed by collecting data from the urine culture logbook at the Clinical Microbiology Laboratory of Dr. Soetomo Hospital in July-October 2019. The sample was UTI patients aged one day – 18 years due to bacterial infection with a colony count of ≥100,000 CFU/ml. In this study, 131 patients showed significant bacterial growth dominated by males and ages one month – 2 years. UTI were caused by gram-negative bacteria (74%) and gram-positive bacteria (26%), with the most bacteria found in each group were Escherichia coli and Enterococcus faecalis. E. coli showed ≥70% resistance to ampicillin, cefazoline, piperacillin, tetracycline, and trimethoprim-sulfamethoxazole. Comorbidities were dominated by hydronephrosis (10.98%), chronic kidney disease (9.79%) and hydrocephalus (8.09%). In conclusion, gram-negative bacteria were the leading cause of UTI in children with E. coli as the most common uropathogen, highly resistant to ampicillin and cefazolin. Gram-positive bacteria were less frequent with varied resistance patterns. Most common comorbidity was hydronephrosis.*

**Keywords:** *antibiotic resistance; bacterial pathogen; urinary tract infection*

***ABSTRAK***

*Infeksi saluran kemih (ISK) merupakan penyakit infeksi yang banyak dijumpai pada anak ditandai dengan pertumbuhan bakteri urin dalam jumlah yang signifikan. Pengobatan ISK anak utamanya dengan pemberian antibiotik. Namun, telah terjadi peningkatan resistensi antibiotik terhadap uropatogen di seluruh dunia akibat penggunaan yang kurang tepat dan terlalu ekstensif. Variasi geografis dalam distribusi bakteri penyebab ISK dan pola resistensi antibiotiknya juga cukup besar. Untuk mencegah*

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*resistensi lebih lanjut dan memberikan pilihan antibiotik empiris, penelitian ini diperlukan untuk mengetahui profil bakteri dan pola resistensi antibiotik pada pasien anak ISK di RSUD Dr. Soetomo. Penelitian ini dilakukan dengan menggunakan data sekunder berupa catatan hasil kultur urin di Laboratorium Mikrobiologi Klinik RSUD Dr. Soetomo pada bulan Juli-Oktober 2019 dengan sampel pasien ISK anak berusia 1 hari – 18 tahun akibat infeksi bakteri dengan hitung koloni sebanyak ≥100,000 CFU/ml. Dalam penelitian ini, 131 pasien menunjukkan pertumbuhan bakteri signifikan, yang didominasi oleh laki-laki dan usia 1 bulan – 2 tahun. ISK disebabkan oleh bakteri gram negatif (74%) dan gram positif (26%) dengan bakteri terbanyak yang ditemukan pada masing-masing kelompok adalah Escherichia coli dan Enterococcus faecalis. E. coli menunjukkan resistensi ≥70% terhadap ampisilin, sefazolin, piperasilin, tetrasiklin, dan trimetoprim-sulfametoksazol. Penyakit penyerta pada pasien ISK anak didominasi oleh hidronefrosis (10,98%), penyakit ginjal kronis (9,79%), dan hidrosefalus (8,09%). Sehingga dapat disimpulkan bahwa bakteri gram negatif merupakan penyebab utama ISK anak dengan E. coli sebagai uropatogen yang paling sering dijumpai, yang resisten terhadap ampisilin dan cefazolin. Sedangkan bakteri gram positif lebih jarang ditemukan dengan pola resistensi yang bervariasi. Penyakit penyerta pasien terbanyak adalah hidronefrosis.*

***Kata kunci:*** *bakteri patogen; infeksi saluran kemih; resistensi antibiotik*

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## INTRODUCTION

Urinary Tract Infection (UTI) is the second most common infectious disease in children after respiratory tract infection characterized by the growth of bacteria in the urine in significant numbers.[1,2] Mostly, UTI in children are caused by gram-negative bacteria with *Escherichia coli* as the most common uropathogen.[3] UTI in children are often underdiagnosed due to their non-specific signs and symptoms, especially in neonates and infants[4], such as fever, decreased appetite, vomiting, diarrhea, jaundice, abdominal distension, weight loss, and failure to thrive.[2] In addition, pediatric UTIs are commonly associated with various congenital abnormalities of the urinary tract, such as posterior urethral valves, ureteropelvic junction obstruction, neurogenic bladder, urethral stricture, and vesicoureteral reflux, which can lead to recurrent UTIs.[5] If the patient is not treated promptly, complications such as renal scarring, hypertension, or chronic kidney disease, will develop progressively. Thus, it is necessary to give empirical antibiotics based on local antimicrobial susceptibility patterns as initial therapy before the urine culture results are available.[3]

Globally, UTI in pediatric are estimated around 150 million cases annually.[6] In the United States, there are an estimated 1.5 million cases of UTI in pediatric outpatients.[7] While at Dr. Soetomo Hospital Surabaya, Indonesia, it obtained 94 urine samples among children with UTI within two months.[8] The incidence of UTI in children is more common in girls (8%) than boys (2%).[9] Boys have a greater incidence of UTI than girls with a ratio of 2:1 to 5:1 in the neonatal period and early infancy.[3,10] In addition, the increasing prevalence of antimicrobial resistance among uropathogens over the past few decades also complicates UTI management.[3] The National Healthcare Safety Network (NHSN) in the United States reported that an increase in multidrug-resistant gram-negative bacteria was found in 2,039 hospitals.[11] A study from South India demonstrated that Extended-Spectrum Beta-Lactamase (ESBL) production was detected in 53% of isolates from patients with community-acquired bacteremia caused by *E. coli* and *Klebsiella* spp.[12]

In the recent years, the increasing trend of bacterial uropathogen resistance against commonly used antimicrobials has become a major concern worldwide. Antibiotic susceptibility patterns vary widely between different geographic areas. In a study in Ethiopia showed that *E. coli*, as the most common isolated uropathogen, was resistant

to ampicillin (100%) and nitrofurantoin (78.6%) whereas sensitive to ciprofloxacin (71.4%), norfloxacin (71.4%) and ceftriaxone (57.1%).[6] In Nepal, the percentage of sensitivity for *E. coli* were high for nitrofurantoin, ceftriaxone, amikacin, gentamicin, and ofloxacin, while a high level of resistance was observed for ampicillin and cotrimoxazole.[13] A study by Patwardhan et al. in North India reported that the incidence of resistance to ampicillin, amoxiclav, nitrofurantoin, co-trimoxazole, and norfloxacin increased significantly over a five-year period. This situation is certainly very concerning because the complexity of UTI treatment can increase the risk of long-term consequences in children.[14]

Given the high prevalence of antibiotic resistance worldwide with the diversity of resistance patterns between geographic areas that change easily over time, continuous monitoring of uropathogens and local antibiotic resistance patterns is needed as a basic consideration in selecting empiric pharmacotherapy which is important to optimize the initial management of pediatric UTIs to reduce risk of unexpected complications.[4] Studies recommend that policies for UTI treatment in children should be re-evaluated every five years according to local resistance levels.[15] Hence, this study was conducted to assess the prevalence of bacterial uropathogens and their susceptibility patterns to antibiotic agents amongst pediatric patients with UTI in Dr. Soetomo Hospital.

## MATERIALS AND METHODS

### Study Design

This descriptive retrospective study was conducted at the Clinical Microbiology Laboratory of Dr. Soetomo Hospital, Surabaya, from September 2020 to June 2021. Data on age, sex, urine culture, antibiotic sensitivity, and patient comorbidities were obtained from the urine culture logbook in July-October 2019. Samples were collected using consecutive sampling techniques from pediatric patients aged one day – 18 years with UTI (inpatient and outpatients). The diagnosis of UTI was established when the result of the bacterial colony count was >100,000 colony-forming units per millilitre (CFU/ml).[17] Bacterial identification and antibiotic susceptibility test were carried out using the automatic microdilution method, BD Pheonix and Vitek, validated and interpreted by Clinical Laboratory Standard International (CLSI). Patients with incomplete urine examination data and medical records were excluded from this study.

### Statistical Analysis

The data were analyzed descriptively with Statistical Package for the Social Sciences (SPSS) 16.0 and Microsoft Excel resulted in the distribution of the number and percentage of each variable.

### Ethical Approval

This research received ethical approval from the health research ethics committee of Dr. Soetomo Hospital on November 26, 2020, with the letter number 0225/LOE/301.4.2/XI/2020.

## RESULTS AND DISCUSSION

### Characteristics of pediatric UTI patients

Based on the urine culture logbook in pediatric UTI in July-October 2019, there were 211 data on patients aged one day – 18 years who performed urine culture examinations and antibiotic sensitivity tests at the Clinical Microbiology Laboratory of Dr. Soetomo Hospital. However, significant bacterial growth (≥100,000 CFU/ml) was found in 131 patients and was dominated by boys (54.2%). Based on age, the results showed that UTI in children mainly occurred in the age group of one month – 2 years.

