

Profile and resistance pattern of *Stenotrophomonas maltophilia* in Dr. Soetomo General Academic Hospital During 2020-2022 Period

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Abstract

Introduction: *Stenotrophomonas maltophilia* is a challenging respiratory tract pathogen with increasing number of cases. *S. maltophilia* also shows a high resistance towards various antibiotics. The aim for this study is to know the antibiotic resistance pattern and profile of patient infected with *S. maltophilia* in order to find out effective antibiotic therapy in treating future cases.

Methods: This cross-sectional study uses descriptive analytic method using medical record data of 36 patients infected with *S. maltophilia* in Dr. Soetomo General Academic Hospital during 2020-2022 period. The measured variables included antibiotic resistance pattern, age, sex, clinical diagnosis, comorbidity, signs and symptoms, medical device usage, total leukocyte count, and mortality rate.

Result: *S. maltophilia* shows highest sensitivity index towards Trimetophrim-sulfomethoxazole (56%). Cases of *S. maltophilia* is most often found in 0-17 years age group (53%) and male (63%). It may cause infection whether alone or alongside other bacteria. The most common clinical diagnosis that occurs in *S. maltophilia* infections is pneumonia (81%). Dyspnea is the most occurred symptoms. Hypertension is a common comorbidity. IV infusion is the most used medical device. Might cause infection alongside other bacteria. Leukocytosis is often present. Mortality rate among subjects is 50%.

Conclusion: Trimetophrim-sulfomethoxazole is the best treatment for *S. maltophilia* infections. Cases most often occurs in age 0-17 years, male, diagnosed with pneumonia, and has hypertension as comorbidity. In the future, antibiotics must be used wisely to prevent bacterial resistance and regular changing of medical device is encouraged to prevent nosocomial infections.

Keywords: *Stenotrophomonas maltophilia*; Antibiotic resistance; Bacterial infection; Patient profile; Pneumonia

1. Introduction

Stenotrophomonas maltophilia is a gram negative aerob bacteria, known as *Bacterium bookeri* during its first discovery in pleural fluid specimen on 1943. In 1961, this bacteria was known as *Pseudomonas maltophilia*, then changed into *Xanthomonas maltophilia* in 1983 until it was finally classified as *S. maltophilia* in 1992⁽¹⁾. Most cases of *S. maltophilia* infection are associated with healthcare associated infections, one of the risk factors is the use of catheters in hospitalized patients. Other risk factors associated with *S. maltophilia* infection are a history of disease, chronic

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respiratory disorders, immunocompromised host, use of antibiotics and a long treatment period in hospital or ICU. In a study conducted by Layanto et al. at X hospital, it was found that the mortality rate of patients whose sputum specimens shows a presence of *S. maltophilia* was 52,94% (2).

One of the challenges in dealing with infections caused by *S. maltophilia* is that its clinical manifestations are often non-specific and indistinguishable from other infections (1). A study conducted by Guerci et al. showed that 86,61% of *S. maltophilia* isolates were often found in lower respiratory tract specimens, such as in cases of pneumonia. In a study conducted by Patmanathan and Waterer in Royal Perth Hospital, *S. maltophilia* were found in sputum culture of patients with acute tracheobronchitis, acute exacerbation of chronic obstructive pulmonary disease, healthcare-associated pneumonia, community-acquired pneumonia, and infective exacerbation of bronchiectasis. Another infections associated with *S. maltophilia* infection includes: skin and soft tissue infections, osteomyelitis, meningitis, urinary tract infections, endocarditis, and biliary sepsis (3).

S. maltophilia does not have high virulence, but recent cases of healthcare-associated infections caused by *S. maltophilia* have been increasing in hospital and ICU. *S. maltophilia* can also be found in various parts of hospital setting and equipment, such as water taps, sinks, air conditioners, disinfectant fluids, nebulizers, IV fluids, catheters, even in hands of health workers working in hospital. In addition to its ability to survive in hospital environment, *S. maltophilia* has also shown 80% resistance to the antibiotic trimethoprim-sulfamethoxazole which is considered the first line of treatment for *S. maltophilia* infection (1).

With the adaptation and changes in *S. maltophilia* that continues to grow rapidly and its ability to cause high mortality, especially in immunocompromised hosts, further studies regarding the pattern of resistance of this microorganism to various antibiotics are needed, especially in Dr. Soetomo General Academic Hospital during 2020-2022 period. It is important to find out effective antibiotic therapy in treating cases of *S. maltophilia* infection. In addition to pattern of antibiotic resistance, profile of infected patients also needs to be identified to get a more specific information about the spread pattern of *S. maltophilia*

2. Methods

A cross-sectional study was conducted in Dr. Soetomo General Academic Hospital, using medical record data from both Microbiology Department and medical record unit. Patients with lower respiratory tract infections (LRTI) such as pneumonia, bacteremia, chronic obstructive pulmonary disease (COPD), and acute tracheobronchitis who are infected by *S. maltophilia* and has a complete medical record data were included in this research. Patient who has incomplete medical record data and has no antibiotic susceptibility test result were excluded from the study. The medical record data needed for the research are as follows: antibiotic resistance pattern, age, sex, comorbid disease, clinical diagnosis, signs and symptoms, medical device usage, total leukocyte count, classification of infection, and mortality rate.

