Microbiological profile of causes of corneal ulcers at sultan agung islamic teaching hospital semarang

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INTRODUCTION

Corneal ulcers are discontinuities or partial loss of the corneal surface due to the death of corneal tissue. The formation of corneal ulcers is due to collagenases formed by new epithelial cells and inflammatory cells. Healed corneal ulcers will cause corneal scarring and are the cause of blindness. Epidemiological data states that corneal ulcer incidence is mainly caused by trauma followed by cornea infection. Men are more than women; the age is mostly the productive age of 21-40 years, the occupation is mostly farmer. Both infectious and non-infectious agents can cause corneal ulcers. The most common corneal ulcers caused by bacteria are Staphylococcus aureus, Staphylococcus epidermidis, Streptococcus pneumoniae.

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Keywords
microbiology; corneal ulcer; Sultan Agung Islamic Teaching Hospital Semarang

ABSTRACT

Background
Corneal ulcer is a medical condition that is the most significant cause of morbidity and blindness worldwide, caused most often by bacteria and fungi. This study aimed to determine the microbiological profile of the causes of corneal ulcers at Sultan Agung Islamic Teaching Hospital, Semarang.

Methods
This research is a descriptive study with a cross-sectional design. Samples were all patients with corneal ulcers at Sultan Agung Islamic Teaching Hospital Semarang from July 1, 2018 – July 31, 2023; the sampling method used consecutive sampling, and the sample size was the total population. Samples were taken using a scraping on the cornea, then implanted directly in Blood Agar Plate and Saboroud Dextrose Agar. Bacterial colonies are identified using API®, and a susceptibility test was performed on Muller Hinton Agar using the Kirby Bauer method. Fungal colonies are identified using Lacto Phenol Cotton Blue, Gram, and Germ Tube.

Results
There were 85 samples, with no growth as many as 41 samples (48%). Fungi cause more infections than bacteria. The fungus that causes the most extensive corneal ulcers is Aspergillus sp as much as 13, while the group of bacteria is Staphylococcus coagulase negative as much as 4 (50%)

Conclusion
Most of the microorganisms that cause corneal ulcers are fungi compared to bacteria. No Multi-Drug Resistant Organisms were found in the causative bacteria, and no azole resistance was found in fungi.

Keywords
microbiology; corneal ulcer; Sultan Agung Islamic Teaching Hospital Semarang

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Streptococcus pyogenes, Moraxella sp, Pseudomonas aeruginosa, Proteus sp, Klebsiella pneumoniae, and Escherichia coli\textsuperscript{4,5}. Fungi can also cause infection in corneal ulcers. The most extensive fungi that cause infection in the cornea are Culvularia sp, Aspergillus sp, Paecilomyces sp, Cladosporium sp, Bipolaris sp, Alternaria sp, and Candida sp\textsuperscript{6,7}. Infection can also be caused by viruses or parasites, namely Herpes Simplex\textsuperscript{8}, or Acanthamoeba\textsuperscript{9}. Causes of non-infectious corneal ulcers include trauma, which is acidic or alkaline, radiation trauma, and temperature\textsuperscript{10}.

Early diagnosis of lesions, profile of causative microorganisms and appropriate antimicrobial therapy can be used to control infection in lesions to prevent complications and improve the patient’s quality of life. Antibiotic sensitivity testing on microorganisms that cause corneal ulcers is also necessary for infection management to carry out appropriate and accurate therapy\textsuperscript{9,11}. Resistant bacteria cause some infection-causing microbes in corneal ulcers. Pseudomonas aeruginosa is reportedly resistant to the antibiotic moxifloxacin\textsuperscript{12} and other fluoroquinolones\textsuperscript{13}. The microbiological profile of one place is different from another. This study aims to determine the microbiological profile of the causes of corneal ulcers at Sultan Agung Islamic Teaching Hospital Semarang. The profile to be studied includes etiology and antimicrobial sensitivity tests.

**METHOD**

This is descriptive research. The samples of this study are all patients with corneal ulcers at Sultan Agung Islamic Teaching Hospital Semarang from July 1, 2018 – July 31, 2023; the sampling method uses consecutive sampling, the sample size is the total population. Samples were taken using scrapings on the cornea, then planted directly in the medium Blood Agar Plate (bacterial growth medium) and Saboroud Dextrose Agar (fungal growth medium), and Gram and Giemsa staining are carried out. Bacterial colonies growing on the Blood Agar medium were then identified using API\textsuperscript{14} and sensitivity tests were carried out on the Muller Hinton Agar medium by the Kirby Bauer method\textsuperscript{14}. Fungal colonies that grow on Saboroud Dextrose Agar medium are followed by a mushroom identification test using LPCB (Lacto Phenol Cotton Blue) staining for mold type fungi, while yeast types are identified using Gram staining and Germ Tube.