If we look at the distribution of age by sex (Table 1), the results show that most boys are found in the age group of one month – 2 years, while most girls are found in the age group of 6–12 years.

**Table 1.** Age and Sex Distribution

| Age | Sex | | Total n (%) |
|---|---|---|---|
| | Girl | Boy | |
| | n (%) | n (%) | |
| 0-30 days | 0(0.00) | 2(1.53) | 2(1.53) |
| 1 month - 2 years | 15(11.45) | 23(17.56) | 38(29.01) |
| 2-6 years | 8(6.11) | 18(13.74) | 26(19.85) |
| 6-12 years | 19(14.50) | 15(11.45) | 34(25.95) |
| 12-18 years | 18(13.74) | 13(9.92) | 31(23.66) |
| Total | 60(45.80) | 71(54.20) | 131(100.00) |

## Bacteria Isolation

Bacteria causing UTI were dominated by gram-negative bacteria (74%) followed by gram-positive bacteria (26%). The most common gram-negative bacteria were *E. coli* (30.5%) while the most common gram-positive bacteria were *E. faecalis* (8.4%). All the data are shown in Figure 1. In this study, there were 17 isolates of *E. coli* and eight isolates of *K. pneumoniae* ESBL-producing gram-negative bacteria.

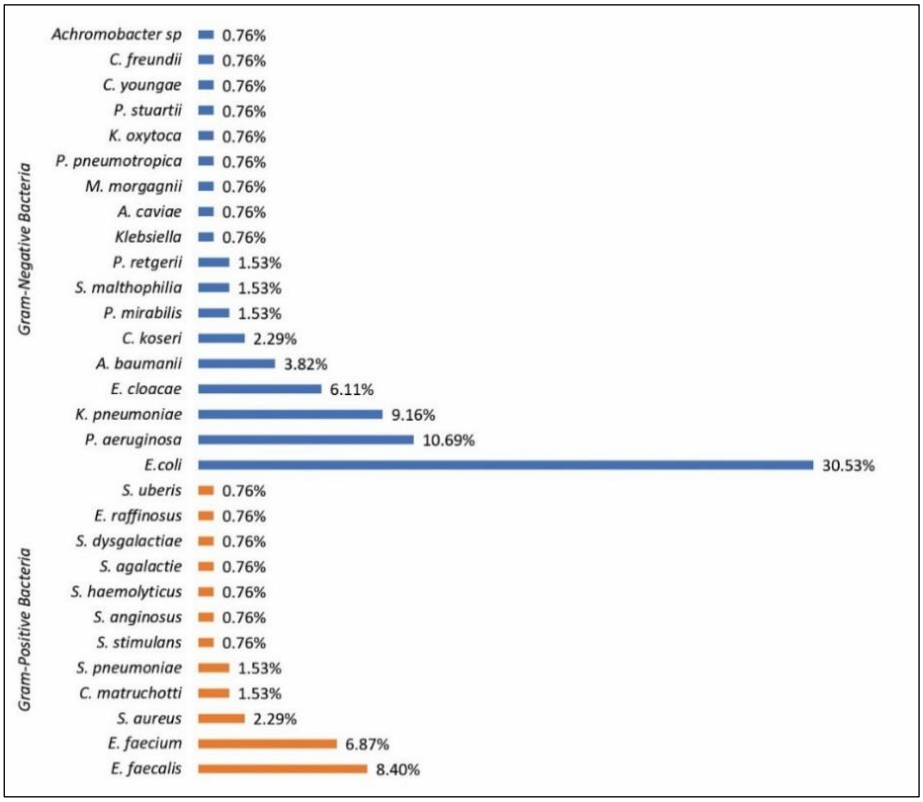


**Figure 1.** Distribution of Bacteria Causing UTI

## Gram-Negative Bacteria Resistance Pattern

In this study, *E. coli*, *P. aeruginosa*, *K. pneumoniae*, *E. cloacae*, and *A. baumannii*, showed resistance to ampicillin and cefazolin. *E. coli* was found to be resistant to ampicillin, cefazolin, piperacillin, sulfamethoxazole, trimethoprim- and tetracycline for about more than 70%. In contrast to *P. aeruginosa* which was resistant to more antibiotics such as ampicillin, cefazolin, amoxicillin-clavulanate, ampicillin-sulbactam, chloramphenicol, cefotaxime, nitrofurantoin, tetracycline, tigecycline, trimethoprim-sulfamethoxazole and ceftriaxone (Table 3).

In addition, the five most common gram-negative bacteria showed high sensitivity to amikacin, imipenem, meropenem, and piperacillin-tazobactam, as shown in Table 3. *E. coli* was also sensitive to tigecycline, nitrofurantoin, gentamicin, and cefoperazone-sulbactam, while *P. aeruginosa* was also found to be sensitive to piperacillin, gentamicin, and ceftazidime.

