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Prevalence and Antibiogram of *Stenotrophomonas maltophilia* in a Tertiary Care Hospital at Trivandrum, Kerala, India

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A B S T R A C T

Stenotrophomonas maltophilia causes opportunistic infections and is an emerging opportunistic pathogen. The rate of infections due to these bacteria has increased in recent years and so is their resistance to antimicrobials. Thus, the present study was conducted with an objective to identify *Stenotrophomonas* isolation from various clinical samples and to study its antimicrobial sensitivity/ resistance pattern which will guide clinicians in prophylactic antibiotic therapy. A total of 400 clinical samples were collected from patients admitted in ICU and other wards of the hospital. All samples were inoculated on to Blood Agar (BA) and MacConkey Agar (MA) plates under strict aseptic conditions, followed by incubation at 37ºC for 24-48 hours under aerobic conditions. Antimicrobial susceptibility testing was performed by Kirby Bauer disc diffusion method on Mueller Hinton agar. Out of 400 samples, 48.57% sputum samples, 34.38% of pus sample, 14.28% blood ssmples and 2.85% of other samples were positive for isolates.

Keywords

Stenotrophomonas maltophilia, antibiogram, antimicrobial susceptibility, antibiotic resistance

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Introduction

Originally classified as *Pseudomonas maltophilia*, *Stenotrophomonas maltophilia* is an obligate aerobe and a ubiquitous organism. It causes opportunistic infections and is an emerging opportunistic pathogen. It is the third most commonly encountered non-fermenter in clinical laboratory next to *Pseudomonas* and *Acinetobacter*. It is an important nosocomial pathogen associated with substantial morbidity and Mortality rate of 43% especially in immunosuppressed patients, patient in intensive care unit, and pulmonary source of the isolate. (1)

The most common site for recovery of *S.maltophilia* is the respiratory tract. It is frequently isolated from patients with ventilator support in ICU. It produces proteolytic enzymes, deoxyribonucleases, ribonucleases, hemolysins, hyaluronidase and mucinase etc. which contribute to its severity in immunosuppressed patients.

The rate of infections caused by *S.maltophilia* is increased in recent years and are being isolated from wound infections, bacteremia, pneumonia, endocarditis, urinary tract infections, meningitis and peritonitis. *S.maltophilia* is oxidase negative, motile, catalase positive, indole negative, citrate variable, urease negative,lysine and DNAse positive. (2, 3)

S.maltophilia is susceptible to colistin and polymyxin. The antibiotic susceptibility pattern can be a clue to the identification of *S.maltophilia.* The most active agents are trimethoprim sulphamethoxazole, colistin and quinolones. Like other nonfermenters it is intrinsically resistant to many common antibiotics like aminoglycosides, carbapenams and many betalactam agents. Development of resistance in these organism is multifactorial.

Factors involved are-mutations in genes encoding porins, efflux pump mechanisms, penicillin binding proteins, chromosomal beta lactamases. Success of antimicrobial therapy depends on the appropriateness of the choice of antibiotics that should be used on the basis of prior knowledge of the susceptibility pattern of the agent.(4, 5)

Epidemiological studies of clinical *S. maltophilia* isolates have shown genetic diversity, probably associated with selection of naturally present *S. maltophilia* from among other bacteria by antibiotic pressure. However, cross-infections between patients, transmitted by healthcare workers, have also been reported. For this reason, detection of antibiotic resistance patterns and typing of *S. maltophilia* isolates is significant in the context of hospital infection control. Itis a readily available commensal of importance, found in water, soil, sewage and frequently on plant or within plant rhizosphere.(6)

The bacteria explore the depression of immune systems to cause infection, though they have also been implicated in infection of immunocompetent subjects. They are therefore important considering their infectivity and the morbidity they initiate, which range from nosocomial to community acquired infections. It propagates in moist environments (water, medical equipment, soil and sewage) and colonizes medical devices.

Dialysed patients are an ideal target for infections: they are immunosuppressed because of uraemia, old age, malnutrition, comorbidities and the increased use of artificial accesses such as prosthetic grafts, central venous or peritoneal catheters.(7)

The present study was conducted with an objective to identify Stenotrophomonas isolation from various clinical samples and to study its antimicrobial sensitivity/ resistance pattern.This study is also directed to guide the clinicians for prophylactic antimicrobial therapy.

Materials and Methods

The study was conducted at Shree Gokulam Medical College and Research centre, Trivendrum from January 2016 to December 2016. A total of 400 clinical samples were collected from patients admitted in ICU and various wards of the hospital of depending upon the clinical diagnosis of respective patients.

Out of these 35 isolates of Stenotrophomonas was isolated. These included: pus, blood, sputum and other samples. All samples were collected and processed as per standard microbiological guidelines. Samples were inoculated on to Blood Agar (BA) and MacConkey Agar (MA) plates under strict aseptic conditions and plates were incubated at 37ºC for 24-48 hours under aerobic conditions. (8)

All isolates that showed non-lactose fermenting colonies on MA and those which grew only on BA and not on MA were subjected to Gram staining and all gram-negative bacilli/cocci/coccobacilli obtained were then subjected to triple sugar iron test. The bacterial isolates which produced alkaline/acid (K/A) reaction and acid/acid (A/A) reaction were excluded.

