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Stenotrophomonas maltophilia an Emerging Opportunistic Bacterial Infection Isolated from Diverse Clinical Samples

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Abstract **Aim:** The aim of this study was to assess the prevalence of infection, antimicrobial susceptibility pattern of *Stenotrophomonas maltophilia* in diverse samples in the Delhi. **Materials and Methods:** This is a retrospective study conducted over a period of three years, i.e., January 2019 to December 2021. All clinical samples received in the microbiology laboratory at *Dr Lal Path Labs*, Delhi during the study period were processed using standard microbiological procedures. Antibiotic susceptibility was performed for Levofloxacin, Minocycline and Trimethoprim-sulfamethoxazole by Vitek 2 system (bioMerieux, India) as per CLSI guidelines. **Results and Discussion:** A total of 9615 non fermenters were isolated, among the non-fermenters, 375 (3.9%) were *Stenotrophomonas maltophilia*. The most prevalent source of *S. maltophilia* was largely isolated from blood (34.7%) followed by fluids (20.3%), respiratory (17.8%) and other specimens. This study highlighted potency and the limitation of available agent in the era of antibiotic resistance especially in Delhi, India. Our study describes the distribution and antibiotic resistance of Levofloxacin, Trimethoprim-sulfamethoxazole and Minocycline based on cumulative interpretation and MIC across all age groups. **Conclusion**: The *Stenotrophomonas maltophilia* isolates collected in our study had relatively high susceptibility to Minocycline, good susceptibility to Trimethoprim/sulfamethoxazole, but low susceptible to Levofloxacin. Minocycline, could be useful alternative treatment options in Trimethoprim/sulfamethoxazole and Levofloxacin resistant strains.

Keywords: *Stenotrophomonas maltophilia (S. maltophilia), Trimethoprim/sulfamethoxazole (TM/SXT), minocycline, Levofloxacin (LVX), non fermenters, nosocomial*

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1. Introduction

Stenotrophomonas maltophilia (*S. maltophilia*) is a motile, gram-negative, oxidase-negative, and catalase-positive, biofilm forming, non-fermenting, as an opportunistic nosocomial pathogen previously known as *Pseudomonas maltophilia* or *Xanthomonas maltophilia* [1,2,3].

Stenotrophomonas maltophilia is the only species of *Stenotrophomonas* known to infect humans and has been recognized as global emerging gram-negative MDRO that is most commonly associated with a cause of severe nosocomial infections with significant mortality, such as bacteremia, pneumonia, urinary tract infection, meningitis, endocarditis [2,5].

In 2019-2021, *S. maltophilia* was the third most frequent, non-fermentative, gram-negative bacterium at our lab. The risk factors for *S. maltophilia* colonization and infections include previous exposure to broad-spectrum antibiotics, prolonged hospitalization, an intensive care unit stay, mechanical ventilation, use of intravascular devices, and an immunocompromised host [3]. The organism has been show to survive several biocides used in the hospital setting. Hospital water sources can serve as a reservoir for *S. maltophilia* [2,6].

The treatment of *S. maltophilia* is challenging due to its multidrug resistance such as intrinsically resistant to the majority of commonly used drugs such as decreased permeability, the production of beta-lactamase and carbapenemase enzymes, the production of aminoglycoside-modifying enzymes, and the presence of multidrug efflux pumps [5,10]. The correct identification of *S. maltophilia* is very important because it is very challenging for a routine laboratory to identify *S. maltophilia*, due to its inert biochemical profile and difficulty in the interpretation of phenotypic characteristics and physicians do not recognize the risk factors and clinical characteristics of *S. maltophilia* infections, which later leads to high mortality.

This study set out to first time in this region to establish the prevalence of *S. maltophilia* infections in different age

groups in diverse samples and the administration of appropriate antibiotics to combat this organism. Knowing such information about *S. maltophilia* infections may increase physicians' abilities to make early diagnoses, thereby improving the clinical outcomes.