**Table 3.** Distribution of Antibiotic Resistance in Gram-Negative Bacteria

| Antibiotic | | *E. coli* (N=40) | *P. aeruginosa* (N=14) | *K. pneumoniae* (N=12) | *E. cloacae* (N=8) | *A. baumanii* (N=5) |
|---|---|---|---|---|---|---|
| Amikacin | R (%) | 0/40 (0.00) | 1/14 (7.14) | 2/12 (16.67) | 4/8 (50.00) | 0/5 (0.00) |
| | I (%) | 0/40 (0.00) | 1/14 (7.14) | 1/12 (8.33) | 0/8 (0.00) | 0/5 (0.00) |
| | S (%) | 40/40 (100.00) | 12/14 (85.71) | 9/12 (75.00) | 4/8 (50.00) | 5/5 (100.00) |
| Amoxicillin-clavulanate | R (%) | 13/40 (32.50) | 14/14 (100.00) | 4/12 (33.33) | 8/8 (100.00) | 5/5 (100.00) |
| | I (%) | 10/40 (25.00) | 0/14 (0.00) | 3/12 (25.00) | 0/8 (0.00) | 0/5 (0.00) |
| | S (%) | 17/40 (42.50) | 0/14 (0.00) | 5/12 (41.67) | 0/8 (0.00) | 0/5 (0.00) |
| Ampicillin | R (%) | 36/39 (92.31) | 13/13 (100.00) | 12/12 (100.00) | 8/8 (100.00) | 5/5 (100.00) |
| | I (%) | 0/39 (0.00) | 0/13 (0.00) | 0/12 (0.00) | 0/8 (0.00) | 0/5 (0.00) |
| | S (%) | 3/39 (7.69) | 0/13 (0.00) | 0/12 (0.00) | 0/8 (0.00) | 0/5 (0.00) |
| Ampicillin-sulbactam | R (%) | 21/40 (52.50) | 13/13 (100.00) | 7/12 (58.33) | 8/8 (100.00) | 0/5 (0.00) |
| | I (%) | 9/40 (22.50) | 0/13 (0.00) | 1/12 (8.33) | 0/8 (0.00) | 0/5 (0.00) |
| | S (%) | 10/40 (25.00) | 0/13 (0.00) | 4/12 (33.33) | 0/8 (0.00) | 5/5 (100.00) |
| Aztreonam | R (%) | 17/40 (42.50) | 8/14 (57.14) | 8/12 (66.67) | 4/8 (50.00) | 5/5 (100.00) |
| | I (%) | 3/40 (7.50) | 3/14 (21.43) | 0/12 (0.00) | 0/8 (0.00) | 0/5 (0.00) |
| | S (%) | 20/40 (50.00) | 3/14 (21.43) | 4/12 (33.33) | 4/8 (50.00) | 0/5 (0.00) |
| Cefazolin | R (%) | 26/26 (100.00) | 14/14 (100.00) | 8/8 (100.00) | 8/8 (100.00) | 5/5 (100.00) |
| | I (%) | 0/26 (0.00) | 0/14 (0.00) | 0/8 (0.00) | 0/8 (0.00) | 0/5 (0.00) |
| | S (%) | 0/26 (0.00) | 0/14 (0.00) | 0/8 (0.00) | 0/8 (0.00) | 0/5 (0.00) |
| Cefepime | R (%) | 18/40 (45.00) | 7/14 (50.00) | 8/12 (66.67) | 4/8 (50.00) | 1/5 (20.00) |
| | I (%) | 1/40 (2.50) | 0/14 (0.00) | 0/12 (0.00) | 0/8 (0.00) | 0/5 (0.00) |
| | S (%) | 21/40 (52.50) | 7/14 (50.00) | 4/12 (33.33) | 4/8 (50.00) | 4/5 (80.00) |
| Cefotaxime | R (%) | 18/40 (45.00) | 14/14 (100.00) | 8/12 (66.67) | 4/8 (50.00) | 1/5 (20.00) |
| | I (%) | 1/40 (2.50) | 0/14 (0.00) | 0/12 (0.00) | 0/8 (0.00) | 3/5 (60.00) |
| | S (%) | 21/40 (52.50) | 0/14 (0.00) | 4/12 (33.33) | 4/8 (50.00) | 1/5 (20.00) |
| Gentamicin | R (%) | 8/40 (20.00) | 2/14 (14.29) | 5/12 (41.67) | 4/8 (50.00) | 2/5 (40.00) |
| | I (%) | 0/40 (0.00) | 1/14 (7.14) | 0/12 (0.00) | 0/8 (0.00) | 0/5 (0.00) |
| | S (%) | 32/40 (80.00) | 11/14 (78.57) | 7/12 (58.33) | 4/8 (50.00) | 3/5 (60.00) |
| Ceftazidime | R (%) | 17/40 (42.50) | 2/14 (14.29) | 8/12 (66.67) | 4/8 (50.00) | 1/5 (20.00) |
| | I (%) | 2/40 (5.00) | 1/14 (7.14) | 0/12 (0.00) | 0/8 (0.00) | 0/5 (0.00) |
| | S (%) | 21/40 (52.50) | 11/14 (78.57) | 4/12 (33.33) | 4/8 (50.00) | 4/5 (80.00) |
| Ceftriaxone | R (%) | 22/39 (56.41) | 11/13 (84.62) | 8/12 (66.67) | 4/8 (50.00) | 2/5 (40.00) |
| | I (%) | 1/39 (2.56) | 2/13 (15.38) | 0/12 (0.00) | 0/8 (0.00) | 2/5 (40.00) |
| | S (%) | 16/39 (41.03) | 0/13 (0.00) | 4/12 (33.33) | 4/8 (50.00) | 1/5 (20.00) |
| Chloramphenicol | R (%) | 1/3 (33.33) | 12/12 (100.00) | 1/1 (100.00) | 4/4 (100.00) | 5/5 (100.00) |
| | I (%) | 0/3 (0.00) | 0/12 (0.00) | 0/1 (0.00) | 0/4 (0.00) | 0/5 (0.00) |
| | S (%) | 2/3 (66.67) | 0/12 (0.00) | 0/1 (0.00) | 0/4 (0.00) | 0/5 (0.00) |
| Ciprofloxacin | R (%) | 12/39 (30.77) | 3/13 (23.08) | 2/12 (16.67) | 4/8 (50.00) | 1/5 (20.00) |
| | I (%) | 1/39 (2.56) | 1/13 (7.69) | 2/12 (16.67) | 0/8 (0.00) | 0/5 (0.00) |
| | S (%) | 26/39 (66.67) | 9/13 (69.23) | 8/12 (66.67) | 4/8 (50.00) | 4/5 (80.00) |
| Ertapenem | R (%) | 0/1 (0.00) | - | - | - | - |
| | I (%) | 0/1 (0.00) | - | - | - | - |
| | S (%) | 1/1 (100.00) | - | - | - | - |
| Fosfomycin | R (%) | 0/11 (0.00) | 1/3 (33.33) | 0/1 (0.00) | - | 2/2 (100.00) |
| | I (%) | 0/11 (0.00) | 1/3 (33.33) | 0/1 (0.00) | - | 0/2 (0.00) |
| | S (%) | 11/11 (100.00) | 1/3 (33.33) | 1/1 (100.00) | - | 0/2 (0.00) |
| Imipenem | R (%) | 0/38 (0.00) | 1/12 (8.33) | 1/12 (8.33) | 4/8 (50.00) | 0/5 (0.00) |
| | I (%) | 3/38 (7.89) | 1/12 (8.33) | 0/12 (0.00) | 1/8 (12.50) | 0/5 (0.00) |
| | S (%) | 35/38 (92.11) | 10/12 (83.33) | 11/12 (91.67) | 3/8 (37.50) | 5/5 (100.00) |
| Levofloxacin | R (%) | 11/40 (27.50) | 3/12 (25.00) | 2/12 (16.67) | 4/8 (50.00) | 1/5 (20.00) |
| | I (%) | 2/40 (5.00) | 3/12 (25.00) | 0/12 (0.00) | 0/8 (0.00) | 0/5 (0.00) |
| | S (%) | 27/40 (67.50) | 6/12 (50.00) | 10/12 (83.33) | 4/8 (50.00) | 4/5 (80.00) |
| Meropenem | R (%) | 0/40 (0.00) | 1/14 (7.14) | 1/12 (8.33) | 4/8 (50.00) | 0/5 (0.00) |
| | I (%) | 0/40 (0.00) | 1/14 (7.14) | 0/12 (0.00) | 0/8 (0.00) | 0/5 (0.00) |
| | S (%) | 40/40 (100.00) | 12/14 (85.71) | 11/12 (91.67) | 4/8 (50.00) | 5/5 (100.00) |

| | | | | | | |
|---|---|---|---|---|---|---|
| Moxalactam | R (%) | - | - | - | 0/1 (0.00) | - |
| | I (%) | - | - | - | 0/1 (0.00) | - |
| | S (%) | - | - | - | 1/1 (100.00) | - |
| Moxifloxacin | R (%) | 13/38 (34.21) | - | 2/12 (16.67) | 4/7 (57.14) | - |
| | I (%) | 0/38 (0.00) | - | 2/12 (16.67) | 1/7 (14.29) | - |
| | S (%) | 25/38 (65.79) | - | 8/12 (66.67) | 2/7 (28.57) | - |
| Nitrofurantoin | R (%) | 4/39 (10.26) | 14/14 (100.00) | 7/12 (58.33) | 6/8 (75.00) | 5/5 (100.00) |
| | I (%) | 1/39 (2.56) | 0/14 (0.00) | 3/12 (25.00) | 0/8 (0.00) | 0/5 (0.00) |
| | S (%) | 34/39 (87.18) | 0/14 (0.00) | 2/12 (16.67) | 2/8 (25.00) | 0/5 (0.00) |
| Piperacillin | R (%) | 31/38 (81.58) | 2/12 (16.67) | 9/12 (75.00) | 5/8 (62.50) | 1/5 (20.00) |
| | I (%) | 4/38 (10.53) | 0/12 (0.00) | 1/12 (8.33) | 1/8 (12.50) | 1/5 (20.00) |
| | S (%) | 3/38 (7.89) | 10/12 (83.33) | 2/12 (16.67) | 2/8 (25.00) | 3/5 (60.00) |
| Piperacillin-tazobactam | R (%) | 4/40 (10.00) | 3/14 (21.43) | 1/12 (8.33) | 4/8 (50.00) | 1/5 (20.00) |
| | I (%) | 1/40 (2.50) | 0/14 (0.00) | 1/12 (8.33) | 0/8 (0.00) | 0/5 (0.00) |
| | S (%) | 35/40 (87.50) | 11/14 (78.57) | 10/12 (83.33) | 4/8 (50.00) | 4/5 (80.00) |
| Tetracycline | R (%) | 27/38 (71.05) | 13/13 (100.00) | 5/12 (41.67) | 5/8 (62.50) | 1/5 (20.00) |
| | I (%) | 0/38 (0.00) | 0/13 (0.00) | 0/12 (0.00) | 0/8 (0.00) | 1/5 (20.00) |
| | S (%) | 11/38 (28.95) | 0/13 (0.00) | 7/12 (58.33) | 3/8 (37.50) | 3/5 (60.00) |
| Tigecycline | R (%) | 1/39 (2.56) | 14/14 (100.00) | 1/12 (8.33) | 2/7 (28.57) | 1/5 (20.00) |
| | I (%) | 1/39 (2.56) | 0/14 (0.00) | 1/12 (8.33) | 2/7 (28.57) | 1/5 (20.00) |
| | S (%) | 37/39 (94.87) | 0/14 (0.00) | 10/12 (83.33) | 3/7 (42.86) | 3/5 (60.00) |
| Trimethoprim-sulfamethoxazole | R (%) | 28/39 (71.79) | 13/13 (100.00) | 6/12 (50.00) | 6/8 (75.00) | 1/5 (20.00) |
| | I (%) | 0/39 (0.00) | 0/13 (0.00) | 0/12 (0.00) | 0/8 (0.00) | 0/5 (0.00) |
| | S (%) | 11/39 (28.21) | 0/13 (0.00) | 6/12 (50.00) | 2/8 (25.00) | 4/5 (80.00) |
| Sefoperazon-sulbaktam | R (%) | 0/38 (0.00) | 0/14 (0.00) | 1/12 (8.33) | 4/8 (50.00) | 0/5 (0.00) |
| | I (%) | 8/38 (21.05) | 5/14 (35.71) | 3/12 (25.00) | 0/8 (0.00) | 0/5 (0.00) |
| | S (%) | 30/38 (78.95) | 9/14 (64.29) | 8/12 (66.67) | 4/8 (50.00) | 5/5 (100.00) |

**Gram-Positive Bacterial Resistance Pattern**

The five most common gram-positive bacteria, are *E. faecalis, E. faecium, S. aureus, C. matruchotii*, and *S. pneumoniae* showed varied resistance patterns. *E. faecalis* showed resistance to ceftriaxone, oxacillin, quinupristin-dalfopristin, tobramycin, trimethoprim, trimethoprim-sulfamethoxazole, gentamicin, clindamycin, cefotaxime, amikacin, cefoxitin, fusidic acid, tetracycline, and ciprofloxacin for about more than 70%. Meanwhile, *E. faecium* was resistant to amikacin, ampicillin, cefotaxime, gentamicin, ceftriaxone, clindamycin, erythromycin, penicillin, trimethoprim-sulfamethoxazole, levofloxacin, ciprofloxacin, and nitrofurantoin. In contrast to *S. aureus, C. matruchotii*, and *S. pneumoniae*, which were only resistant to one or two types of antibiotics (Table 4).

