

Evaluation of *Sphingomonas paucimobilis* as an emerging nosocomial pathogen in a teaching hospital in Uttarakhand

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Received: June 2021, Accepted: August 2021

ABSTRACT

Background and Objectives: *Sphingomonas paucimobilis* is an opportunistic pathogen and was rarely encountered in clinical specimens previously. This study aimed to investigate the clinical features, associated co-morbidities, and antimicrobial susceptibility patterns of *S. paucimobilis* infection in a tertiary hospital in Uttarakhand.

Materials and Methods: *S. paucimobilis* isolates cultured from various sections of hospital and OPDs were identified and analyzed for their antibiograms in the microbiology laboratory for a duration of one year from January 2020 to December 2020.

Results: *S. paucimobilis* was isolated from 49 samples (0.01%) out of 3792 samples processed in VITEK 2 Compact automated ID/AST instrument. The maximum number of isolates were obtained from urine samples (31%), followed by blood (24%). Septicemia (41%), meningitis (17%), lower respiratory tract infections and ventilator associated pneumonia (14%) constituted a major portion of infections caused by this organism. Diabetes mellitus (22%) and steroid usage (16%) were major associated co-morbid conditions. Third and Fourth generation cephalosporins like ceftriaxone (81%) and cefepime (86%) were found to be the most susceptible drugs whereas 61% of isolates were resistant to colistin.

Conclusion: This organism is an up-and-coming pathogen and should not be simply labeled as a contaminant. Although the organism is not grossly virulent and still might not be associated with serious life-threatening infections; however their evolving resistance patterns and increased spectrum of infections should be seriously taken into account.

Keywords: *Sphingomonas*; Nosocomial; paucimobilis; Septicemia; Antimicrobial; Steroid

INTRODUCTION

Sphingomonas paucimobilis, an emergent pathogenic bacterium is aerobic, motile, non-fermenting Gram-negative bacilli. It is being implicated as growing cause of health care associated infections in hospitals in recent years (1). It is catalase and oxidase-positive and also exhibits the production of a yellow pigment (2). The organism is present everywhere and has been isolated from natural environmental conditions like seawater, sea ice, river water,

wastewater, mineral water, and soil. It has a peerless sphingoglycolipid in the cell wall and lacks the lipopolysaccharide constituent in conjunction with its endotoxin activity. This could be the explanation for the low virulence of this organism (3). In fact, this organism can propagate in hemodialysis devices, nebulizers, ventilators, sterile drug solutions and distilled water (4). Both nosocomial and community-acquired infections can be caused by this organism; which were sparse previously but now their occurrence, particularly in hospital environment has augmented

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(2). Blood, sputum, urine, wound, bile, cerebrospinal fluid, vagina, and cervix infections have been reported by this organism (5). *Sphingomonas* has plethora of resistant phenotypes, contributing to resistance to many antimicrobial agents tested. Individualized and appropriate antimicrobial therapy may need to be given to every patient (6). *S. paucimobilis* usually shows susceptibility to carbapenems, aminoglycosides, trimethoprim-sulfamethoxazole, and piperacillin/tazobactam whereas resistant patterns are majorly reported for penicillins and first-generation cephalosporins (7).

Till recent times *S. paucimobilis* was seldom encountered in the clinical milieu especially in immunocompromised patients and those with co-morbidities, however now there are many case reports to support the mounting body of evidence that this may be a budding infectious pathogen creditable of further probe and investigation (8). It is an emerging pathogen that should be dealt with cautiously (8, 9).

Thus, the current study aims to observe the clinical features of patients with *S. paucimobilis* infections and the antimicrobial susceptibility pattern of the isolated strains among the hospitalized patients in a tertiary health care institute for a duration of one year.

MATERIALS AND METHODS

A prospective study was conducted in the Department of Microbiology, Shri Guru Ram Rai Institute of Medical and Health Sciences; a tertiary care teaching hospital from January 2020 to December 2020. A study protocol was designed, written consent was taken from all the study participants, and approval was sought by the ethical and research committee of the institution.

Inclusion criteria was as follows: All clinical specimens from the patients attending outpatient departments (OPDs) and those admitted in the wards and ICUs of Shri Mahant Indires Hospital (SMIH), Patel Nagar Dehradun. Exclusion criteria was as follows: Unacceptable sample as per laboratory protocol and repeat samples from the same patient. Various clinical samples from patients like urine, pus, wound swabs, blood, other sterile fluids, respiratory specimens like Broncho-alveolar lavage (BAL), sputum, central line tips, bile, and cerebrospinal fluid (CSF) were analyzed in the Department of Microbiology.