Since the 1980s, the drug of choice in *S maltophilia* infections is sulfamethoxazole-trimethoprim (SMX/TMP); SMX/TMP resistance is a serious concern in clinical practice. *S. maltophilia* is not a highly virulent pathogen, but it has emerged as an important nosocomial pathogen associated with crude mortality rates ranging from 14 to 69% in patients with bacteremia and pneumonia [1,5,11].

2. Method

In this retrospective study 375 *S. maltophilia* isolated from different clinical specimens during three-year period (Jan 2019 to Dec 2021) at Microbiology department of *Dr Lal Path Labs*, Delhi. More advanced and standardized methods, such as MALDI-TOF MS (Bruker, Daltonics) were used for identification and the antimicrobial susceptibility was evaluated by VITEK® 2 using susceptibility card (AST 281, BioMerieux, India) as per as CLSI M100-S-31 [8]. Isolates were tested against with the following antibiotics: Trimethoprim-sulfamethoxazole, Levofloxacin and Minocycline.

3. Statistical Analysis

Descriptive statistical analysis was performed using the statistical software package MYLA (Biomerieux). Age, gender, *S. maltophilia* causing infections and their antibiotic sensitivity and resistance with MIC were included as variables in this study.

4. Results

A total of 9615 non fermenters were isolated, out of which 375 were *S. maltophilia*. Among the non-fermenters, 375 (3.9%) were *S. maltophilia* which were isolated from various clinical specimens such as, blood, respiratory tract (sputum, Broncho alveolar lavage, endotracheal tip) pus, urine, sterile body fluids. The most prevalent source of *S. maltophilia* was largely isolated from blood (34.7%) followed by fluids (20.3%), respiratory (17.8%) and other specimens. [Figure 1]

Out of the 375 patients, 239 (63.7%) were males and 136 (36.2%) were females. Data were then analyzed for variables such as age range was 0 to 99 years. In our study the most predominant age group infected with *Stenotrophomonas* were elderly adults (>=66 years) constituted 28.5% followed by adults (36-50) (21.6%), children (0-12) (20.3%) respectively [Table 1].