Isolates which produced an alkaline/alkaline (K/K) reaction were provisionally identified as non-fermenters and were included in this study and subjected to identification upto genus/species level by a battery of biochemical tests.8 Oxidative/Fermentative (O/F) test for glucose, lactose, sucrose, mannitol and xylose, oxidase test, motility test, nitrate reduction test, lysine and ornithine decarboxylase test, arginine dihydrolase test, gelatin liquefaction test, urease test, indole production test, citrate utilization test, growth at 42ºC and 44ºC.

Antimicrobial susceptibility testing was performed by Kirby Bauer disc diffusion method on Mueller Hinton agar as per CLSI guidelines using commercially available discs. (9, 10, 11) Following antimicrobial discs were used: ceftazidime (30µg), cefepime (30µg), piperacillin-tazobactum (100µg/10 µg), aztreonam(30µg), imipenem (10µg), meropenem(10 µg), gentamicin (10µg), amikacin (30µg) netilmicin (30 µg), ciprofloxacin (5µg), norfloxacin (30µg; for urinary isolates), polymyxin B (300 units) and colistin (10µg).

Plates were incubated at 37º C for 18-24 hours and results were interpreted according to zone sizes mentioned in the CLSI guidelines. (12)All dehydrated media and antibiotic discs were procured from HiMedia Labs, Mumbai, India.

Statistical analysis was done by descriptive statistics using percentages and ratios method. Sensitivity was performed using control strains of *Staphylococcus aureus* ATCC25923, *E. coli* ATCC25922, and *Pseudomonas* ATCC 27853.

Results and Discussion

Between Jan 2016 to Dec 2016, 35 patients with underlying haematological or oncological disease were diagnosed with *S. maltophilia* bacteraemia. Of these, 15 had Diabetes mellitus, 10 had COPD, 5 patients were on ventilator and 5 patients were immunocompromised. The demographical data and patients' sample wise distribution are listed in Table 1 and 2.

Table.1 Gender Distribution (n=35)

Sex	Number	Percentage (%)
Male	**23**	**65.72**
Female	**12**	**34.28**

Table.2 Sample wise distribution (n=35)

Sample	Size	Isolates	Percentage (%)
Sputum	**120**	**17**	**48.57**
Pus	**202**	**12**	**34.28**
Blood	**45**	**5**	**14.28**
Others	**33**	**1**	**2.85**
Total	**400**	**35**	**100**

Table.3 Comorbidity conditions (n=35)

Underlying conditions	Number	Percentage (%)
COPD	**10**	**28.57**
Ventilator	**5**	**14.28**
Diabetes mellitus	**15**	**42.85**
Immunocompromised	**5**	**14.28**

Maximum isolates were obtained from sputum and pus samples followed by blood and others. Out of 400 samples, 48.57% sputum samples, 34.38% of pus sample, 14.28% blood samples and 2.85% of other samples were positive for isolates.

Table 3 and 4 represents the results of the comorbid conditions and antibiogram conducted on the isolates. *S. maltophilia* was also found to be multidrug resistant pathogen showing resistance to various groups of antibiotics. All isolates of *S. maltophilia* were resistant towards Amikacin and Gentamicin, Sensitive to Ceftazidime, Cefoperazone-Sulbactum, Piperacillin-Tazobactum and to Cotrimoxazole.

Out of 35 patients, 10 patients (28.57%) suffered from COPD, 15 patients were diabetic, 5 patients (14.28%) were on ventilator and 5 patients (14.28%) were immunocompromised.

Of all the isolates, 100% resistance was observed towards Amikacin and Gentamicin. 100% sensitivity was observed towards Ceftazidime, 96% sensitivity towards Cafoperazone-sulbactam combination, 94% sensitivity towards Piperacilin-tazobactam combination and 93% sensitivity towards Cotrimoxazole.

Non-fermenters were usually considered as commensals or contaminants in the past but have now emerged as important health care pathogens. These organisms are associated with life threatening infections such as-septicaemia, pneumonia, UTI, meningitis, surgical site infections, ventilator associated pneumonia, osteomyelitis etc. and resistance to antimicrobials have resulted in difficulty in treatment of infections caused by these bacteria. (13)

NFGNB are intrinsically resistant to various antimicrobials and are known to produce extended spectrum betalactamases (ESBL's) and metallobetalactamases (MBL's).

