Original Article

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Microbiology Section

Stenotrophomonas maltophilia: An Emerging Pathogen in Paediatric Population

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ABSTRACT

Introduction: *Stenotrophomonas maltophilia (formerly Pseudomonas maltophilia/Xanthomonas maltophilia*), a Gram- negative, non-fermenting bacillus, is being increasingly recognized as a threatening nosocomial pathogen, associated with significant mortality.

Aim: To determine the prevalence of infection, antimicrobial susceptibility pattern and clinical outcome of *S. maltophilia* in a paediatric population.

Materials and Methods: This was a retrospective study conducted over a period of eight months, i.e., October 2015 to May 2016. All clinical samples received in the microbiology laboratory during the study period were processed using standard microbiological procedures. *S. maltophilia* isolates were selected. Antibiotic susceptibility was performed for levofloxacin and trimethoprim-sulphamethoxazole by Vitek 2C system (Biomerieux, France). Average length of stay and mortality caused by *S. maltophilia* infection was compared with age and sex matched controls without *S. maltophilia* infection.

Results: A total of 16,234 clinical specimens were received in the microbiology laboratory in the study period, with 2,734 pathogenic bacteria isolated. A total of 1,339 (1.7% of total isolates) Gram-negative bacteria were isolated, out of which 414 were non-fermenters. Among the non-fermenters, 23 (5.5%) were *S. maltophilia*. Out of the 23 isolates, 15 (65.2%) were isolated from blood, 4 (17.3%) were isolated from urine and tracheal aspirate each. A total of 91.3% of strains were susceptible and 8.6% were resistant to trimethoprim-sulphamethoxazole. Total 80% of strains were sensitive and 20% had intermediate susceptibility for levofloxacin. None of the strains were resistant to levofloxacin. Average length of stay of patients with *S. maltophilia* infection was found out to be 23.3 days as compared to 44.8 days in controls. The average mortality of patients with *S. maltophilia* infection was found to be same as that of controls (35.2%).

Conclusion: *S. maltophilia* is becoming an important nosocomial pathogen and its isolation rate is reported to be increasing. Trimethoprim-sulphamethoxazole still remains the drug of choice but resistance has been reported for this drug as well. As its isolation is increasing, it is important to study the epidemiology, antimicrobial susceptibility profile and clinical outcomes of these isolates.

Keywords: Gram-negative, Levofloxacin, Trimethoprim-sulphamethoxazole

INTRODUCTION

Stenotrophomonas maltophilia (*S. maltophilia*) (formerly *Pseudomonas maltophilia/Xanthomonas maltophilia*), is becoming an important gram negative nosocomial pathogen associated with significant mortality [1]. The various infections caused by *S. maltophilia* include bacteraemia, pneumonia, urinary tract infection, etc., [2]. It is also known to reside in medical devices and thus leads to device associated infections like catheter associated blood stream infections, urinary tract infections etc., [3]. Among the non-fermenting bacteria, *S. maltophilia* stands next only to *Pseudomonas aeruginosa* and *Acinetobacter* spp. among all the clinical isolates [4]. *S. maltophilia* is intrinsically resistant to a wide range of commonly used drugs (including all carbapenems) making treatment of such infections very difficult [5-8]. Clinical and Laboratory Standards Institute (CLSI) recommends testing for following antibiotics, minocycline, ticarcillin-clavulanate, ceftazidime, levofloxacin and trimethoprim-sulphamethoxazole and chloramphenicol [9]. There is an increasingly reported resistance to levofloxacin [7]. Strains are usually susceptible to trimethoprim-sulphamethoxazole. Susceptibility to ceftazidime is variable [5,6].

The present study was conducted to determine the prevalence of epidemiology, antimicrobial susceptibility pattern and clinical outcome of *S. maltophilia* in the paediatric hospital setting in a tertiary care hospital in Delhi.

MATERIALS AND METHODS

This was a retrospective study done over a period of eight months, October 2015 to May 2016. Data was collected from a hospital information management system. All non fermenting Gram-negative bacilli from any clinical specimen like pus, tracheal aspirate, blood, urine etc., were selected. The clinical samples were processed using standard microbiological procedures. Out of all the non-fermenters, *S. maltophilia* isolates were further selected. Final identification and antibiotic susceptibility of these isolates for levofloxacin and trimethoprim-sulphamethoxazole was performed by VITEK 2C system (Biomerieux, France).