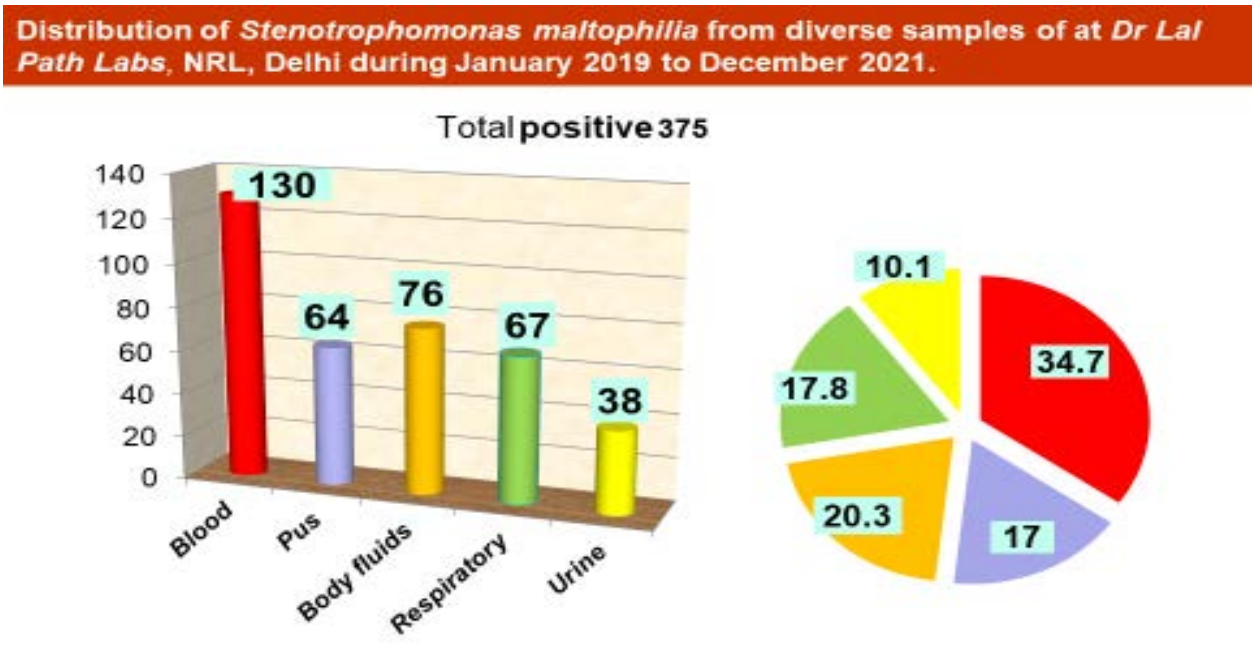

Figure 1. Distribution of *S. maltophilia* in Diverse Samles

Table 1. Distribution and Percentage of cumulative interpretation of *S. maltophilia* in different age groups in diverse samples

Age groups	Blood N (%)	Pus N (%)	Fluid N (%)	Respiratory N (%)	Urine N (%)	Total N (%)
0-12	38 (50%)	19 (25%)	17 (22.3%)	2 (2.6%)	0	76 (20.3%)
13-35	19 (37.3%)	5 (9.8%)	15 (29.4%)	6 (11.8%)	6 (11.8%)	51 (13.6%)
36-50	24 (29.6%)	14 (17.3%)	16 (19.8%)	12 (14.8%)	15 (18.5%)	81 (21.6%)
51-65	18 (30%)	6 (10%)	10 (16.7%)	20 (33.3%)	6 (10%)	60 (16%)
>=66	31 (28.9%)	20 (18.7%)	18 (16.8%)	27 (25.2%)	11 (10.3)	107 (28.5%)

Table 1: also depicts correlation with the prevalence of *S. maltophilia* isolates among samples were stratified by age group, the most frequently identified *S. maltophilia* in blood of all age groups, but it was especially high among pediatric age group (50%). The prevalence of *S. maltophilia* infection in respiratory samples increased by age group for example,>=51 age group [Table 1].

In addition, we assessed the antimicrobial susceptibilities with cumulative MIC activity of TM/SXT and LVX against 375 and Minocycline for 79 isolates that comprises *S. maltophilia* that were isolated from various clinical specimens with the help of Myla statistical analysis (Biomerieux, India) in *Dr Lal Path Labs* during the study period.

All the isolates of *S. maltophilia* shown highly resistant to Levofloxacin 23.2 %. Levofloxacin activity (MIC50/90, 1/8 µg/ml) against 375 *S. maltophilia* demonstrated that 50 % and 90% isolates were within 1µg/ml and 8 µg/ml respectively. 89% sensitive to TM/SXT was having MIC50/90 (<=20/80 µg/ml) were noted, in Delhi.

On the other hand, 79 tested isolates of *S. maltophilia* were recorded high susceptibilities to Minocycline 99.2% (MIC at which 50% and 90% of isolates were inhibited (MIC50 & MIC90), <=0.5 and 4µg/ml respectively). [Table 2]

In this study, selected antimicrobials included which possessed sensitivity patterns against *S. maltophilia* among different samples. The best antimicrobials among non-fermenter gram-negative *S. maltophilia* were Minocycline, TM/SXT and moderate resistance rate were reported in Levofloxacin. In Blood and other samples TM/SXT found to be sensitive against >90% and >80% individuals respectively [Figure 2] whereas highly resistant drug were levofloxacin in Urine, Fluid and Pus demonstrated that 42.9%, 35.7% and 30% respectively. In other hand levofloxacin were showed moderate resistance in blood and respiratory [Figure 2]. Although minocycline was tested for susceptibility in only 21% of cultures, 99.2% of isolates were found to be susceptible in diverse samples [Table 2].