The data was collected using a formulated case report form integrated to Microsoft Office Excel. After collection, data will be processed and analyzed using statistic descriptive method, using data processing software *Microsoft Office Excel*. The processed data showing distribution of each variables is presented in table, diagram, and chart. This study was approved by the ethics committee of Dr. Soetomo General Academic Hospital with ethical clearance certificate number of 1411/LOE/301.4.2/VIII/2023.

3. Results

Of the 46 patients that shows positive culture of *S. maltophilia*, 36 patients with complete medical record data is included in this research. Most cases of *S. maltophilia* infections occurs in age range of 0-17 years old (53%) and least in 41-40 years old (3%). Male patients are more susceptible towards *S. maltophilia* infections compared to female patients. The most common comorbidity to occurs in *S. maltophilia* infection cases is hypertension (8%). Pneumonia often happened in cases of *S. maltophilia* infection in lower respiratory tract, with the percentage as follows: pneumonia (61%) and pneumonia with sepsis (25%). Signs and symptoms occurring in *S. maltophilia* infections are often related to its clinical diagnosis, most often being pneumonia. The signs and symptoms that might occurs such as dyspnea (61%), cough (31%), nausea (17%) and vomiting (17%). Mortality rate of patients infected with *S. maltophilia* in Dr. Soetomo General Academic Hospital during 2020-2022 period is 50%. These data are presented in Table 1.

Table 1 Subject Demographic

Variable	Category	Percentage
Age (years old)	0-17	53%
	18-30	6%
	31-40	11%
	41-50	3%
	51-60	6%
	>61	3%
Sex	Male	64%
	Female	36%
Comorbidities	SLE	3%
	UTI	3%
	DMT 2	3%
	Hypertension	8%
	Anemia	6%
	LBW	6%
	HIV	3%
Clinical Diagnosis	Pneumonia	61%
	Pneumonia with sepsis	25%
	COPD	3%
	Acute tracheobronchitis	0%
Signs and Symptoms	Dyspnea	61%
	Cough	31%
	Nausea	17%
	Fever	8%
	Breath retraction	8%
	Vomiting	17%
Status	Dead	50%
	Alive	50%

S. maltophilia can manifest as a single bacterial infection, where it is the sole infectious agent, or alongside other bacteria. The most common bacteria that can cause co-infection with *S. maltophilia* are *Klebsiella pneumoniae* (14%), *Pseudomonas aeruginosa*, *Candida tropicalis*, *Candida glabrata*, and *Staphylococcus coagulase negative* (6%). 50% of cases found are single infection of *S. maltophilia*, whereas 50% are multiple infection of *S. maltophilia* and another bacteria as presented in Table 2.

Generally, bacterial infections shows an increased number in leukocytes since it's considered to be a marker of inflammation. In *S. maltophilia* infection cases, *Leukocytosis* or elevation of white blood cell count is a common finding in cases of infection, including *S. maltophilia*. When the number of white blood cells in human body exceeds 11.000/mm³, it is considered as leukocytosis. However, leukocytosis is not the ultimate indicator for infection. Normal amount of leukocyte does not rule out the possibility of bacterial infections. More cases of leukocytosis are found before the patient received any treatment compared to after receiving treatment as presented on Table 3.

Table 2 Profile of patients based on infection type (single/multiple)

Infection type		Percentage
Single		50%
Multiple	<i>Klebsiella pneumoniae</i>	14%
	<i>Candida tropicalis</i>	6%
	<i>Candida albicans</i>	3%
	<i>Pseudomonas aeruginosa</i>	6%
	<i>Candida glabrata</i>	6%
	Staphylococcus coagulase negative	6%
	<i>Enterobacter cloacae</i>	3%
	<i>Corynebacterium striatum</i>	3%
	<i>Acinetobacter baumannii</i>	3%

Table 3 Total Leukocyte Count (TLC) before and after treatment

Reference Number (/mm ³)	Before Treatment	After Treatment
<4.500	0%	3%
4.500-11.000	8%	19%
>11.000	92%	78%

The most used medical device in patients infected with *S. maltophilia* is intravenous (IV) infusion, followed by ventilator. Infusion and ventilator are medical devices that is installed in the body for some period of time, not immediately discharged upon use. The usage of medical device is also associated with a definitive risk of bacterial infections, especially bacteria who can encourage the growth of biofilms such as *S. maltophilia*. The data is presented on Table 4.