After receiving specimens in the laboratory under all aseptic precautions, processing and reporting was done as per the standard methods. Microscopic examination was done by direct Gram staining followed by their culture onto Sheep Blood agar (5%) and MacConkey agar \pm Chocolate agar except for blood specimens. Blood specimens were first inoculated in culture bottles of the automated blood culture system (BacT/Alert system, Organon Teknika Corporation, Durham, NC) followed by aerobic incubation for 5 days. If bottles flagged positive, subculture was taken on Blood agar and MacConkey agar. The inoculated plates were incubated aerobically at 37°C for 48 hours. For primary identification basic microbiological features and biochemical characteristics such as colony morphology, Gram staining, catalase, and oxidase tests were taken into account. Automated system (VITEK-2 Biomerieux) was used to detect bacteria from clinical specimens and the final identification and antibiotic susceptibility testing was reported based on it.

Data was entered and analyzed on Microsoft Excel and interpreted by descriptive methods in terms of frequency distribution in percentages, proportions, rates, ratios etc. Non-parametric tests i.e. chi-square tests were applied to ascertain the significance of the association.

RESULTS

In the study duration of one year, the total clinical samples received in the laboratory were 96,309. Significant growth was processed in 3792 samples using VITEK 2 Compact automated ID/AST instrument. *S. paucimobilis* was isolated in 1.3% (49/3792) of samples. 23 out of 49 (46.9%) patients had history of taking antibiotics before presenting to the hospital. 19 patient had devices on them (foley's catheter (8), endotracheal tube (6), central venous catheter in-situ (2), ventriculo-peritoneal shunt (1), intercostal drainage tube (1), and hemodialysis catheter (1)) but none had prosthetic implant.

Table 1 shows the distribution of *S. paucimobilis* isolates according to gender and age. Clinical manifestations of these patients (n=49) were as illustrated in Fig. 1. Table 2 Shows distribution of samples from which *S. paucimobilis* was isolated (n=49). Table 3 shows the frequency distribution of *S. paucimobilis* isolated from various wards. The maximum

number of isolates were obtained from and Intensive care units (ICUs) and High dependency units (HDUs) (51%), followed by various wards (37%) and outpatient departments (12%). Diabetes (22%) and steroid use (16%) were the most frequent associated co-morbid conditions (Table 4). Table 5 depicts antibiotic

Table 1. Demographic parameters of the patients in whom *Sphingomonas paucimobilis* was isolated (n=49)

Demographics	Particulars	Number (%)
Gender (n=49)	Male	28 (58%)
	Female	21 (42%)
Age in years (n=49)	<20	3 (6%)
	21-40	14 (29%)
	41-60	26 (53%)
	>60	6 (13%)

susceptibility patterns of isolates to various antibiotics agents (as per MIC breakpoints given in CLSI 2021 Guidelines) (10). Table 6 shows distribution of Multi-drug resistant and Extensively drug resistant isolated in various critical and non-critical area of the hospital. Of the 49 patients, 3 patients expired (6.1%). All other cases (93.8%; 46/49) were successfully managed with antibiotics and were followed up as outpatients.

DISCUSSION

In the study, the majority of the samples from which *S. paucimobilis* was isolated were urine samples (31%) followed by blood (24%) and lower respiratory tract specimens (16%). However, UTI was reported

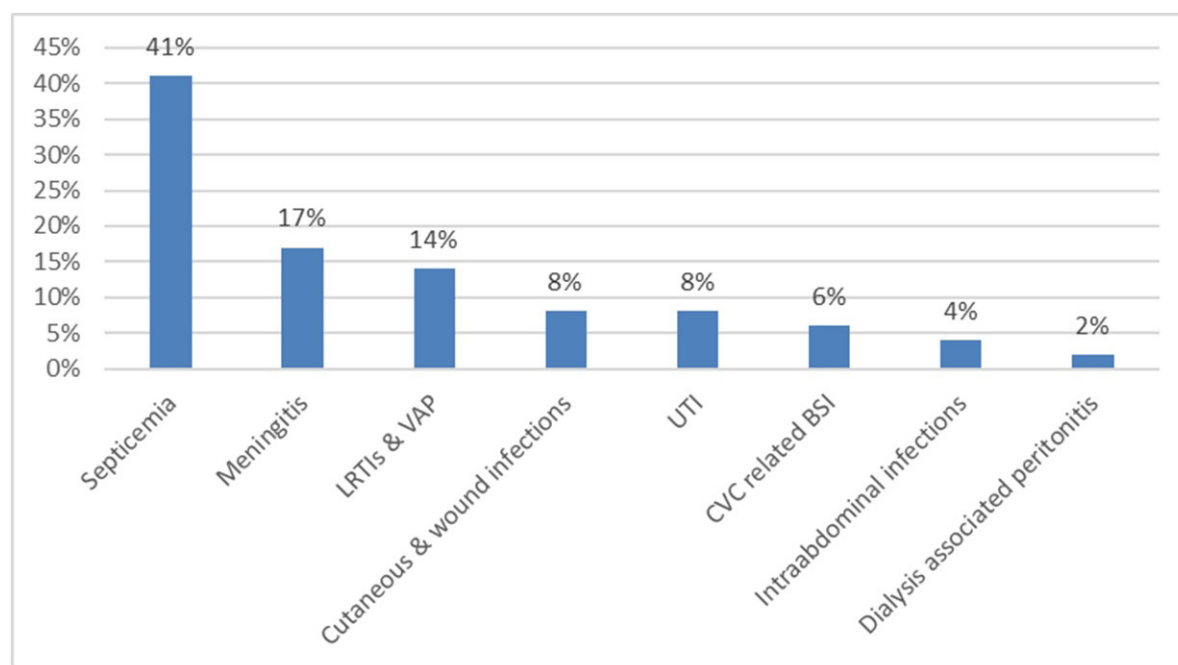


Fig. 1. Frequency distribution of clinical manifestations of the patients (n=49)

