

Stenotrophomonas maltophilia in Lower Respiratory Tract Infections

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ABSTRACT

Background: *Stenotrophomonas maltophilia* infection is gaining importance as an important cause of nosocomial pneumonia due to its characteristic inherent resistance to many broad-spectrum antibiotics. In this study we evaluated the demographic, clinical and microbiological profile of patients with lower respiratory tract infection due to *Stenotrophomonas maltophilia*.

Materials and Methods: A retrospective analysis of 33 patients diagnosed with *Stenotrophomonas maltophilia* lower respiratory tract infections during a period of two years from 2012 - 2013 was done.

Results: The predominant predisposing factor observed was mechanical ventilation in 17(51.5%) cases. Fluoroquinolones

were the most effective antibiotic (26;78.8%) followed by trimethoprim-sulfamethoxazole (24;72.7%). Among the 19 patients treated with proper antibiotic, 13(68.4%) showed clinical improvement. Among the 14 patients who did not receive appropriate antibiotic for *Stenotrophomonas maltophilia* infection, 8(57.1%) showed improvement. Two (6%) had blood culture positive for *Stenotrophomonas maltophilia*. Mortality rate was 21.2%.

Conclusion: *Stenotrophomonas maltophilia* is emerging as an important nosocomial pathogen with increased risk in patients on mechanical ventilation in ICU. Empiric therapy should include agents active against *S.maltophilia* such as newer fluoroquinolones and trimethoprim-sulfamethoxazole.

Keywords: Antimicrobial drug resistance; Quinolones, *Stenotrophomonas maltophilia*, Trimethoprim-sulfamethoxazole

INTRODUCTION

Stenotrophomonas maltophilia was first classified within the genus *Pseudomonas* in 1961, then as *Xanthomonas* in 1983 and finally as *Stenotrophomonas* in 1993 [1]. *S. maltophilia* is the only species of *Stenotrophomonas* known to infect humans. It is an obligate aerobic, non-fermentative gram negative bacillus that is present in almost any aquatic or humid environment [2].

Though it is not a virulent bacterium, today *S.maltophilia* has emerged as an important multi-drug resistant pathogen in hospitalized patients [3]. Respiratory infections constitute the predominant infection caused by this pathogen. Risk factors for acquiring respiratory infections by *S.maltophilia* are patients on ventilator; prolonged stay in hospital, underlying malignancy or obstructive pulmonary disease and extended exposure to a broad spectrum antibiotics [4].

Due to the property of biofilm formation it often colonizes the respiratory tract of hospitalized patients. In such cases to differentiate between colonisation and infection can be challenging. Moreover, the patients who are initially colonized with this pathogen may later develop infection. The pathogen has gained importance due to production of Chromosomally encoded zinc-dependent β -lactamases that confer resistance to carbapenems and other β -lactams [2]. Trimethoprim-sulfamethoxazole (TMP-SMX) as monotherapy or in combination with another bactericidal antibiotic is considered as the treatment of choice for serious clinical infection [1,3]. There are only few planned studies done earlier especially in India, assessing the microbiological and clinical significance of *S.maltophilia* in lower respiratory tract infections (LRTIs). Majority of studies have focused on multi-drug resistant *Pseudomonas* spp. and *Acinetobacter* spp. isolation from patients having LRTIs. Hence this study was undertaken to evaluate the demographic, microbiological and clinical details of patients diagnosed with LRTIs due to *S.maltophilia*.

MATERIALS AND METHODS

This retrospective study was conducted in a tertiary care hospital of Coastal Karnataka, India for two years duration (Jan 2012–Dec

2013). All respiratory samples from patients having LRTIs, which were culture positive for *S.maltophilia* during the study period were included in the study. Lower respiratory tract samples including sputum, endotracheal aspirates or bronchoalveolar lavage fluid (BAL) from patients with symptoms and signs of LRTIs were processed by microscopy and culture. Microscopy was done according to Bartlett's grading system. Culture for all the respiratory samples was done on sheep blood agar, MacConkey agar and chocolate agar and incubated at 37°C for 18-24 hours in 5-10% CO₂. Culture for ET aspirates and BAL specimens was done quantitatively. Cut-offs for ET aspirates and BAL were taken as $\geq 10^5$ and $\geq 10^4$ CFU/ml. Isolates were identified based on the biochemical reactions as per standard guidelines and were further confirmed by Vitek2 system. The antibiotic susceptibility testing of *S.maltophilia* was performed by Kirby-Bauer disc diffusion method using commercially available discs (Span Diagnostics Ltd, Surat, India) according to Clinical Laboratory Standards Institute (CLSI) guidelines [5]. The isolates were tested against TMP-SMX (1.25/23.75 μ g) and levofloxacin (5 μ g).