Table 4 Medical device usage in *S. maltophilia* infections

Medical Device Used	Percentage
Intravenous (IV) Infusion	67%
Catheter	17%
Ventilator	56%
NGT	8%
Transfusion	22%
Injection	22%
Central Venous Catheter (CVC)	19%

In this research, not every antibiotics are tested on each subject. The percentage mentioned above is obtained by using 36, which is the total sample number as the denominator. Only 35 subjects are tested for SAM, KZ, and CTX. 34 subjects are tested for MEM, 31 subjects are tested for SCF, 25 subjects tested for TGC, and 19 subjects tested for FOS.

Trimethoprim-sulfomethoxazole (SXT) shows the highest sensitivity rate against *S. maltophilia* infections with the percentage of 56% or tested sensitive in 20 subjects infected with *S. maltophilia*. Followed by Levofloxacin (LEV) with 53% or tested sensitive in 19 subjects and Tigecycline (TGC) with 42%, tested sensitive in 15 subjects. Antibiotics with

sensitivity percentage above 50% is considered effective in treating the infection. As for the resistance, SXT has 44% resistance against *S. maltophilia*, LEV has 39%, and TGC has 25%. Some antibiotics are also ineffective in treating *S. maltophilia* infections, such as AMP, ATM, CRO, and TE, showing 100% resistance towards *S. maltophilia*, which is highly associated with a likelihood of therapeutic failure. Information regarding antibiotic resistance pattern of *S. maltophilia* can be seen in Table 5

Table 5 Antibiotic Resistance Pattern percentage

Antibiotic	Sensitive (S)%	Intermediate (I)%	Resistant (R)%
AK	3%	0	97
AMC	0%	3%	97%
AMP	0%	0%	100%
ATM	0%	0%	100%
C	17%	28%	94%
CAZ	28%	11%	58%
CN	0%	0%	61%
CRO	6%	0%	100%
CTX	0%	0%	97%
FOS	22%	3%	31%
IMP	3%	0%	97%
KZ	0%	0%	97%
LEV	53%	8%	39%
MEM	3%	0%	94%
PIPE	0%	0%	97%
SAM	0%	0%	97%
SCF	36%	14%	47%
SXT	56%	0%	44%
TE	0%	0%	100%
TGC	42%	6%	25%
TZP	0%	3%	97%

4. Discussion

S. maltophilia shows the highest sensitivity index towards its first-line treatment, Trimetophrim-sulfomethoxazole or SXT with the percentage of 56%. The second highest, Levofloxacin or LEV, has a 53% sensitivity in *S. maltophilia* cases in Dr. Soetomo General Academic Hospital during 2020-2022 period. Having a sensitivity percentage above 50%, SXT and LEV is considered to be the effective treatment regimens against *S. maltophilia* infections. However, this might cause another problem in the future regarding the treatment of *S. maltophilia* infections. As there are not many antibiotics that shows high effectivity in treating *S. maltophilia*, SXT and LEV, which are broad spectrum antibiotics, will be used frequently in cases of *S. maltophilia*. However, Levofloxacin might cause serious damage to the muscles such as tendonitis or Achilles tendon rupture and Trimetophrim-sulfomethoxazole might cause hypersensitivity reactions (4).

Due to its ability to form biofilms, *S. maltophilia* often colonizes the respiratory tract of hospitalized patients. In this study, 29 out of 36 patients (81%) is diagnosed with pneumonia. This aligns with previous findings of *S. maltophilia* that is mainly linked to acute exacerbations of COPD and respiratory tract infections, such as pneumonia (5).

Children's immune system are not yet fully developed, hence why they're more likely to catch infections. Treatment of *S. maltophilia* in children is also more challenging compared to adults because of the possible adverse effects of drugs that is often used in *S. maltophilia* treatment, such as Trimetophrim-sulfomethoxazole and fluoroquinolones such as levofloxacin (6).

Females generally have stronger adaptive and innate immune response compared to males, thus making the pathogen clearance and response to vaccination better in females. On the other hand, stronger immune response make females more susceptible to autoimmune and inflammatory diseases. Compared to males, females also express more pathogen-associated molecular pattern receptor, higher B cell numbers, higher IgM and IgG levels, and greater antibody responses (7).