For the sensitivity pattern, these five bacteria were sensitive to vancomycin and linezolid (Table 4). *E. faecalis* is also sensitive to ampicillin, nitrofurantoin, and teicoplanin, while for *E. faecium*, another antibiotic sensitivity was only found in teicoplanin. In contrast to their resistance, *S. aureus, C. matruchotii*, and *S. pneumoniae* were found to be sensitive to many types of antibiotics.

**Table 4.** Distribution of Antibiotic Resistance in Gram-Positive Bacteria

| Antibiotic | | *E. faecalis* (N=11) | *E. faecium* (N=9) | *S. aureus* (N=3) | *C. matruchotti* (N=2) | *S. pneumoniae* (N=2) |
|---|---|---|---|---|---|---|
| Amikacin | R (%) | 6/7 (85.71) | 4/4 (100.00) | - | - | 0/1 (0.00) |
| | I (%) | 0/7 (0.00) | 0/4 (0.00) | - | - | 0/1 (0.00) |
| | S (%) | 1/7 (14.29) | 0/4 (0.00) | - | - | 1/1 (100.00) |
| Amoxicillin-clavulanate | R (%) | 0/1 (0.00) | - | 1/3 (33.33) | - | - |
| | I (%) | 0/1 (0.00) | - | 0/3 (0.00) | - | - |
| | S (%) | 1/1 (100.00) | - | 2/3 (66.67) | - | - |
| Ampicillin | R (%) | 2/11 (18.18) | 6/6 (100.00) | 3/3 (100.00) | - | - |
| | I (%) | 0/11 (0.00) | 0/6 (0.00) | 0/3 (0.00) | - | - |
| | S (%) | 9/11 (81.82) | 0/6 (0.00) | 0/3 (0.00) | - | - |
| Cefotaxime | R (%) | 7/8 (87.50) | 9/9 (100.00) | - | 0/2 (0.00) | 0/2 (0.00) |
| | I (%) | 0/8 (0.00) | 0/9 (0.00) | - | 0/2 (0.00) | 0/2 (0.00) |
| | S (%) | 1/8 (12.50) | 0/9 (0.00) | - | 2/2 (100.00) | 2/2 (100.00) |
| Gentamisin | R (%) | 10/11 (90.91) | 9/9 (100.00) | 1/3 (33.33) | 1/1 (100.00) | 0/2 (0.00) |
| | I (%) | 0/11 (0.00) | 0/9 (0.00) | 0/3 (0.00) | 0/1 (0.00) | 0/2 (0.00) |
| | S (%) | 1/11 (9.09) | 0/9 (0.00) | 2/3 (66.67) | 0/1 (0.00) | 2/2 (100.00) |
| Cefoxitin | R (%) | 6/7 (85.71) | 3/3 (100.00) | 1/2 (50.00) | - | - |
| | I (%) | 0/7 (0.00) | 0/3 (0.00) | 0/2 (0.00) | - | - |
| | S (%) | 1/7 (14.29) | 0/3 (0.00) | 1/2 (50.00) | - | - |
| Ceftriaxone | R (%) | 9/9 (100.00) | 8/8 (100.00) | - | 0/2 (0.00) | 0/2 (0.00) |
| | I (%) | 0/9 (0.00) | 0/8 (0.00) | - | 0/2 (0.00) | 0/2 (0.00) |
| | S (%) | 0/9 (0.00) | 0/8 (0.00) | - | 2/2 (100.00) | 2/2 (100.00) |
| Chloramphenicol | R (%) | 0/1 (0.00) | 0/1 (0.00) | - | 1/2 (50.00) | - |
| | I (%) | 0/1 (0.00) | 1/1 (100.00) | - | 0/2 (0.00) | - |
| | S (%) | 1/1 (100.00) | 0/1 (0.00) | - | 1/2 (50.00) | - |
| Ciprofloxacin | R (%) | 8/10 (80.00) | 5/6 (83.33) | 2/3 (66.67) | - | 0/1 (0.00) |
| | I (%) | 0/10 (0.00) | 1/6 (16.67) | 0/3 (0.00) | - | 0/1 (0.00) |
| | S (%) | 2/10 (20.00) | 0/6 (0.00) | 1/3 (33.33) | - | 1/1 (100.00) |
| Clindamycin | R (%) | 10/11 (90.91) | 8/8 (100.00%) | - | 0/2 (0.00) | 1/2 (50.00) |
| | I (%) | 0/11 (0.00) | 0/8 (0.00) | - | 0/2 (0.00) | 0/2 (0.00) |
| | S (%) | 1/11 (9.09) | 0/8 (0.00) | - | 2/2 (100.00) | 1/2 (50.00) |
| Erythromycin | R (%) | 6/9 (66.67) | 9/9 (100.00) | - | 0/2 (0.00) | 1/2 (50.00) |
| | I (%) | 2/9 (22.22) | 0/9 (0.00) | - | 1/2 (50.00) | 0/2 (0.00) |
| | S (%) | 1/9 (11.11) | 0/9 (0.00) | - | 1/2 (50.00) | 1/2 (50.00) |
| Fusidic Acid | R (%) | 6/7 (85.71) | 3/3 (100.00) | - | - | - |
| | I (%) | 0/7 (0.00) | 0/3 (0.00) | - | - | - |
| | S (%) | 1/7 (14.29) | 0/3 (0.00) | - | - | - |
| Levofloxacin | R (%) | 6/9 (66.67) | 7/8 (87.50) | 2/3 (66.67) | 0/2 (0.00) | 1/2 (50.00) |
| | I (%) | 1/9 (11.11) | 1/8 (12.50) | 0/3 (0.00) | 0/2 (0.00) | 0/2 (0.00) |
| | S (%) | 2/9 (22.22) | 0/8 (0.00) | 1/3 (33.33) | 2/2 (100.00) | 1/2 (50.00) |
| Linezolid | R (%) | 2/11 (18.18) | 1/9 (11.11) | 0/3 (0.00) | 0/2 (0.00) | 0/2 (0.00) |
| | I (%) | 6/11 (54.55) | 1/9 (11.11) | 0/3 (0.00) | 0/2 (0.00) | 0/2 (0.00) |
| | S (%) | 3/11 (27.27) | 7/9 (77.78) | 3/3 (100.00) | 2/2 (100.00) | 2/2 (100.00) |
| Moxalactam | R (%) | 0/1 (0.00) | - | - | - | - |
| | I (%) | 0/1 (0.00) | - | - | - | - |
| | S (%) | 1/1 (100.00) | - | - | - | - |
| Moxifloxacin | R (%) | 2/3 (66.67) | - | - | 0/2 (0.00) | 0/1 (0.00) |
| | I (%) | 0/3 (0.00) | - | - | 0/2 (0.00) | 0/1 (0.00) |
| | S (%) | 1/3 (33.33) | - | - | 2/2 (100.00) | 1/1 (100.00) |
| Nitrofurantoin | R (%) | 2/11 (18.18) | 7/9 (77.78) | 0/3 (0.00) | - | 1/2 (50.00) |
| | I (%) | 0/11 (0.00) | 1/9 (11.11) | 0/3 (0.00) | - | 0/2 (0.00) |
| | S (%) | 9/11 (81.82) | 1/9 (11.11) | 3/3 (100.00) | - | 1/2 (50.00) |
| Oxacillin | R (%) | 5/5 (100.00) | 2/2 (100.00) | 1/3 (33.33) | - | - |
| | I (%) | 0/5 (0.00) | 0/2 (0.00) | 0/3 (0.00) | - | - |
| | S (%) | 0/5 (0.00) | 0/2 (0.00) | 2/3 (66.67) | - | - |
| Penicillin | R (%) | 4/10 (40.00) | 8/8 (100.00) | 3/3 (100.00) | 0/2 (0.00) | 1/2 (50.00) |
| | I (%) | 0/10 (0.00) | 0/8 (0.00) | 0/3 (0.00) | 0/2 (0.00) | 0/2 (0.00) |
| | S (%) | 6/10 (60.00) | 0/8 (0.00) | 0/3 (0.00) | 2/2 (100.00) | 1/2 (50.00) |