Demographic and clinical details of the patients which included age, gender, clinical presentation, associated risk factors and comorbidities, radiological findings, use of antimicrobial therapy and prognostic outcomes were collected from the medical records. Blood culture reports of the patients, wherever possible, were also collected to study bacteremia due to *S.maltophilia*. Clinical and radiological findings of the patient were correlated and compared to assess the clinical significance of the *S.maltophilia* isolates. Descriptive analysis of results was performed using statistical software, SPSS version 16.0.

RESULTS

During the study period, *S.maltophilia* was isolated from 33 respiratory samples that include sputum (17, 51.5%) and endotracheal aspirates (16, 48.5%). Eighteen (54.5%) of the patients were admitted in intensive care units. The predominant predisposing factor observed

Parameter	Number of cases (%)
Median Age in years (range)	55 (13-98)
Gender	
Male	24 (72.7)
Female	09 (27.3)
Presenting clinical features	
Fever	14 (42.4)
Cough with expectoration	14 (42.4)
Breathlessness	25 (75.8)
Risk factors	
Mechanical ventilation	17 (51.5)
Chronic respiratory disease	10 (30.3)
Nebulisation	07 (21.2)
Malignancy	02 (6.1)
Chemotherapy	02 (6.1)
Co-morbidities	
Tuberculosis	05 (15.2)
COPD	02 (6.1)
Bronchial asthma	03 (9.1)
Diabetes mellitus	06 (18.2)
Ischaemic heart disease	04 (12.1)
Hypertension	13 (39.4)
Chronic kidney disease	02 (6.1)
Abdominal disease	02 (6.1)
Blood Investigations	
Total leucocyte count(mean \pm SD)	15030.30 \pm 6001.5 (mm ³)
Blood culture	2/27 (7.4)
Chest radiography	
Normal	06 (18.1)
Pneumonia	24 (72.7)
Pneumothorax	02 (6.0)
Hemothorax	01 (3.0)

[Table/Fig-1]: Demographic and clinical profile of patients with *S. maltophilia* LRTI

	Total no. of cases	Improvement No. (%)	No Improvement No. (%)	All-cause mortality No. (%)
Treatment with appropriate antibiotic	19	13(68.4)	1(5.3)	5(26.3)
Treatment with inappropriate antibiotic	14	8(57.1)	4(28.6)	2(14.3)

[Table/Fig-2]: Outcome of patients infected with LRTI due to *S. maltophilia*

was mechanical ventilation in 17(51.5%) patients. Radiologically, 24(72.7%) patients showed features suggestive of pneumonia. Details of demographic and clinical details of patients are shown in [Table/Fig-1]. Sensitivity to levofloxacin was observed in 26 (78.8%) strains whereas sensitivity to TMP-SMX was noticed in isolates 24 (72.7%). *S. maltophilia* was isolated as monomicrobial flora from 20 (60.6%) patients and as part of polymicrobial flora in the rest 13 (39.4%) cases. The other bacteria which were isolated as part of polymicrobial flora include, *K. pneumoniae* (4), *P. aeruginosa* (4), *S. aureus* (3) and *Acinetobacter* sp. (2). *S. maltophilia* was repeatedly isolated from 2(6.1%) patients.

