



## ANTIMICROBIAL RESISTANCE PATTERNS IN ARTHRITIS GOUT PATIENTS WITH INFECTION

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### ABSTRACT

**Background:** Gout arthritis is a metabolic disease characterized by the accumulation of monosodium urate (MSU) in the joints and soft tissues that cause inflammation. If this inflammatory process continues it will cause severe pain that can decrease the quality of life. The incidence of gout arthritis disease increases from year to year and often coincides with infectious arthritis so analysis of infected joint fluid aspiration is essential to establish an accurate diagnosis and initiate appropriate antimicrobial therapy. The limited data on antimicrobial resistance patterns in gout arthritis patients in Indonesia is the basis for this study. **Objective:** To investigate the pattern of antimicrobial resistance in gout arthritis patients with infection. **Methods:** Descriptive research was conducted at Haji Adam Malik General Hospital Medan and Boloni Hospital from April to July 2018 with 20 samples of gout arthritis patients with infection. **Results:** 20 patients with gout arthritis who had infection, with the most sex was male (60%) with mean age  $52,1 \pm 9,25$  years old and mean of uric acid level  $10,01 \pm 1,73$  mg/dL. The most common microorganisms identified were *Acinetobacter baumannii* and *Escherichia coli*. Cefazolin, Ciprofloxacin and Ampicillin are antimicrobials with high resistance rates  $\geq 80\%$  in this study. **Conclusion:** *Acinetobacter baumannii* and *Escherichia coli* are the most common microorganisms in gout arthritis patients with infections at RSUP H. Adam Malik Medan and RS Boloni Medan whereas high-resistance antimicrobials are Cefazolin, Ciprofloxacin and Ampicillin

**KEYWORDS :** gout arthritis, infection, antimicrobial resistance

### INTRODUCTION

Gout arthritis is one of the metabolic diseases caused by the accumulation of monosodium urate (MSU) in the joints and soft tissues which is associated with impaired purine metabolism.<sup>1</sup> Gout arthritis is the most common inflammatory joint disease in men aged more than 40 years old, with an average global prevalence of 1-4%. In the West, gout arthritis occurs 3-6% in males and 1-2% in females, even in some countries may reach 10% in males and 6% in elderly women.<sup>2,3</sup> Inflammatory responses that occur in the joint will trigger a variety of enzymatic reactions that will eventually cause joint damage and severe pain.<sup>4</sup>

The progression of gout arthritis generally consists of various stages, ranging from asymptomatic hyperuricemia, intermittent uric acid attacks, and long-term chronic gout without remission that can degrade the quality of life of patients and may even lead to complications of renal failure.<sup>1</sup>

The differential diagnosis of gout arthritis and infectious arthritis can be difficult and often missed when these two diseases coincide. Symptoms that occur usually include joint pain involved, redness, swelling and palpable heat, even systemic fever. Hyperuricemia is one of the characteristics that can be used to differentiate gout arthritis with other bacterial infections. Crystal demonstrations in synovial fluid do not rule out the coincidence of bacterial infectious arthritis. The culture of microorganisms should also be performed in cases of arthritis caused by crystals.<sup>5,6</sup> In relation to the background and data, the investigators wanted to investigate the pattern of antimicrobial resistance in gout arthritis patients with the infection.

### METHODS

#### Data Collection

This descriptive study was conducted at Adam Malik Medan General Hospital and Boloni Hospital from April to July 2018

with total sampling method in 20 gout arthritis patients with infection. The determination of infection in gout arthritis patients were based on positive culture results at each gout arthritis infection focus with uric acid levels  $> 7$  mg/dL in male patients and  $> 6$  mg/dL in female patients.