| | | | | | | |
|---|---|---|---|---|---|---|
| Quinupristin-dalfopristin | R (%) | 11/11 (100.00) | 1/6 (16.67) | 1/3 (33.33) | - | - |
| | I (%) | 0/11 (0.00) | 3/6 (50.00) | 0/3 (0.00) | - | - |
| | S (%) | 0/11 (0.00) | 2/6 (33.33) | 2/3 (66.67) | - | - |
| Rifampin | R (%) | - | - | 0/3 (0.00) | 0/2 (0.00) | - |
| | I (%) | - | - | 0/3 (0.00) | 0/2 (0.00) | - |
| | S (%) | - | - | 3/3 (100.00) | 2/2 (100.00) | - |
| Streptomycin | R (%) | 0/2 (0.00) | 1/2 (50.00) | - | - | - |
| | I (%) | 0/2 (0.00) | 0/2 (0.00) | - | - | - |
| | S (%) | 2/2 (100.00) | 1/2 (50.00) | - | - | - |
| Teicoplanin | R (%) | 2/11 (18.18) | 0/6 (0.00) | 0/3 (0.00) | - | - |
| | I (%) | 0/11 (0.00) | 0/6 (0.00) | 0/3 (0.00) | - | - |
| | S (%) | 9/11 (81.82) | 6/6 (100.00) | 3/3 (100.00) | - | - |
| Tetracycline | R (%) | 9/11 (81.82) | 2/6 (33.33) | 2/3 (66.67) | 0/2 (0.00) | 0/1 (0.00) |
| | I (%) | 0/11 (0.00) | 0/6 (0.00) | 0/3 (0.00) | 0/2 (0.00) | 0/1 (0.00) |
| | S (%) | 2/11 (18.18) | 4/6 (66.67) | 1/3 (33.33) | 2/2 (100.00) | 1/1 (100.00) |
| Tigecycline | R (%) | - | - | - | 0/2 (0.00) | - |
| | I (%) | - | - | - | 0/2 (0.00) | - |
| | S (%) | - | - | - | 2/2 (100.00) | - |
| Tobramycin | R (%) | 7/7 (100.00) | 3/3 (100.00) | - | - | - |
| | I (%) | 0/7 (0.00) | 0/3 (0.00) | - | - | - |
| | S (%) | 0/7 (0.00) | 0/3 (0.00) | - | - | - |
| Trimethoprim | R (%) | 6/6 (100.00) | 3/3 (100.00) | - | - | - |
| | I (%) | 0/6 (0.00) | 0/3 (0.00) | - | - | - |
| | S (%) | 0/6 (0.00) | 0/3 (0.00) | - | - | - |
| Trimethoprim-sulfamethoxazole | R (%) | 11/11 (100.00) | 9/9 (100.00) | 1/3 (33.33) | 1/2 (50.00) | 1/1 (100.00) |
| | I (%) | 0/11 (0.00) | 0/9 (0.00) | 0/3 (0.00) | 0/2 (0.00) | 0/1 (0.00) |
| | S (%) | 0/11 (0.00) | 0/9 (0.00) | 2/3 (66.67) | 1/2 (50.00) | 0/1 (0.00) |
| Vancomycin | R (%) | 2/11 (18.18) | 1/9 (11.11) | 0/3 (0.00) | 0/2 (0.00) | 0/2 (0.00) |
| | I (% | 0/11 (0.00) | 0/9 (0.00) | 0/3 (0.00) | 0/2 (0.00) | 0/2 (0.00) |
| | S (%) | 9/11 (81.82) | 8/9 (88.89) | 3/3 (100.00) | 2/2 (100.00) | 2/2 (100.00) |

## Co-morbidities

In this study, children with UTI were diagnosed with more than one disease. The patient's comorbidities were dominated by hydronephrosis, chronic kidney disease, and hydrocephalus (Figure 2).

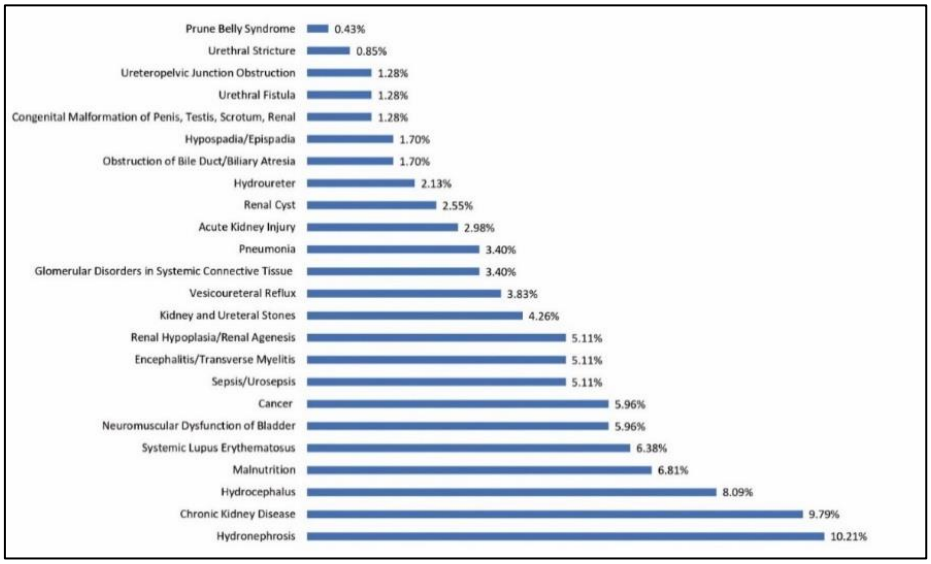


**Figure 2.** Distribution of Comorbidities

## DISCUSSION

UTI is one of the most common bacterial infectious diseases in children with non-specific symptoms. Epidemiologically, it is estimated that Emergency Department visits by children diagnosed with UTI reach more than 500,000 visits and 50,000 hospitalizations.[18] The incidence of UTI is influenced by two important interrelated variables, namely age and gender.[19] According to the American Academy of Pediatrics, the highest prevalence of UTI in children is found at the age of two months - two years, which is about 5% of children with fever complaints.[20] Similar to this study, which found that there were 54.2% of 131 children with UTI were male, dominated by one month – 2 years. Similar with Mirsoleymani et al in their study in Bandar Abbas, South Irian, UTI incidence in boys reached 54.9%.[21] The high incidence of UTI in boys at this age may be due to their uncircumcised status, so that uropathogens colonize the foreskin and cause ascending infection.[22] Poor diaper hygiene during infancy is also an important predisposition to UTI.[23]

In addition, the incidence of UTI in boys in early life is also possible because males have a higher risk of Congenital Anomalies of The Kidney and Urinary Tract (CAKUT) than females, so boys are more prone to UTI.[24]

Based on gender, the tendency of UTI among children will change with age. The dominance of uncircumcised male of UTI in infants will change to female preponderance in older children.[17] At the age of 7 years, it is estimated that approximately 7.8% of girls and 1.7% of boys are diagnosed with UTI.[25] This study found that boys were most commonly found at the age of one month – 2 years, while girls were most commonly found at the age of 6-12 years. UTI in girls is due to the relatively shorter urethral structure of girls so that bacteria more easily cause ascending infection to the bladder. It could also be due to heavy colonization of enteric bacteria in the perineal uropathogens.[22]

In the majority, UTIs in children are caused by gram-negative bacteria from the intestinal flora that colonize the perineum and cause ascending infection to the urinary tract. It is estimated that approximately 80% of pediatric UTIs are caused by *E. coli*.[3] In concordance with this study, which found a predominance of gram-negative bacteria (74%) with *E. coli* as the most common gram-negative bacteria, followed by *P. aeruginosa, K. pneumoniae, E. cloacae,* and *A. baumannii*. *E. coli* has various virulence factors, namely P fimbriae, a type of surface fimbriae that induces attachment to host-specific receptors on the uroepithelium. In addition, flagella, lipopolysaccharide, capsule polysaccharide, and hemolysin are also important virulence factors in infecting the host. Most uropathogenic *Escherichia coli* (UPEC) can produce aerobactin, a high affinity iron-binding protein that causes acute pyelonephritis.[2] While the gram-positive bacteria were only found in 26%, dominated by *E. faecalis*, followed by *E. faecium, S. aureus, C. matruchotii*, and *S. pneumoniae*. Similar to Benachinmardi et al in their study in India where 82.22% gram-negative bacteria were found, with *E. coli* (52.9%) as the most common bacterial isolate followed by *K. pneumoniae* (7.6%) while gram-positive bacteria were only found in 16% of isolates dominated by *Coagulase negative Staphylococcus* (9.8%) followed by *Enterococcus spp.* (5.8%).[4]

Currently, the management of UTI is becoming more difficult as various resistance mechanisms emerge, such as members of the *Enterobacteriaceae* family including *E. coli* and *K. pneumoniae* that produce ESBL. Kitagawa et al stated that ESBL-producing *E. coli* and *K. pneumoniae* were found to be more dominant than non-ESBL-producing isolates[8], in contrast to this study which found non-ESBL-producing *E. coli* and ESBL-producing *K. pneumoniae* strains are more dominant. This difference can be attributed to risk factors for ESBL infection including comorbidities, frequent use of health resources for a long time, previous use of antibiotics, experiencing recurrent UTI, older age, and male gender.[26]

To reduce the risk of acute and chronic complications in pediatric UTIs, prompt and appropriate initial treatment with empirical antibiotics plays an important role.