Outcome of patients was compared in two groups of patients [Table/Fig-2]. Group I included patients (n=19) who were treated with appropriate antibiotic according to susceptibility pattern and Group II (n=14) included patients who did not receive antibiotics according to the susceptibility pattern of *S. maltophilia* isolates. In group I, 13/19(68.4%) patients showed clinical improvement whereas 5/19(26.3%) cases expired. In group II, 8/14(57.1%)

patients showed improvement, 4/14(28.6%) showed status quo whereas mortality was noticed in 2 (14.3%) cases [Table/Fig-2]. Overall mortality rate was 21.2% (7 cases) and the main causes of mortality among these patients were acute respiratory distress syndrome (ARDS) and septic shock.

DISCUSSION

The study has revealed the isolation of *S. maltophilia* predominantly in elderly males (>55 years). Males are more prone to infections due to their outdoor activities. The susceptibility of infection more so in old age can be described by decreased immunity. Risk factors associated with *S. maltophilia* infections include immunosuppressive and invasive therapies, admission to the intensive care unit, advanced age, prolonged hospitalization, surgical procedures and prior therapy with broad-spectrum β -lactam antibiotics, aminoglycosides or quinolones [6-8]. Present study has shown that half of the patients (51.5%) were on ventilator and another 30% were having chronic respiratory disease [Table/Fig-1].

An interesting finding of this study was that 18% of these cases were having normal chest X-ray whereas 72.7% were having features suggestive of pneumonia. Tsang et al., have described the importance of CT-scan in these patients [9]. Both of his patients described were having normal chest radiology but CT-scanning helped to diagnose the lung involvement.

Inherent drug resistance of this pathogen towards beta lactam antibiotics, quinolones and aminoglycosides is of major concern [6,8]. It limits the options for the treatment of infections due to *S. maltophilia*. TMP-SMX, ticarcillin-clavulanate, doxycycline, minocycline and some new fluoroquinolones are the only agents with activity against this organism [6,10]. Low membrane permeability that contributes to resistance to β -lactams including cefepime, ticarcillin-clavulanate, ceftazidime, and piperacillin-tazobactam; chromosomally encoded multidrug resistance efflux pumps; β -lactamases; and antibiotic-modifying enzymes contribute to the intrinsic antibiotic resistance of *S. maltophilia* [11]. CLSI has published disc-diffusion interpretative standards for *S. maltophilia* towards trimethoprim-sulfamethoxazole, levofloxacin and minocycline; and dilution MIC standards including other drugs, ticarcillin-clavulanic acid, ceftazidime and chloramphenicol. Our study has demonstrated maximum susceptibility to levofloxacin (78.8%) followed by TMP-SMX (72.7%). Though latter is considered the first treatment of choice but recently resistance to this antibiotic is also being observed. Many studies have demonstrated the emergence of strains resistant to TMP-SMX. Resistance is attributed to sul1 and sul2 genes present on integrons, transposons or plasmids. Combination treatment is viewed as a better option as compared to monotherapy. Combination therapy like TMP-SMX with levofloxacin or with ticarcillin-clavulanic acid is considered better. A study done by Toleman et al., has shown the resistance to TMP-SMX in 45% of strains [12]. However, present study has shown lower rates of resistance (18.5%) towards TMP-SMX.

Another important observation made by the study was that in patients who were given treatment according to the susceptibility pattern displayed better clinical improvement (68%) as compared to the group that was not given appropriate treatment (57%) [Table/Fig-2]. Earlier Kwa et al., have reported in their study that either inability to institute appropriate therapy or delay in treatment of infection caused by *S. maltophilia* can increase the mortality rate of such cases [13]. Though more mortality is seen in group of patients treated with appropriate antibiotics as compared to other group, it may be due to severity of disease or underlying morbidity. The dilemma the clinicians face is whether to consider the isolation of *S. maltophilia* as colonization or infection. More studies are needed to be done to answer this question. But in patients having underlying malignancy or other comorbidities and patients already undergoing treatment in intensive care unit, *S. maltophilia* should be considered

as a pathogen. Being a retrospective study, the study has few limitations. First, differentiation of colonized vs infected cases could not be done. Second, the source of infection was not studied.

CONCLUSION

S.maltophilia is an important respiratory pathogen in hospital settings. Early identification and appropriate therapy is advocated. The treating clinicians should be aware of inherent resistance of *S.maltophilia* to multiple antibiotics so as to manage these patients effectively.

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