The VITEK 2C is an automated microbiology system utilizing growth-based technology. It has colorimetric reagent cards that are incubated and interpreted automatically. A total of 16234 clinical specimens were received from our hospital in the microbiology laboratory between October 2015 to May 2016, with 2734 pathogenic bacteria isolated.

All the patients were followed up and their clinical outcome and average length of stay in the hospital was calculated. Average length of stay and mortality caused by *S. maltophilia* infection was compared with controls. Controls were taken as double the number of cases, were matched for age and sex with cases and were inpatients with infection other than *S. maltophilia.*

As the sample size was very small, statistics could not be employed. Ethical clearance was not required as it was a retrospective study. All the samples were routine samples and no special intervention was done.

RESULTS

A total of 1339 gram negative bacteria were isolated, out of which 414 were non fermenters. Among the non fermenters, 23 (5.5%) were *S. maltophilia*. Out of the 23 isolates, 15 (65.2%) were isolated from blood, 4 (17.3%) were isolated from urine and tracheal aspirate each [Table/Fig-1].

Out of the 23 patients, 18 (78.2%) were males and 5 (21.7%) were females. Maximum patients were above five years of age (34.7%) followed by one month-one year (26%), one to five year (21.7%) and below one month of age 4 (17.3%) [Table/Fig-2]. Out of the 23 patients, 9 (39.1%) were admitted to wards, 5 (21.7%) were in ICU, 5 (21.7%) were seen in OPD and 4 (17.3%) were in emergency [Table/Fig-3].

A total of 21 (91.3%) of strains were susceptible and 2 (8.6%) were resistant to trimethoprim-sulphamethoxazole. A total of 12 (80%) of strains were sensitive and 3 (20%) had intermediate susceptibility for levofloxacin. None of the strains were resistant to levofloxacin [Table/Fig-4].

Sample	No.(%)
Blood	15 (65.2)
Tracheal aspirate	4 (17.3)
Urine	4 (17.3)
Total	23

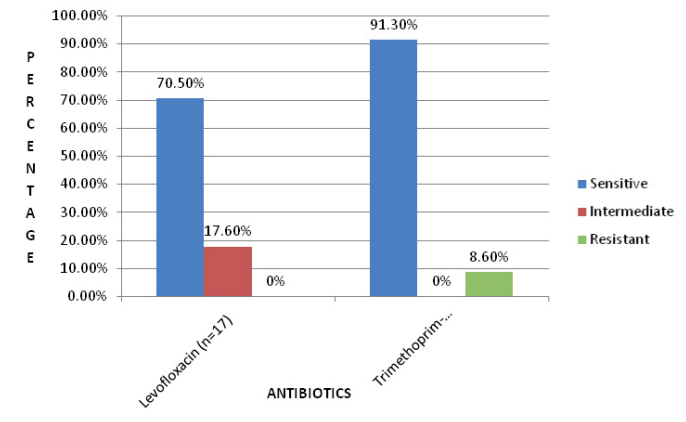
[Table/Fig-1]: Sample wise distribution of the *S. maltophilia* isolates.

Gender	No. (%)
Female	5 (21.7)
Male	18 (78.2)
Age	
<1 month	4 (17.3)
1 month-1 year	6 (26.0)
1-5 year	5 (21.7)
>5 year	8 (34.7)
Total	23

[Table/Fig-2]: Demographic profile of the patients with *S. maltophilia* infection.

Location	No.(%)
In-patients/wards	9 (39.1)
ICU	5 (21.7)
OPD	5 (21.7)
Emergency	4 (17.3)
Total	23

[Table/Fig-3]: Location wise distribution of the *S. maltophilia* isolates.



[Table/Fig-4]: Antimicrobial susceptibility pattern of the *S. maltophilia* isolates.