Unfortunately, an increase in resistant strains

has been widely reported, especially in developing countries due to the habit of consuming over-the-counter antibiotics without a prescription and prior consultation.[14] Antimicrobial resistant pattern varies by geographic area. Therefore, local antimicrobial susceptibility patterns are needed in selecting empirical antibiotics for initial treatment of pediatric UTIs considering potential side effect and economic consequences.[4] This study showed that the most resistant antibiotics to *E. coli, P. aeruginosa, K. pneumoniae, E. cloacae,* and *A. baumannii*, were ampicillin and cefazolin, similar with Kitagawa et al in their study of UTI patients in Surabaya.[8] The high resistance to these two antibiotics may be due to their frequent use considering that UTI management in Indonesia generally uses ampicillin, cephalosporins, and fluoroquinolones.[27]

Carbapenems are the broadest spectrum beta-lactam antibiotics that have become the gold standard for treating infections caused by ESBL-producing *Enterobacteriaceae*. They have high stability against hydrolysis reactions by beta-lactamase enzymes[28], however, its use should be limited to avoid irresponsible prescribing, resulting in the emergence of carbapenem-resistant organisms.[29] In contrast to amikacin, Poey et al explain that amikacin monotherapy can be used as the first line of empirical treatment in febrile UTI among pediatric patients so that amikacin may be a more appropriate empiric therapy option.[30] However, this still requires further research in the form of randomized controlled trials (RCT).[31] This study showed that the five most common gram-negative bacteria were sensitive to carbapenems (imipenem, meropenem), amikacin, and piperacillin-tazobactam, similar to Rahmadi in his research on UTI patients at the Department of Internal Medicine Dr. Soetomo Hospital.[32]

In Taiwan, Wu et al reported that *E. coli* was resistant to ampicillin, piperacillin, trimethoprim-sulfamethoxazole, and sensitive to amikacin, imipenem, ceftazidime, ceftriaxone, and cefuroxime, gentamicin.[33] Similar to this study in which *E. coli* was also resistant to ampicillin, cefazolin, piperacillin, trimethoprim-sulfamethoxazole, tetracycline exceeded 70%, and sensitive to amikacin, imipenem, meropenem, and piperacillin-tazobactam, tigecycline, nitrofurantoin, gentamicin, cefoperazone-sulbactam. A study in India stated that trimethoprim-sulfamethoxazole resistance increased significantly over a five-years period.[14] The increasing resistance of trimethoprim-sulfamethoxazole in various regions has resulted in this antibiotic being no longer recommended as empiric therapy unless it is proven to be sensitive according to local antibiogram data.[31] Meanwhile, cefoperazone-sulbactam showed a sensitivity of more than 90% in ESBL-producing *Enterobacteriaceae*.[34] Tigecycline is well tolerated in cases of serious Extensively Drug-Resistant (XDR) gram-negative bacterial infections[35], but should not be used as monotherapy in pediatric UTIs because of its limited excretion and some side effects, enamel hypoplasia.[36] According to the American Academy of Pediatrics, nitrofurantoin is not recommended for febrile infants because serum and parenchymal concentrations may be insufficient to treat urosepsis or pyelonephritis. In addition, nitrofurantoin is contraindicated in cases of decreased renal function with creatinine clearance <60 millilitre per minute (ml/min).[37]

The second largest gram-negative bacteria, *P. aeruginosa* was also found to be resistant to amoxicillin-clavulanate, ampicillin-sulbactam, cefotaxime, chloramphenicol, nitrofurantoin, tetracycline, tigecycline, trimethoprim-sulfamethoxazole, ceftriaxone and sensitive to piperacillin, gentamicin, ceftazidime. In previous studies, *P. aeruginosa* was reported to be highly resistant to trimethoprim-sulfamethoxazole, nitrofurantoin, cefotaxime, ampicillin, amoxicillin/clavulanate, cephalexin, cefuroxime, ceftriaxone, nalidixic acid[38,39] and more sensitive to piperacillin-tazobactam, ceftazidime, imipenem, ciprofloxacin, gentamicin, and tobramycin.[40]

It is different with gram-positive bacteria, which show high sensitivity to vancomycin and linezolid with varying resistance patterns. Both of *E. faecalis* and *E. faecium* showed resistance

to ceftriaxone, trimethoprim-sulfamethoxazole, gentamicin, cefotaxime, amikacin, ciprofloxacin for about more than 70%, and sensitive to vancomycin, linezolid, teicoplanin. This is in accordance with Hameed et al and Benachinmardi et al which showed that *Enterococcus spp*. resistant to trimethoprim-sulfamethoxazole (100%), amikacin (71.43%), gentamicin (85%), erythromycin (76.92%), and ciprofloxacin (60%) and completely sensitive to vancomycin, linezolid, and teicoplanin.[4,41] Enterococci are resistant to antibiotics because they are naturally resistant to low levels of aminoglycosides, cephalosporins, clindamycin and trimethoprim/sulfamethoxazole. Beta-lactams have also been reported to have limited clinical efficacy on enterococci due to the low affinity Penicillin-binding proteins (PBPs).[42]

In pediatric UTI, urinary tract abnormalities contribute to increasing recurrent UTI and resulting in the development of multi drug resistance organisms.[43] In this study, comorbidities in pediatric UTI patients were dominated by hydronephrosis (10.98%) followed by chronic kidney disease (9.79%), and hydrocephalus (8.09%). According to Coelho et al, the increasing severity of hydronephrosis leads to an increased risk of UTI due to urinary tract dilatation.[44] Hydronephrosis or dilation of the renal collecting system can be caused by partial or complete obstruction of urine flow caused by vesicoureteral reflux, posterior urethral valves, ureteropelvic junction obstruction, ureterocele, or duplication of the collecting system.[45] The most severe long-term sequelae as a complication of UTI is renal scarring that may progress to end-stage renal disease.[46] On the other hand, chronic kidney disease can also be a contributing factor to UTI due to oxidative stress and inflammatory cytokines, which can result in impaired immunity and increase susceptibility to various infections, especially UTI.[47]

Non-urinary disorders that can also increase the risk of UTI is hydrocephalus. Hydrocephalus is generally caused by myelomeningocele, the most common form of open spina bifida that can increase the incidence of UTI in children.[48,49] Hydrocephalus has an additional effect at the central level on the micturition process controlled by the pons, brain stem, and cerebral cortex which can aggravate the neurogenic bladder which results in impaired bladder emptying and increases the risk of UTI.[50]

The limitations found in this study are related to the instruments used. In this study, the researcher used secondary data in the form of a urine culture logbook, so that there could be bias because the researcher was not directly involved during the examination process and some of the data were found to be incomplete. However, this study is essential to evaluate the antibiotic resistance pattern among uropathogens in Dr. Soetomo Hospital, who could be considered in selecting the appropriate empirical antibiotics to optimize initial UTI therapy.

## CONCLUSIONS

This study revealed gram-negative bacteria isolates as the preponderance uropathogen, with *E. coli* as the most common bacteria found. Gram-negative bacteria are highly resistant to ampicillin and cefazoline, while gram-positive bacteria showed varied antibiotics resistance. UTI comorbidities are dominated by hydronephrosis, chronic kidney disease, and hydrocephalus. This research can be useful for health workers, especially in Dr. Soetomo Hospital, Surabaya, as an initial consideration in selecting empirical antibiotics before culture results are available. In addition, this study can be used as a reference for further research on children with UTI in order to develop public health services.

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## CONFLICT OF INTEREST

All authors declared that they do not have any conflict of interest.

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***Original Article***

# Knowledge and Attitudes of Dengue Virus Infection Transmission and Its Relationship with Eradication Action Program in Surabaya, Indonesia

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***ABSTRACT***

*Dengue virus infection is caused by a dengue virus transmitted through mosquito bites from species Aedes albopictus and Aedes aegypti. The Ministry of Health takes action to reduce the prevalence of DHF by regulating the management of PSN 3M Plus. This study aimed to determine the knowledge, attitude, and compliance with the management of PSN 3M Plus strategies of those living in Surabaya. A cross-sectional population-based google form questionnaire was conducted in January 2022 for four weeks (January 3, 2022, to January 29, 2022). Based on the bivariate analysis, gender and age of respondents were no relationship between compliance with the PSN 3M Plus (p-value >0.05). The results also showed no relationship between education and adherence to PSN 3M Plus (p-value > 0.05). However, based on previous studies, people with higher education showed better compliance. Public knowledge and attitude about the dengue virus and its transmission process can be increased by developing, modifying, and intervening in the people controlling dengue virus infection. Most people of Surabaya believe that dengue prevention is the complete responsibility of every people. Based on the bivariate analysis, the characteristics of respondents had no relationship with the PSN 3M Plus compliance (p-value > 0.05). Knowledge and attitudes of the Surabaya people toward PSN 3M Plus are still good. However, the characteristics of the respondents did not significantly affect their knowledge and attitudes*