Table 2. Antimicrobial susceptibilities with cumulative MIC for *S. maltophilia* by broth dilution

Stenotrophomonas maltophilia	Range	Total No.	MIC 50/90 (µg/ml)	% Sensitive	% Resistant
Trimethoprim Sulfamethoxazole	**≤ 20 - ≥80**	375	<=20/80	89	11
Levofloxacin	**≤ 0.5 - ≥2**	375	1/8	76.8	23.2
Minocycline	**≤ 4 -≥ 16**	79	<=0.5/4	99.2	0.8

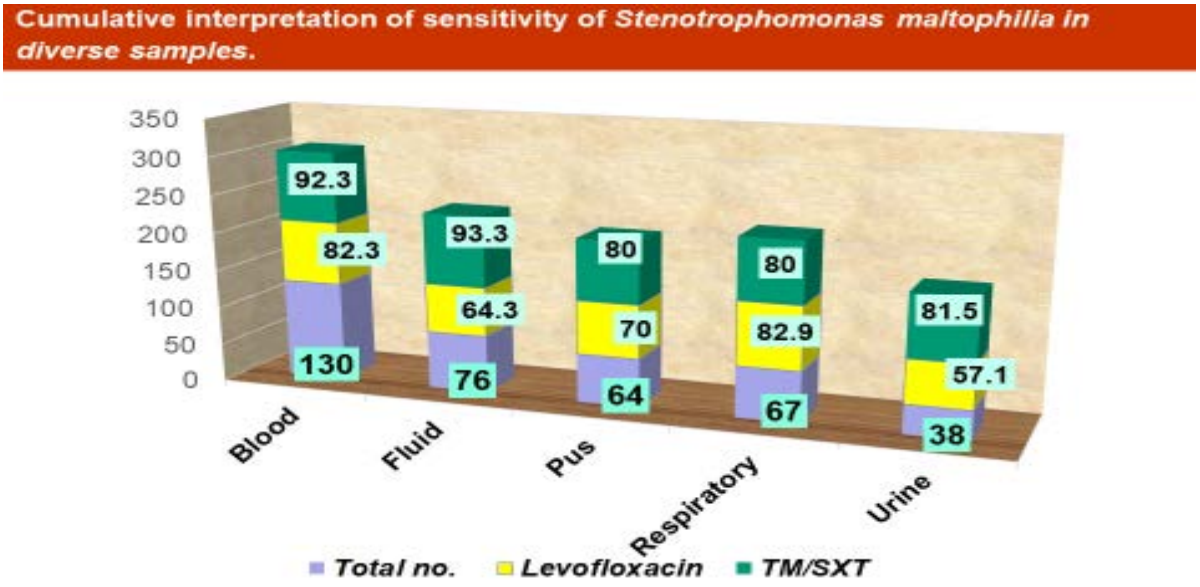

Figure 2. Percentage of cumulative interpretation of sensitivity of *S. maltophilia* in diverse samples

5. Discussion

In this study we tested 375 cases with an *S. maltophilia* infection during a 3-year period at a large tertiary care laboratory, Dr Lal path labs in Delhi capital of India. *S. maltophilia* has been recognized as a cause of severe nosocomial infections that is ICU patients or patient with a long hospital stay, mainly in debilitated patients such as extensive surgeries, mechanical ventilation, and dialysis, patients with chronic illnesses (e.g., bloodstream infections and pneumonia) or cancer [1,6,11].

In this Study *S.maltophilia* was the third most frequent, non-fermentative, gram-negative bacterium causing bacteremia in the children (0-12) and in elderly adults (>=66 years) *S. maltophilia* isolates had most with respiratory infection which was similar to the findings of several other studies. [1,11,13,15,17] The significance in children of isolation from other sites is less clear that is concordance with other study [3,18].

S. maltophilia infections have been associated with high mortality, in many study reporting that the mortality related to bacteremia in children and adults has been reported to be high, with crude mortality rates ranging from 14 to 54% [1,6,9-13]. In our study, main type of infection caused by *S. maltophilia* was bloodstream infection followed by respiratory, body fluids, Pus and this finding correlated with the other study [12]. In contrast many studies reported that respiratory specimen were most prevalent [9,13]

Treatment of infection caused by *S. maltophilia* is complicated because this pathogen exhibits multi drug resistance (MDR). The intrinsic resistance of *S. maltophilia* to multiple antibiotics, including Cephalosporins and Carbapenem, which are commonly used for empiric therapy, makes it a therapeutic challenge. This study highlighted potential and the limitation of available agent in the era of antibiotic resistance especially in Delhi, India. Our study describes the distribution and antibiotic resistance of LVX, TM/SXT and Minocycline based on cumulative interpretation and MIC across all age groups. Pathogen isolates were tested for antimicrobial susceptibility following the CLSI M 31 guidelines [8].