Table.4 Antibiogram (n=35)

Antibiotics	Sensitive	Resistant
Ceftazidime	**100**	**0**
Cotrimoxazole	**93**	**7**
Cefoperazone-sulbactam	**96**	**4**
Piperacillin-tazobactam	**94**	**6**
Amikacin	**0**	**100**
Gentamicin	**0**	**100**

The recovery rate of this bacterium appears to be increasing with time compared to when the bacteria was initially discovered. (14)

Fluoroquinolone and polymycin B, both of which showed good activities against the *S. maltophilia* isolates, are usually the antibiotics of choice in the treatment of infections by the bacteria. The activities of these antibiotics against the bacteria have been similarly reported by Gales *et al.,* and Tripodi *et al.,* (15, 16) However, it is known that trimethoprim-sulfamethoxazole is the drug of therapeutic choice against *S. maltophilia* infections ; but several reports have shown that the prevalence of *S. maltophilia* strains that are resistant to trimethoprim-sulfamethoxazole are increasing. (17)

S. maltophilia causes infections mainly in hospitals and is a particular risk for debilitated patients. This organism is ubiquitous in the environment and in the hospital setting. Since it is able to grow in many different media in the presence of most antimicrobial agents, *S. maltophilia* is isolated with increasing frequency as a nosocomial pathogen.

The annual isolation rate per 10 000patient discharges rose from 7.1 in 1981 to 14.1 in 1984 at a university hospital in the USA. (18)
A widespread study between 1997 and 2001, including data from Asia-Pacific, Europe and America, showed that *S. maltophilia* was the third most frequently isolated non-fermentative bacterium, following P. aeruginosa and *Acinetobacter*, with a rate of isolation from clinical specimens of 8%. (19)

As described above, the isolation frequency of *S. maltophilia* increased during the period of the present study (8.5%), but further investigations are needed to clarify the underlying reasons for this increase.

In the present study, *S. maltophilia* isisolated most often from respiratory specimens (sputum), pus and blood. Valdezate *et al.,* described about 105 *S. maltophilia* isolates obtained between 1995 and 1998, 79 of which were from the respiratory tract and 19 from blood. (20).

Isolation of *S. maltophilia* from polymicrobial cultures may be related to a true infection, and is an important consideration in determining initial treatment, since b-lactamases leaking from *S. maltophilia* cells can facilitate the survival of b-lactam-susceptible microorganisms (21, 22).

The many risk-factors that predispose to the development of *S. maltophilia* infection include prolonged hospitalisation, especially in ICUs, consumption of broad-spectrum antibiotics, malignancy, immune suppression, and a breakdown in mucocutaneous defence

barriers (e.g., following catheterisation, artificial implants, tracheostomy, or peritoneal dialysis). (23) Most of the patients (85.4%) in the present study had underlying diseases, including 14.6% who had malignant diseases. These results are in accordance with previously published data. *S. maltophilia* is resistant to a wide spectrum of antimicrobial agents.

In a worldwide surveillance study that included 1488 isolates obtained between 1997 and 2001, resistance to the antimicrobial agents tested was > 50%, withthe exception of co-trimoxazole (5%), gatifloxacin (5%), levofloxacin (6%), ticarcillin–clavulanate (14%) and ceftazidime (34%). (24) Similarly, the present study found resistance rates of > 60% for all antimicrobial agents except co-trimoxazole.

When an isolate is identified as *S. maltophilia*, cotrimoxazole, ticarcillin–clavulanate, doxycycline, minocycline and the newer quinolones, such asofloxacin, levofloxacin, sparfloxacin and moxifloxacin, may be possible options for treatment. (21)
Although the NCCLS suggests the use of dilution methods for testing antimicrobial susceptibilities of *S. maltophilia*, the correlation between in-vitro resistance and the clinical response is unknown. (25, 26)

The incubation time and temperature for susceptibility testing remain controversial, with an increase in incubation time influencing the resistance rates of *S. maltophilia* forco-trimoxazole, ciprofloxacin, b-lactams and aminoglycosides. According to the susceptibility of the bacterium, a prolonged combination therapy of endovenous aminoglycosides plus levofloxacin or ceftazidime or trimethoprim/ sulfamethoxazole, and a locked-in instillation of gentamicin or ceftazidime, is safe, with an excellent outcome for both the patient and the catheter. (27,28)

S. maltophilia is an emergent pathogen in dialysis units, causing infection in peritoneal and haemodialysis patients. As it is a natural inhabitant in most environments inside and outside the hospital setting, it can induce infections in immunosuppressed subjects.

From the present study it can be concluded that maximum isolates of *Stenotrophomonas maltophilia* can be obtained from sputum and pus of affected patients.

It has also been demonstrated from the present study that S.maltophilia is multidrug resistant to various groups of anitbiotics. In the present study, the antibiogram conducted showed that all isolates of S.maltophilia were resistant towards most commonly used penicillin Amikacin and Gentamicin. At the same time, they were sensitive to other individual and combination antimicrobials such as Ceftazidime, Cefoperazone-Sulbactum, Piperacillin-Tazobactum and to Cotrimoxazole.

The treatment of *S. maltophilia*-related infection could be cumbersome because of several bacterial and host characteristics. Antibiotic therapy, if well conducted, shall be able to cure the infection in most cases; in a few cases, it preserves patient safety and dialysis access patency too.

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