Drugs	Blood (n=15)	Tracheal aspirate (n=4)	Urine (n=4)
Levofloxacin (Numerator/Denominator)	80%	75%	100%
Trimethoprim-sulphamethoxazole (Numerator/Denominator)	100%	75%	75%

[Table/Fig-5]: Sample wise antimicrobial sensitivity pattern of the *S. maltophilia* isolates.
Numerator- Number of resistant isolates, Denominator- Length of stay

Variables	Cases (n=17)	Controls (n=34)
LOS (days)	23.3	44.8
Mortality	35.2%	35.2%

[Table/Fig-6]: Comparison of outcome of patients with *S. maltophilia* infection with those of controls.
LOS- Length of stay

Maximum resistance was seen in the blood isolates followed by urine and tracheal aspirate [Table/Fig-5].

MIC value of trimethoprim-sulphamethoxazole ranged between ≤20 to ≥320 µg/ml and levofloxacin ranged between 0.12 to 4 µg/ml.

Average length of stay of patients with *S. maltophilia* infection was found out to be 23.3 days as compared to 44.8 days in controls. The average mortality of patients with *S. maltophilia* infection was found to be same as that of controls (35.2%) [Table/Fig-6].

DISCUSSION

S. maltophilia is a Gram-negative bacterium generally considered as having low virulence, is becoming an emerging multi-drug resistant opportunistic pathogen in hospital as well as community settings, especially among immunocompromised hosts. Various risk factors associated with *S. maltophilia* infection include underlying malignancy, cystic fibrosis, cortico-steroid or immunosuppressant therapy, the presence of an indwelling central venous catheter and exposure to broad spectrum antibiotics [10,11]. There is paucity of information on the world wide prevalence of *S. maltophilia* infections in the paediatric population [11].

In our hospital *S. maltophilia* was found to be the third most common non-fermenters after *Acinetobacter* spp and *Pseudomonas aeruginosa* accounting for 5.5% of total non-fermenters. This finding was similar to that reported by Rit K et al., from Eastern India [12] and Jia W et al., from China [6].

Abdel-Aziz N et al., reports the total isolation of *S. maltophilia* among Gram-negative bacteria to be 1.5% which was comparable to our study (1.7%) [5]. Jia W et al., reports the total prevalence of *S. maltophilia* among the non-fermenters to be 10.1% [6] which was higher than that of our study. In another study from Eastern India, *S. maltophilia* represented 2.8% of total non fermenters [12].

In this study, *S. maltophilia* was most commonly isolated from blood (65.2%) followed by urine and tracheal aspirate each (17.3%). Jia W et al., reports maximum isolation from respiratory specimens [6]. Abdel-Aziz N et al., reports maximum isolation from urine sample followed by swabs and blood [5].

In our study, 78.2% isolates were from males as compared to 21.7% in females. Similar rates were seen in a study conducted in Karnataka, India [13]. Risk factors associated with *S. maltophilia* infections include immunosuppressive therapy, admission to the Intensive Care Unit (ICU), advanced age, prolonged hospital stay, long term antimicrobial therapy and surgical procedures [14]. In our study, 21.7% patients were admitted to ICU, 39.1% were in wards and rest were OPD patients. Among this population, we found maximum isolation in children more than five years of age followed by infants with one month to one year of age. To the best of our

S. No.	Year	Age/sex	Diagnosis	Site of isolation	Antibiotics given	Outcome
1	2009	30 year/male	Endophthalmitis	Vitreous fluid	Ciprofloxacin	Recovered
2	2010	Newborn/female	Early onset neonatal sepsis	Blood	Cefotaxime, Amikacin	Expired
3	2010	Newborn/female	Early onset neonatal sepsis	Blood	Piperacillin-tazobactam, Amikacin	Expired
4	2012	44 year/male	Conjuctival ulcer	Conjuctival scraping	Moxifloxacin	Recovered
5	2015	2 year/female	Sepsis	Blood	Amoxyclav, Antimalarials, Ceftriaxone	Recovered
6	2015	9 year/female	Sepsis	Blood	Amoxyclav, Antimalarials,	Recovered
7	2015	7 year/female	Sepsis	Blood	NA *	Recovered
8	2015	60 year/male	End stage renal diseases	Blood	Levofloxacin	Recovered
9	2015	Newborn/female	Early onset neonatal sepsis	Blood	Levofloxacin, Ceftazidime	Recovered

[Table/Fig-7]: Summary of case reports of *S. maltophilia* reported from India in the last decade [1,2,10,18-20].
*NA-Not available

knowledge, this is the first study conducted in India in paediatric population.