### Table 1. Etiology of Corneal Ulcer

<table>
<thead>
<tr>
<th>Fungal</th>
<th>n</th>
<th>%</th>
<th>Bacteria</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspergillus sp*</td>
<td>13</td>
<td>36,1</td>
<td>Staphylococcus coagulase negative</td>
<td>4</td>
<td>50</td>
</tr>
<tr>
<td>Fusarium sp</td>
<td>6</td>
<td>16,7</td>
<td>Pseudomonas aeruginosa</td>
<td>3</td>
<td>37,5</td>
</tr>
<tr>
<td>Penicillium sp</td>
<td>3</td>
<td>8,3</td>
<td>Enterobacter cloacae</td>
<td>1</td>
<td>12,5</td>
</tr>
<tr>
<td>Acremonium sp</td>
<td>3</td>
<td>8,3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Culvularia sp</td>
<td>2</td>
<td>5,6</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alternaria sp</td>
<td>2</td>
<td>5,6</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paecilomyces sp</td>
<td>1</td>
<td>2,8</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trichophyton sp</td>
<td>1</td>
<td>2,8</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Candida sp</td>
<td>5</td>
<td>13,8</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Aspergillus flavus:11, Aspergillus fumigatus:2
Table 2. Antibiotic Sensitivity Test

<table>
<thead>
<tr>
<th>Bacteria</th>
<th>Ampicillin</th>
<th>Cefotaxime</th>
<th>Ceftazidime</th>
<th>Cefepime</th>
<th>Ciprofloxacin</th>
<th>Gentamicin</th>
<th>Meropenem</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Staphylococcus coagulase negative</em></td>
<td>25</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td><em>Pseudomonas aeruginosa</em></td>
<td>0</td>
<td>0</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td><em>Enterobacter cloacae</em></td>
<td>0</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>

**DISCUSSION**

The results of the antibiotic sensitivity test show that many etiology-causing bacteria are still sensitive to various classes of antibiotics, for example, *Pseudomonas aeruginosa* is still sensitive to anti-pseudomonal antibiotics, such as cephalosporins (ceftazidime, cefepime), fluoroquinolone group (ciprofloxacin), aminoglycoside group (gentamicin), and carbapenem group (meropenem). *Staphylococcus coagulase-negative* bacteria are mainly resistant to ampicillin.

The results of culture ethology of corneal ulcer causes at Sultan Agung Islamic Teaching Hospital Semarang are no different from other places, where most of them are dominated by fungi, and the most significant causes are *Aspergillus sp* and *Fusarium sp*. Fungi are the most common cause of corneal ulcers. There are 70 species of fungi that can cause corneal ulcers, but the most common are yeast and molds. *Aspergillus* and *Fusarium* are fungi responsible for 1/3 of traumatic corneal ulcer cases, so proper diagnosis and effective therapy are needed. Predisposing factors to corneal ulcers due to fungi are mainly caused due to trauma with parts of the plant. Trauma can damage normal defence mechanisms and allow normal conjunctival flora or pathogenic flora to enter to invade damaged corneal tissue. Tissue damage will significantly threaten vision and potential corneal perforation. Management of fungal infections is more difficult because most antifungals are fungistatic, so they require a longer time to eradicate. The yeast group antifungal sensitivity test (*Candida sp*) results at Sultan Agung Islamic Teaching Hospital Semarang are all sensitive to azole group antifungals. This study needs to improve due to limited infrastructure for mold antifungal sensitivity tests.

The pattern of microorganisms that cause keratitis varies based on variations in geography as well as local climate. The bacteria that cause corneal ulcers in Sultan Agung Islamic Teaching Hospital Semarang in the gram-negative group are *Pseudomonas aeruginosa*, while in the gram-positive group by *Staphylococcus coagulase negative*. The results of this study are the same as results elsewhere. *Pseudomonas aeruginosa* is a causative...
bacterium that is often found in cases of corneal ulcers. These bacteria can cause corneal perforation if the diagnosis and treatment of infection is inappropriate. The attachment of *Pseudomonas aeruginosa* to the cornea is caused by its piles containing magnesium and calcium, as well as biofilms that can damage the epithelium. The antibiotic sensitivity pattern in the bacteria that cause corneal ulcers at Sultan Agung Islamic Teaching Hospital Semarang is still sensitive in the gram-positive and gram-negative groups. This is different from other regions, where many resistant organisms or MDRO (Multi Drug Resistant Organism) have begun to be found, for example *Pseudomonas aeruginosa* resistance to fluoroquinolone antibiotics, and the discovery of *Staphylococcus aureus* Resistance to Metisillin as a cause of corneal ulcers. 48% of samples with clinical corneal ulcers did not grow on culture. This is likely because Sultan Agung Islamic Teaching Hospital Semarang is a referral hospital, and patients have received antimicrobial therapy for a long time before being referred.

**CONCLUSION**

The microorganism that causes the most corneal ulcers is the fungus with the most isolate, namely *Aspergillus flavus*, while for the most bacteria caused by *Staphylococcus coagulase negative* in the Gram positive group, and *Pseudomonas aeruginosa* in the

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**Figure 1.** a) Corneal ulcers due to bacteria, b) Corneal ulcers due to fungi, c) Corneal scraping hyphae in gram staining, d) *Culvularia sp* in Lacto Phenol Cotton Blue staining, e) *Aspergillus sp* in Lacto Phenol Cotton Blue staining, f) *Aspergillus sp* colonies in saboroud dextrose agar medium.
gram negative group. No MDRO was found in the causative bacteria, and no azole resistance was found in the fungal sensitivity test. The limitations of this study are that it has not been able to display identification and sensitivity tests for mold class antifungals, and does not test on the causes of other microorganisms such as viruses or parasites.

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Author Contribution:

Study design: Masfiyah, Rahayu, Nika Bellarinasari
Data gathering: Masfiyah, Rahayu, Nika Bellarinasari
Data analysis: Masfiyah, Rahayu, Nika Bellarinasari
Writing and submitting the manuscript: Masfiyah, Rahayu, Nika Bellarinasari, Putri R Ayuningtyas
Editing and approval of final draft: Masfiyah, Putri R Ayuningtyas

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