#### Statistics

All data is analyzed using SPSS 22 software. Demographic data is described in number and percentage, then if normal data distribution will be reported in mean  $\pm$  standard deviation whereas if abnormal data distribution will reported with median value (minimum - maximal)

### RESULTS

This study was followed by 20 patients who had been diagnosed with gout arthritis infection at Adam Malik General Hospital Medan and Boloni Hospital from April to July 2018. A total of 12 patients (60%) were male and 8 patients (40%) are women with an average age of  $52,1 \pm 9,25$  years old. Based on the level of education, the majority of respondents in this study were senior high school students (55%), followed by bachelor (20%), primary school (15%) and junior high school (10%). For occupation, 6 patients were housewives (30%), 6 patients were civil servants (30%), entrepreneurs (20%), farmers (10%) and private employees (10%). The results of this study showed that the mean of uric acid level were  $10,01 \pm 1,73$  mg/dL.

**Table 1. Characteristics of Research Subjects**

Characteristics	n = 20
Gender, n (%)	
Male	12 (60)
Female	8 (40)
Age (mean $\pm$ SD), years old	52,1 $\pm$ 9,25
Education, n (%)	
Primary School	3 (15)
Junior High School	2 (10)

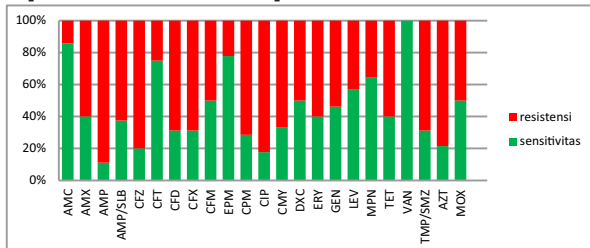
Senior High School	11 (55)
Bachelor	4 (20)
Occupation, n (%)	
Housewives	6 (30)
Civil Servant	6 (30)
Entrepreneurs	4 (20)
Farmers	2 (10)
Private employees	2 (10)
Uric acid, mg/ dL	10,01 ± 1,73

Based on the type of microorganisms of gout arthritis patients with infections, the results showed that the most microorganisms were *Acinetobacter baumannii* and *Escherichia coli* (20%), followed by *Klebsiella pneumonia* by 3 samples (15%). Other microorganisms identified were *Enterococcus faecalis* and *Staphylococcus aureus* each of 2 samples (10%), *Kocuria kristinae*, *Streptococcus pyogen*, *Serratia liquerfaciens group*, *Pseudomonas aeruginosa* and *Proteus mirabilis* each of 1 sample (5%).

**Table 2. Pathogenic microorganism in gout arthritis patients with infection**

Microorganism	n (%)
<i>Acinetobacter baumannii</i>	4 (20)
<i>Escherichia coli</i>	4 (20)
<i>Klebsiella pneumonia</i>	3 (15)
<i>Enterococcus faecalis</i>	2 (10)
<i>Staphylococcus aureus</i>	2 (10)
<i>Kocuria kristinae</i>	1 (5)
<i>Streptococcus pyogen</i>	1 (5)
<i>Serratia liquerfaciens group</i>	1 (5)
<i>Pseudomonas aeruginosa</i>	1 (5)
<i>Proteus mirabilis</i>	1 (5)

The pattern of antimicrobial resistance and sensitivity in gout arthritis patients with infection can be seen in Figure 1. The picture shows that some types of antimicrobials have good sensitivity such as Vancomycin (100%), Amikacin (86%) and Ertapenem (78%). While some antimicrobials have high resistance (≥ 80%) in this study that is Cefazolin (80%), Ciprofloxacin (82%) and Ampicillin (89%).



**Figure 1. Resistance and Antimicrobial Sensitivity in Arthritis Gout Patients with Infection**

Note: AMC: Amikacin; AMX: Amoxicillin; AMP: Ampicillin; AMP/SLB: Ampicillin/ Sulbactam; CFZ: Cefazolin; CFT: Cefotaxime; CFD: Ceftazidime; CFX: Ceftriaxone; CFM: Cefuroxime, EPM: Ertapenem; CPM: Cefepime; CIP: Ciprofloxacin; CMY: Clindamycin; DXC: Doxycycline; ERY: Erythromycin; GEN: Gentamycin; LEV: Levofloxacin; MPN: Meropenem; TET: Tetracycline; VAN: Vancomycin; TMP/SMZ: Trimethoprim/ Sulfamethoxazole; AZT: Aztreonam; MOX: Moxifloxacin