For the treatment of *S. maltophilia* infections, Trimethoprim/sulfamethoxazole (TMP/SMX) is the most effective as the drug of choice; this study demonstrated that Trimethoprim-sulfamethoxazole were still highly active against *S. maltophilia* isolates, despite increasing resistance to Trimethoprim-sulfamethoxazole (11%) which is similar from the findings of previous studies [9,12,13,15] who reported 13% resistant to TM/SXT although, a resistance rates vary geographically but are generally less than 10% has been reported [7].

Few multi-center studies have investigated the efficacy of fluoroquinolones against *S. maltophilia*, the rates of susceptibility of fluoroquinolones have varied in different studies reveals a decrease in sensitivity of *S. maltophilia* to Levofloxacin, from 83.4% during the period 2003–2008 to 77.3% in 2011 [6,16]. Low susceptibility rates ranging from 64–69.6% have also been reported in Korea [7]. However, our finding seems that the high level of Levofloxacin resistance (23.2%) which were similar to a study conducted by other group [16, 17]. As a results of our study, there is need to think about clinical efficacy of this drug in India.

In this study, *S. maltophilia* was the most susceptible to Trimethoprim-sulfamethoxazole (92.1%), followed by Levofloxacin (82.7%) in bacteremia. In most reports, over 90% of strains are susceptible to trimethoprim-sulfamethoxazole in bacteremia which is similar to our findings [1,3]. In addition, it was found that *S. maltophilia* strains, isolated from patients with pneumonia, were slightly more resistant to TM/SXT and Levofloxacin [4,12]. Nevertheless, those two agents are frequently prescribed by treating physicians in hospitals as the empirical and targeted therapy for patients who have *S. maltophilia* infections. When the isolates were susceptible to those agents, Levofloxacin did not show significantly more benefit over Trimethoprim-sulfamethoxazole in patients with *S. maltophilia* infections in UTI [6]. The current study expected that the *S. maltophilia* strains isolated from patients with pneumonia and other site infections tended to be more resistant to antibiotics [11].

However, the increasing prevalence of Levofloxacin and Trimethoprim-sulfamethoxazole resistant isolates highlights the need of finding new therapeutic approaches. Although recent antibiotics, like Minocycline, has demonstrated very promising in vitro activity against *S. maltophilia* from diverse samples in Delhi and have been proposed as useful alternatives for treating infections by Levofloxacin and Trimethoprim-sulfamethoxazole resistant *S. maltophilia* isolates and these results are consistent with those of a recent study by other [4,10,13,14].

Our study had some limitations. The important one was its retrospective design, which prevented us from accurately differentiating between true infections and colonization with *S. maltophilia* isolates and the sensitivity of Chloramphenicol drug which is used for treatment in *S. maltophilia* infection is not available in Vitek. In addition, we do not have mortality data. A prospective, well-designed study should be conducted to more precisely evaluate the risk factors of *S. maltophilia* infections, the impact of appropriate antimicrobial therapy, and the mortality outcome.

6. Conclusion

In conclusion, *S. maltophilia* infection can occur in patients with various types of underlying comorbidity and risk factors in the hospital setting. The S. maltophilia isolates collected in our study had relatively high susceptibility to Minocycline, good susceptibility to Trimethoprim/sulfamethoxazole, but low to Levofloxacin. The Minocycline, could be useful alternative treatment options to Trimethoprim/sulfamethoxazole and Levofloxacin resistant strains.

Ethical Approval

It is not applicable.

Conflicts of Interest

There are no conflicts of interest.

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