**Keywords:** *attitude; dengue virus infection; knowledge; prevention; Surabaya.*

***ABSTRAK***

*Infeksi virus dengue merupakan penyakit yang disebabkan oleh virus dengue yang ditularkan melalui gigitan nyamuk Aedes aegypti dan Aedes albopictus. Kementerian Kesehatan melakukan tindakan untuk menurunkan prevalensi DBD dengan mengatur pengelolaan PSN 3M Plus. Penelitian ini bertujuan untuk menganalisis korelasi antara pengetahuan dan kebiasaan terhadap kepatuhan manajemen strategi PSN 3M Plus pada masyarakat yang berdomisili di Surabaya. Kuesioner google form berbasis populasi cross-sectional dilakukan pada Januari 2022, 4 minggu (3 Jan 2022 hingga 29 Jan 2022). Berdasarkan analisis bivariat, jenis kelamin dan usia responden tidak ada hubungan antara kepatuhan mengikuti PSN 3M Plus (p-value >0,05). Hasil analisis statistik juga menunjukkan bahwa tidak ada hubungan antara pendidikan dengan kepatuhan terhadap PSN 3M Plus (p-value >0,05). Hasil penelitian sebelumnya menunjukkan bahwa orang-orang dengan pendidikan lebih tinggi menunjukkan kepatuhan yang lebih baik, karenan pendidikan merupakan aspek penting dari pengendalian infeksi virus dengue. Pengetahuan dan sikap masyarakat tentang virus dengue dan proses penularannya dapat ditingkatkan dengan mengembangkan, memodifikasi dan mengintervensi masyarakat*

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*yang mengendalikan infeksi virus dengue. Sebagian besar masyarakat Surabaya percaya bahwa pencegahan DBD adalah tanggung jawab penuh setiap orang. Berdasarkan analisis bivariat, karakteristik responden tidak memiliki hubungan dengan kepatuhan masyarakat dalam menjalankan PSN 3M Plus (p-value > 0.05). Pengetahuan dan sikap masyarakat Surabaya terhadap PSN 3M Plus masih baik. Meskipun karakteristik responden tidak berpengarus signifkan terhadap pengetahuan dan kepatuhan.*

***Kata kunci:*** *infeksi virus dengue; pencegahan; pengetahuan; sikap; Surabaya*

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## INTRODUCTION

Dengue virus infection is a mosquito-borne infectious disease with more than 100 tropical and subtropical countries globally reported endemic.[1] It was transmitted through the bites of *Aedes aegypti* and *Aedes albopictus* mosquitoes which have previously been infected by Dengue virus from dengue sufferers. According to the World Health Organization, the estimated annual fatality rate was 2.5%, among individuals with severe dengue, with complications like hemorrhagic fever and fluid accumulation. Dengue infection is prevalent in Southeast Asia because of its primary vector, *Aedes aegypti* mosquitos.[2] Dengue infection was commonly reported among children and teenagers, but the prevalence among older age groups also increased in recent decades.[3,4]

In Indonesia, Dengue Hemorrhagic Fever (DHF) cases in 2020 with 108,303 cases.[5] The incidence of Dengue virus infection is caused, among others, due to high mobility, population density, environmental conditions, and the community's behaviour.[6] Cases of dengue virus infection in East Java Province in 2020 were 8,567 cases.[7] Surabaya City is one of the cities in east java with the highest number of dengue virus infection cases in all work areas, with 73 cases.[5] The Ministry of Health issued a policy with the number PM.01.11/MENKES/591/2016 to reduce dengue prevalence by regulating the management with Eradication Action Program (PSN 3M Plus). The movement of the program consists of draining the water storage, closing the landfill, and reusing used items that have the potential for mosquito breeding, plus sprinkling larvicides, using mosquito repellent, keeping larvae eating fish in the landfill, planting mosquito repellent, and others. According to the Ministry of Health (2019), the one house and one larva hunter effectively prevent dengue fever.[8]

The other effective strategy is that the authorities need to ensure that local people have decent knowledge about vector control and follow the recommendations. The only method for controlling the dengue virus infection is vector control, as no specific treatment or vaccine is available.[9–12] Knowledge and behaviour greatly influence the dynamics of the Aedes mosquito population, which in turn affects dengue virus transmission. Therefore, vector control is critical, with knowledge and fundamental aspects of infection control and prevention of dengue virus. Presently, the recommended control effort is the eradication of mosquito breeding nests. However, the local people need to have a sufficient understanding of the routes of dengue virus transmission, as their behaviour plays a vital role in limiting dengue disease transmission.[13] This study aimed to determine the knowledge, attitude, and compliance with the management of PSN 3M Plus strategies of those living in Surabaya. Study findings of this research are expected to help policymakers develop strategies for more effective prevention and control of dengue virus infection and increase community participation in dengue prevention programs.

## MATERIALS AND METHODS

### Ethics statement

This study was approved by the Lembaga Penelitian dan Pengabdian Kepada Masyarakat Universitas Airlangga with approval number 24-934/UN3.14/PPd/2013.

### Study design and study population

A cross-sectional population-based google form questionnaire was conducted in January 2022 for four weeks (January 3, 2022, to January 29, 2022). The population in this study was residents with Surabaya ID cards concerning their age, gender, profession, monthly income, and education. This study used a random sampling method. The data processing techniques in this study were editing, coding, entry, cleaning, and saving.

### Statistical Analysis

The statistical test used is chi-square using $\alpha = 0.05$ with SPSS software.

## RESULTS AND DISCUSSION

### Dengue Virus Infection in Surabaya

The first dengue outbreak in Surabaya was reported in Surabaya in 1968.[14] Since then, the incidence of dengue has been increasing, with several outbreaks occurring in 1973, 1988, 1988, 2007, and 2010.[15] Even though dengue is a big problem in Surabaya, Indonesia, the incidence of dengue virus infection in Surabaya has decreased over the last five years, as shown in Figure 1.

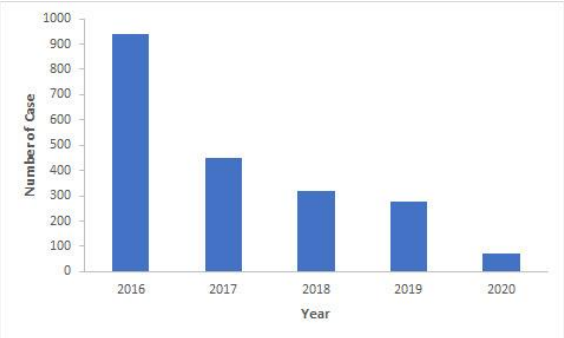


**Figure 1.** Dengue Virus Infection Cases in Surabaya[5,7,16–19]

### Demographic Characteristics of the Respondents in Surabaya

Respondents in this study came from 5 territories of the city of Surabaya (Table 1). The total respondent in this study was 60, with the characteristic of respondents shown in Table 2.

**Table 1.** Total of Respondent

| Territory | Total Respondent (%) |
|---|---|
| East Surabaya | 33.3 |
| North Surabaya | 13.3 |
| Central Surabaya | 5 |
| South Surabaya | 26.7 |
| West Surabaya | 21.7 |

**Table 2.** The Characteristic of Respondent

| Characteristic | Study Site Total (%) |
|---|---|
| **Sex** | |
| Male | 11 (18.3) |
| Female | 49 (81.7) |
| **Age (y.o)** | |
| 19-32 | 35 (58.3) |
| 33-45 | 10 (16.7) |
| 46-60 | 15 (25.0) |
| **Profession** | |
| Work | 34 (56.7) |
| Doesn't | 36 (43.3) |
| **Education** | |
| Senior High School/equal | 22 (36.7) |
| Bachelor/Diploma | 34 (56.7) |
| Master | 4 (6.7) |
| **Monthly income** | |
| <Rp. 1.000.000 | 19 (31.7) |
| Rp. 1.000.000 – Rp. 2.500.000 | 10 (16.7) |
| Rp. 2.500.000 – Rp. 4.000.000 | 15 (25.0) |
| Rp. 4.000.000 – Rp. 5.000.000 | 7 (11.7) |
| >Rp. 5.000.000 | 9 (15.0) |
| **Respondent's dengue virus infection history** | |
| Yes | 3 (5.0) |
| Not yet | 57 (95.0) |
| **Family history of dengue virus infection** | |
| Yes | 8 (13.3) |
| Not yet | 52 (86,7) |

### Knowledge of the Surabaya City People Regarding Dengue and Its Transmission

The respondent's knowledge in Surabaya about dengue virus infection like symptoms, vector transmission, and prevention was high (Table 3).