**DISCUSSION**

This study shows data on demography of 20 gout arthritis patients with infection, 12 men (60%) versus 8 women (40%). This result is in accordance with previous research conducted by Chai et al that reported a comparison of incidence of gout arthritis between men versus women was 4: 1.4.<sup>7</sup> The results of this study also corresponded to data obtained in 2017 which reported that in Western countries, gout arthritis occurs in 3-6% of males and 1-2% in females and the prevalence

continues to increase to 10% in males and 6% in females.<sup>8</sup>

The average age of gout arthritis patients with infection in this study is 52,1 ± 9,25 years old. This is in accordance with the results of a metaanalysis by Lu et al that reported that the prevalence of gout arthritis increased in elderly so that would greatly affect the quality of life.<sup>9</sup> Another study conducted by Choi et al involving 67 patients with gout arthritis reported that the average age of gout arthritis were 53,7 ± 17,1 years old.<sup>5</sup>

This study also shows that the most microorganisms that cause gout arthritis with infection are *Acinetobacter baumannii* (20%), *Escherichia coli* (20%) and *Klebsiella pneumonia* (15%). This is appropriate with the research conducted by Chiu et al in 2013, they found that gram-negative bacteria is the most common bacteria found in patients with gout arthritis who have an infection. Gram negative bacteria include *Acinetobacter baumannii*, *Serratia marcescens*, *Stenotrophomonas malthophilia*, *Pseudomonas mendocina*, *Ralstonia spp* and *Ochrobactrum athropi*. While *Staphylococcus aureus* is the most common gram-positive bacteria from the culture.<sup>10</sup> Another study by Crane et al in the United States mentions that *Escherichia coli* is the most common gram-negative bacteria identified in gout- arthritis patients with infection.<sup>11</sup> Another study conducted by Yu KH et al reported that the most gram-positive microorganisms in gout with infections were *Staphylococcus aureus* (16 cases), *Streptococcus sp* (5 cases) and *Pediococcus sp* (1 case).<sup>12</sup>

The pattern of antimicrobial resistance and sensitivity in gout arthritis patients with infections shows that some antimicrobials have good sensitivity to gout-causing microorganisms with infections such as Vancomycin (100%), Amikacin (86%) and Ertapenem (78%). This is in accordance with previous research by Panicker et al who reported that antimicrobial types Vancomycin and Piperacillin/ Tazobactam are antimicrobials with good sensitivity in cases of gout arthritis with infection.<sup>13</sup> The adequate management of gout arthritis with infection should be based on the culture/ isolation of microorganisms from the infected joint. The infectious microorganisms may spread haematogenously to the synovial membrane from one joint to another. The results of this study are in accordance with antimicrobial therapy recommended as an empirical therapy for gram positive bacteria which is Vankomisin 15-20 mg/ kg body weight given every 8-12 hours, can also be treated with Ceftriaxon 1 gr every 12 hours combined with azithromycin 1 gr every day (or doxycycline 2 x 100 mg for 7 days). While empirical therapy for gram-negative bacteria can be given Vancomycin 15-20 mg/ kg body weight given every 8-12 hours combined with Ceftriaxone 1 gr every 24 hours, can also with Vancomycin 15-20 mg/ kg body weight given every 8-12 hours combined with Cefepime 2 gr every 8-12 hours (for elderly and immunocompromised patients).<sup>14</sup> While some antimicrobials have high resistance rates (≥ 80%) in this study: Cefazolin (80%), Ciprofloxacin (82%) and Ampicillin (89%). Nowadays, It's very important to give an appropriate empirical antimicrobial therapy guideline in accordance with local antimicrobial bacteria surveillance as the treatment of gout arthritis with infection in order to manage this disease comprehensively.

**CONCLUSION**

*Acinetobacter baumannii* and *Escherichia coli* are the most common microorganisms in gout arthritis patients with infections at Adam Malik Hospital and Boloni Hospital. Some antimicrobials have high resistance rates (≥ 80%) in gout arthritis patients with infections such as Cefazolin, Ciprofloxacin and Ampicillin.

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