Trimethoprim-sulphametoxazole is considered as the treatment of choice for *S. maltophilia* infections [11]. In our study, 70.5% strains were susceptible to levofloxacin, none were resistant and 91.3% strains were sensitive to trimethoprim-sulphamethoxazole and 8.6% were resistant. Our results were similar to a study done in South Africa in 2015 which reported 98.3% resistance to trimethoprim-sulphamethoxazole and 1.3% resistance to levofloxacin [15]. Abdel-Aziz N et al., reports 100% sensitivity for trimethoprim-sulphamethoxazole and 16.67% susceptibility to fluoroquinolones [5]. Another study conducted in Hungary reports 99% susceptibility to trimethoprim-sulphamethoxazole and 75% susceptibility to levofloxacin [16] Chawla K et al., reported 78.8% susceptibility for levofloxacin and 72.7% for trimethoprim-sulphamethoxazole [13]. Many studies have demonstrated the emergence of strains resistant to trimethoprim-sulphamethoxazole. Our study reports a lower resistance for both the drugs. A probable explanation could be that this study has been conducted on a relatively antibiotic naïve population.

Most infections caused by *S. maltophilia* were associated with severe morbidity and long-term, extensive ICU treatment. According to previous reports, the mortality rates vary between 14-62% [17].

Our study reports a mortality rate of 35.2% which is in accordance with the known data. A study conducted in India reports the mortality rate to be 21.2%, which was a little lower than our study [13]. The study conducted in Hungary reports the mortality rate to be 45%, however, the attributable mortality rate was 11%. In our study we did not calculate the attributable mortality rate.

In our study the average length of stay in patients with *S. maltophilia* infection was found to be 23.3 days as compared to 44.3 days in the control cases. However, the mortality rate was found to be same in both the groups (35.2%). As compared to the controls, the relative mortality of children infected with *S. maltophilia* was higher. Thus, concluding that *S. maltophilia* causes more serious infections in paediatric population leading to a higher fatality.

To the best of our knowledge, no study has been reported from India highlighting the prevalence, antibiotic susceptibility and clinical outcome of *S. maltophilia* in paediatric population. Rit K et al., and Chawla K et al., have done a similar study in adult population [12,13]. A few case reports have been reported from India. We provide a summary of all the cases reported from India for past decade [Table/Fig-7] [1,2,10,18-20].

LIMITATION

There were many limitations in our study. First of all, it was a very short study, conducted over eight months. A larger study with better planning should be conducted to find out the current epidemiology and resistance burden. Secondly, the identification and antimicrobial susceptibility testing was done only by VITEK. The results should have been confirmed with manual MIC calculations as well. Thirdly, although patients were followed-up to find out the outcome of disease, but the clinical risk factors could not be evaluated. We plan to conduct a bigger study to overcome the limiting factors and to find out the actual burden of the resistant isolates and their clinical implications as well.

CONCLUSION

Many multi-institutional studies done on a worldwide level have confirmed that *S. maltophilia* is an emerging multi-drug resistant opportunistic pathogen in hospital and community settings, especially among immunocompromised hosts. Trimethoprim-sulphamethoxazole still remains the drug of choice in the general population. There is an alarming trend in resistance to previously known susceptible drugs such as ceftazidime, ticarcillin-clavulanate, and fluoroquinolones. A better understanding of the epidemiology, antimicrobial susceptibility profile and clinical outcomes of *S. maltophilia* is required, so as to control the increasing trend in isolation rate of this pathogen from various clinical samples. Regular surveillance and continuous monitoring should be done for better management of patients.