**Table 3.** Respondent's Knowledge

| Characteristic | Category | Knowledge | | | Total |
|---|---|---|---|---|---|
| | | Low | Medium | High | |
| **Sex** | Male | 0 | 0 | 11 | 49 |
| | Female | 0 | 3 | 46 | 11 |
| | **Total** | **0** | **3** | **57** | **60** |
| **Age (y.o)** | < 30 | 0 | 1 | 26 | 27 |
| | 30-40 | 0 | 2 | 11 | 13 |
| | 40-50 | 0 | 0 | 9 | 9 |
| | >50 | 0 | 0 | 11 | 11 |
| | **Total** | **0** | **3** | **57** | **60** |
| **Profession** | Work | 0 | 2 | 32 | 34 |
| | Does not work | 0 | 1 | 25 | 26 |
| | **Total** | **0** | **3** | **57** | **60** |
| **Monthly income** | < Rp. 1.000.000 | 0 | 0 | 19 | 19 |
| | Rp. 1000.000 – Rp. 2.500.000 | 0 | 3 | 7 | 10 |
| | Rp. 2.500.000- Rp. 4.000.000 | 0 | 0 | 15 | 15 |
| | Rp. 4.000.000-Rp. 5.000.000 | 0 | 0 | 7 | 7 |
| | < Rp. 5.000.000 | 0 | 0 | 9 | 9 |
| | **Total** | **0** | **3** | **57** | **60** |
| **Respondent's dengue virus infection history** | Yes | 0 | 0 | 3 | 3 |
| | Not yet | 0 | 3 | 54 | 57 |
| | **Total** | **0** | **3** | **57** | **60** |
| **Family history of dengue virus infection** | Yes | 0 | 0 | 8 | 8 |
| | Not yet | 0 | 3 | 49 | 52 |
| | **Total** | **0** | **3** | **57** | **60** |

## The Attitude of the Surabaya City People Regarding Dengue Virus Infection

The respondents' knowledge about dengue virus infection is high, and their compliance with PSN 3 M Plus recommendations was far from satisfactory. Non-compliance can be explained by the respondent's attitude (Table 4).

**Table 4.** Respondents Attitude

| Characteristic | Category | Attitude | | | Total |
|---|---|---|---|---|---|
| | | Bad | Medium | Good | |
| **Sex** | Male | 1 | 4 | 6 | 11 |
| | Female | 5 | 23 | 21 | 49 |
| | **Total** | **6** | **27** | **27** | **60** |
| **Age (y.o)** | < 30 | 4 | 14 | 9 | 27 |
| | 30-40 | 2 | 7 | 4 | 13 |
| | 40-50 | 0 | 3 | 6 | 9 |
| | >50 | 0 | 3 | 8 | 11 |
| | **Total** | **6** | **27** | **27** | **60** |
| **Profession** | Work | 4 | 15 | 15 | 34 |
| | Does not Work | 2 | 12 | 12 | 26 |
| | **Total** | **6** | **27** | **27** | **60** |
| **Monthly income** | < Rp. 1.000.000 | 2 | 8 | 9 | 19 |
| | Rp. 1.000.000- Rp. 2.500.000 | 1 | 4 | 5 | 10 |
| | Rp. 2.500.000- Rp. 4.000.000 | 2 | 6 | 7 | 15 |
| | Rp. 4.000.000- Rp. 5.000.000 | 0 | 5 | 2 | 7 |
| | < Rp. 5.000.000 | 1 | 4 | 4 | 9 |
| | **Total** | **6** | **27** | **27** | **60** |
| **Respondent's dengue virus infection history** | Yes | 1 | 2 | 0 | 3 |
| | Not yet | 5 | 25 | 27 | 57 |
| | **Total** | **6** | **27** | **27** | **60** |
| **Family history of dengue virus infection** | Yes | 2 | 2 | 4 | 8 |
| | Not yet | 4 | 25 | 23 | 52 |
| | **Total** | **6** | **27** | **27** | **60** |
| **Knowledge** | High | 5 | 26 | 26 | 57 |
| | Medium | 1 | 1 | 1 | 3 |
| | Low | 0 | 0 | 0 | 0 |
| | **Total** | **6** | **27** | **27** | **60** |

Based on the bivariate analysis, gender and age of respondents were no relationship between compliance with the PSN 3M Plus (p-value >0.05). Therefore, every male and female person should be taking action to eradicate the dengue virus infection vector to control the dengue epidemic.

The characteristics of respondents had no relationship with the PSN 3M Plus compliance (p-value > 0.05). The results of previous studies about the PSN 3M Plus stated a relationship between program adherence and profession.[20–22]

Regardless of their characteristics, people have good knowledge and attitude toward DHF prevention. Many programs and information are available and can be easily acquired by people. There are several DHF-related health promotion programs, such as PSN 3M plus. Some are even socialized through television. Therefore PSN 3M Plus are popular in society. Besides that, due to the number of DHF cases in Indonesia, many mosquito repellent products such as insecticide spray, repellent lotion, mosquito coil, and others are easily found.

Public knowledge and attitude about the dengue virus and its transmission process can be increased by developing, modifying, and intervening in the people controlling dengue virus infection. Prevention and control of dengue virus infection is a shared responsibility. For example, routine fogging carried out by the Health Service, this activity only kills adult mosquitoes, so it does not eliminate the risk of transmission of dengue virus infection, especially larvae and eggs. If fogging cannot kill the larvae in water, 3M Plus prevention must still be conducted by the people, such as closing or covering water containers and reservoirs to become mosquito breeding sites potentially.

Most respondents showed good attitudes and habits toward preventing dengue fever outbreaks. They also took action to protect the whole family from dengue fever and mosquito bites by following the recommendation. DHF prevention practices have been implemented, and they believe that knowledge comes from both educational background and experience.

The present study showed that most people surveyed had experienced dengue virus infection. Mosquitoes like to breed in an environment with clean water. Therefore, most people of Surabaya believe that dengue prevention is the complete responsibility of every people. Discipline in enforcing PSN 3M Plus cannot be based on the high education of an individual. Highly educated individuals are usually busy with their work routines, so they cannot focus on the environment around their homes. This study found that respondents from South Surabaya, Sawahan District, one of the endemic areas of DHF in Surabaya, have complied with the PSN 3M Plus policy based on the questionnaires we distributed. The high rate of dengue virus infection in this area is possible because of the poorly maintained settlements and a large number of nomadic residents.

Understanding the spreading pattern of dengue fever and the risk factors associated with transmission in Surabaya is essential to prevent future outbreaks through targeted vector control of dengue virus infection. Furthermore, disseminating appropriate behaviour change communication messages to improve household level environmental modification of destruction of breeding sites around homes, encourage adherence to personal protection, and identification of disease symptoms as successfully applied in many endemic countries.[23–25]

**Study Limitations**

The limitation of this research study is that author unable to verify the congruence between the respondent's answers with the actions practised in everyday life. However, the strength is that respondents were recruited and information obtained based on criteria in endemic areas. Therefore, the results of this research study are easily applied to the community setting. Furthermore, the study's

eligibility criteria further strengthen the quality of the findings.

## CONCLUSIONS

Respondents have a good level of knowledge and attitude towards dengue prevention efforts. However, the characteristics of the respondents did not significantly affect their knowledge and attitudes. One of the factors that influenced the results was probably the easy access to information related to DHF programs in the community.The results of this study suggest the need for future research regarding Information, education and communication strategies along with current implemented intervention efforts evaluation.

## ACKNOWLEDGEMENT

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## CONFLICT OF INTEREST

The authors declare that they have no competing interests.

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Elsevier Saunders; 2012.

2. Calder PC, Field CJ, Gill HS, editors. Nutritional and immune function. Oxon: CABI Publishing; 2002.

More than 6 authors/editors (Book, Chapter in a book & etc.)

3. Fauci AS, Braunwald E, Kasper DL, Hauser SL, Longo DL, Jameson JL, et al. Harrison's Principles of Internal Medicine. 17th ed. New York: McGraw Hill; 2008.

Chapter in a book

4. Vidyadaran S, Ramasamy R, Seow HF. Stem cells and cancer stem cells: Therapeutic Applications in Disease and Injury. In: Hayat MA, editor. New York: Springer; 2012.

Corporate/Organization as Author

5. Canadian Dental Hygienists Association. Dental hygiene: defi nition and scope. Ottawa: Canadian Dental Hygienists Association; 1995.E-book6. Frank SA. Immunology and Evolution of Infectious Disease [Internet]. Princeton: Princeton University Press; 2002 [cited 2014 December 17]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK2394/pdf/TOC.pdf

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2. Abdullah M, Chai PS, Chong MY, Tohit ERM, Ramasamy R, Pei CP, et al. Gender eff ect on in vitro lymphocyte subset levels of healthy individuals. Cellular Immunology. 2012;272(2):214-9.

Journal article in press

3. Clancy JL, Patel HR, Hussein SM, Tonge PD, Cloonan N, Corso AJ, et al. Small RNA changes enroute to distinct cellular states of induced pluripotency. Nature communications.2014; 5:5522.Epub 2014/12/11.

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An original article is a report on the research objectives and analytical process, as well as a discussion of the implications of the results of a study

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- Materials and Methods
- Results
- Discussion
- Conclusions
- Acknowledgements
- Conflict of Interest
- References (minimum 25 references)

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