S. maltophilia is an opportunistic pathogen that can cause infections by itself or alongside other bacteria. The most frequent bacterial infection that occurs in the same time as *S. maltophilia* is *Klebsiella pneumoniae*. However, not many studies are present regarding co-infection of *S. maltophilia* and *Klebsiella pneumoniae*. On the other hand, it is possible for *S. maltophilia* and *P. aeruginosa* to build a polymicrobial biofilm, with each organism in its own separate stratum, according to analysis of in vitro biofilms that they have formed. *P. aeruginosa* also promoted the persistence of *S. maltophilia* in the Live *P. aeruginosa* was necessary for this higher persistence, and there was a direct correlation between *S. maltophilia* numbers and the quantity of present *P. aeruginosa* (1).

There is no specific signs and symptoms that indicates *S. maltophilia* infection because it's usually undistinguishable from other bacterial infection and related to the affected organ systems. *S. maltophilia* often occurs in various diagnosis of respiratory tract infection such as pneumonia, thus making most of the patients showing typical respiratory symptoms such as dyspnea and cough (8).

Most patients found in this research has hypertension as comorbidity. Though the relationship regarding *S. maltophilia* infection and hypertension has not been studied, hypertension can have significant interactions with infection in general. Infections may cause inflammatory responses, which can impact blood pressure regulation. Chronic inflammation is known to affect the cardiovascular system and may worsen hypertension. Numerous physiological processes, such as renal abnormalities, endothelial cell dysfunction, and central nervous system dysregulation, play a role in the development of hypertension.. Many cell types and released substances are involved in the intricate process of inflammation, which has been linked to hypertension in numerous instances (9).

In bacterial infections, leukocytosis or tend to happen because the body produces more white blood cells to fight off invading pathogens. This align with the findings of this research, which shows leukocytosis in 28 out of 36 patients (78%). However, the fact that leukocytosis is associated with infection does not mean that the white blood cell count is a reliable test for infection.

S. maltophilia has the ability to form biofilms on moist surfaces, whether in direct or indirect contact to patients, such as IV infusion, catheters, respiratory tubing, IV lines, dialysis equipment, dental equipment, and hospital plumbing systems such as faucets and sinks. In this research, it was found that patients infected with *S. maltophilia* mostly use IV infusion and ventilator device. *S. maltophilia* also shows a potency for biofilm formation, being able to attach to surfaces within two hours of incubation and reach maximum biofilm intensity within 24 hours of incubation. With the usage of IV infusion and ventilator that usually lasts for a prolonged period of time, risk of infection and biofilm formation also increases (8).

For a considerable amount of time, *S. maltophilia* has been linked to high death rates and has been identified as a source of serious nosocomial infections such as bloodstream infections and pneumonia primarily in patients who are incapacitated. *S. maltophilia* is an important nosocomial pathogen associated with crude mortality in the hospitalized ranging between 14 and 69%. In this research, a 50% mortality rate of *S. maltophilia* infection is obtained. Due to the fairly high mortality rate and multitude of resistance mechanisms, *S. maltophilia* infection is a serious issue that needs to be treated wisely (10)

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Abbreviations

- AK: Amikacin
- AMC: Amoxicillin-clavulanic acid
- AMP: Ampicillin
- ATM: Aztreonam
- C: Chloramphenicol
- CAZ: Ceftazidime
- CN: Gentamycin
- CRO: Ceftriaxone
- CTX: Cefotaxime
- FOS: Fosfomycin
- IMP: Imipenem
- KZ: Cephazolin
- LEV: Levofloxacin
- MEM: Meropenem
- PIPE: Piperacillin-tazobactam
- SAM: Ampicillin-Sulbactam
- SCF: Sulbactam
- SXT: Trimethoprim-sulfomethoxazole
- TE: Tetracycline
- TGC: Tigecycline
- TZP: Tazobactam-piperacillin

5. Conclusion

Cases of *S. maltophilia* is most often found the age range of 0-17 years old and is least found in age group of 41-50 years old. Cases of *S. maltophilia* is more often found in male. Hypertension is the most common comorbidity that occurs in patients infected with *S. maltophilia*. Most common diagnosis found in *S. maltophilia* infection is pneumonia. Most common symptoms found in *S. maltophilia* infection is dyspnea. Most cases of *S. maltophilia* shows leukocytosis. Number of leukocytosis cases decreases after patient has been treated. The most frequent medical device that is used in patients infected with *S. maltophilia* is IV infusion followed by ventilator *S. maltophilia* infection may occur as a single infection or alongside other bacteria, especially *Klebsiella pneumoniae*. Mortality rate of *S. maltophilia* in Dr. Soetomo General Academic Hospital during 2020-2022 is 50%. Trimetoprim-sulfomethoxazole or SXT is the most effective drug in treating *S. maltophilia* .

Compliance with ethical standards

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Disclosure of conflict of interest

The authors declared there is no conflict of interest.

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Authors' Contributions

Fauzia Rachma Diena, Eko Budi Koendhori, Anna Surgean Veterini, and Tutik Kusmiati participated in research design formulation, collecting and analysing data, and paper writing.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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