REFERENCES

[1] Viswanathan R, Singh AK, Ghosh C, Basu S. *Stenotrophomonas maltophilia* causing early onset neonatal sepsis. Indian Paediatric. 2011;48:397-99.
[2] Das T, Deshmukh HS, Mathai A, Reddy AK. *Stenotrophomonas maltophilia* endogenous endophthalmitis: Clinical presentation, sensitivity spectrum and management. Journal of Medical Microbiology. 2009;58:837-38.
[3] Cheong HS, Lee JA, Kang CI, Chung DR, Peck KR, Kim ES, et al. Risk factors for mortality and clinical implications of catheter-related infections in patients with bacteraemia caused by *Stenotrophomonas maltophilia*. Int J Antimicrob Agents. 2008;32(6):538-40.
[4] Looney WJ, Narita M, Muhlemann K. *Stenotrophomonas maltophilia*: An emerging opportunist human pathogen. Lancet Infect Dis. 2009;9:312–23.
[5] Abdel-Aziz N, Morsy MMF, Amin SS, Mohammed KI, Alharbi AE, et al. Threatening problem of *Stenotrophomonas maltophilia* producing extended-spectrum beta-lactamases: Prevalence and automated antibiotic susceptibility pattern. Clin Microbial. 2013;2:108.
[6] Jia W, Wang J, Xu H, Li G. Resistance of *Stenotrophomonas maltophilia* to fluoroquinolones: Prevalence in a university hospital and possible mechanisms. Int. J Environ Res Public Health. 2015;12:5177-95.
[7] Nicodemo AC, Paez JI. Antimicrobial therapy for *Stenotrophomonas maltophilia* infections. Eur J Clin Microbiol Infect Dis. 2007;26:229-37.
[8] Waters V. New treatments for emerging cystic fibrosis pathogens other than *Pseudomonas*. Curr Pharm Des. 2012;18:696–725.
[9] Clinical and Laboratory Standards Institute (CLSI). Performance standards for Antimicrobial Susceptibility Testing. 26th ed. Wayne, Pennsylvania. USA. 2016.
[10] Galate L, Bangde S. *Stenotrophomonas maltophilia* - A rare cause of bacteraemia in a patient of end stage renal disease on maintenance haemodialysis. IOSR Journal of Dental and Medical Sciences (IOSR-JDMS). 2015;14(2):73-75.
[11] Chang YT, Lin CY, Chen YH, Hsueh PR. Update on infections caused by *Stenotrophomonas maltophilia* with particular attention to resistance mechanisms and therapeutic options. Frontiers in Microbiology. 2015;6:893.
[12] Rit K, Nag F, Raj HJ, Maity PK. Prevalence and susceptibility profiles of non fermentative gram-negative bacilli infection in a tertiary care hospital of Eastern India. Indian Journal of Clinical Practice. 2013;24(5):451-55.
[13] Chawla K, Vishwanath S, Gupta A. *Stenotrophomonas maltophilia* in lower respiratory tract infections. Journal of Clinical and Diagnostic Research. 2014;8(12):20-22.

[14] Neela V, Rankouhi SZR, van Belakum A, Goering RV, Awang R. *Stenotrophomonas maltophilia* in Malaysia: Molecular epidemiology and trimethoprim-sulphamethoxazole resistance. Inter J Infec Dis. 2012;16:603-07.
[15] Adegoke AA, Okoh AI. Antibiogram of *Stenotrophomonas maltophilia* isolated from Nkonkobe municipality, Eastern Cape Province, South Africa. Jundishapur J Microbiol. 2015;8(1):e13975.
[16] Juhász E, Krizsán G, Lengyel G, Grósz G, Pongrácz J, Kristóf K. Infection and colonization by *Stenotrophomonas maltophilia*: Antimicrobial susceptibility and clinical background of strains isolated at a tertiary care centre in Hungary. Annals of Clinical Microbiology and Antimicrobials. 2014;13:333.
[17] Wang YL, Scipione MR, Dubrovskaya Y, Papadopoulos J. Monotherapy with fluoroquinolone or trimethoprim-sulfamethoxazole for treatment of *Stenotrophomonas maltophilia* infections. Antimicrob Agents Chemother. 2014;58(1):176-82.
[18] Mahendradas P, Avadhani K, Anandula V, Shetty R. Unilateral conjunctival ulcer due to *Stenotrophomonas maltophilia* infection. Indian J Ophthalmol. 2012;60:134-36.
[19] Hawaldar R, Sodani S. Bacteremia due to *Stenotrophomonas maltophilia* – A series of three cases. Indian J Microbiol Res. 2015;2(2):128-32.
[20] Basany L, Aepala R. Early onset sepsis with pneumonia in a full term neonate due to *Stenotrophomonas maltophilia*. International Journal of Contemporary Paediatrics. 2015;2(2):148-50.

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