Table 2. Distribution of samples from which *Sphingomonas paucimobilis* was isolated (n=49)

Samples	Isolation of <i>Sphingomonas paucimobilis</i> in% (n=49)
Urine	31% (15/49)
Blood	24% (12/49)
Endotracheal aspirate/ Endotracheal tip/suction tips/Bronchoalveolar lavage/ Sputum	16% (8/49)
Pus/wound swabs	12% (6/49)
Cerebrospinal fluid	8% (4/49)
Sterile fluid (Peritoneal fluid/Pleural fluid/Ascitic fluid)	8% (4/49)

Table 3. Ward-wise distribution of isolates

Ward	Percentage of isolates (n=49)
Intensive care units (ICUs) and High dependency Units (HDUs)	
ICUs HDUs	37% (18/49)
Wards	14% (7/49)
Medicine	
Surgery	12% (6/49)
Nephrology	8% (4/49)
Cardiothoracic Vascular surgery (CTVS)	6% (3/49)
Obstetrics & Gynecology	4% (2/49)
Pediatrics	2% (1/49)
Respiratory	2% (1/49)
Outpatient departments	2% (1/49)
Outpatient departments	
	12% (6/49)

Table 4. Underlying predisposing conditions in patients (n=49)

Underlying conditions	Percentage (Number)	P-value
Diabetes	22% (11/49)	0.008725 (s)*
Steroid use	16% (8/49)	0.00001 (s)
Malignancy	8% (4/49)	0.00001 (s)
Chronic renal failure or end-stage renal disease	6% (3/49)	0.083699 (ns)**
Central venous catheter in-situ	6% (3/49)	<0.00001 (s)
Arthritis	2% (1/49)	0.127686 (ns)
Alcoholism	2% (1/49)	0.110655 (ns)
Chronic obstructive pulmonary disease	2% (1/49)	0.77744 (ns)
Acquired immunodeficiency syndrome (AIDS)	2% (1/49)	0.93382 (ns)
No predisposing factors	33% (16/49)	<0.00001 (s)

*s: significant **ns: not significant

in 8% of patients from whom *S. paucimobilis* was isolated and all of the patients with UTI had associated co-morbidities. There are few documented reports suggesting UTI caused by *S. paucimobilis* and most of them had underlying conditions like malignancy, diabetes mellitus, and renal transplantation (11, 12). Moist hospital environment aids the survival of *Sphingomonas* spp. Contact with a contaminated medical device, catheters, implants, etc. can result in colonization and development of infection in the immunocompromised patients (11).

The majority of the patients in our study (41%) were reported to have bloodstream infections caused by *S. paucimobilis* followed by meningitis (17%) and lower respiratory tract infections (14%). Similar reports of *S. paucimobilis* as an etiological agent of bacteremia

have also been reported by Iugito, Puca E et al. (7,13). In fact, cases of community-acquired primary bacteremia have been reported by Puca E et al. (13). It has been isolated from blood in most cases presented in the literature. *S. paucimobilis* bacteremia has been reported mainly in patients with indwelling devices or immunocompromised hosts, especially those with neutropenia (14). In 2017, Goker T et al. have also reported *S. paucimobilis* from CSF samples (2). The patient presented with dizziness and headache and *S. paucimobilis* was subsequently isolated from CSF (15). The second case of meningitis in the literature was the one report by Tai and Velayuthan (16). It may also cause both nosocomial and community-acquired pneumonia with a mortality potential as was evident also in our study where 14% of patients also

Table 5. Antibiotic susceptibility pattern of isolates to various antibiotics agents (as per MIC breakpoints for non-fermenters given in CLSI 2021) (n=49)

	Sensitive (%)	Resistant (%)
Amikacin	29 (59%)	20 (41%)
Gentamicin	29 (59%)	20 (41%)
Aztreonam	29 (59%)	20 (41%)
Piperacillin-tazobactam	29 (59%)	20 (41%)
Ticarcillin clavulanic acid	37 (76%)	12 (24%)
Cefoperazone sulbactam	37 (76%)	12 (24%)
Ceftazidime	35 (72%)	14 (28%)
Ceftriaxone	40 (81%)	9 (19%)
Cefepime	42 (86%)	7 (14%)
Meropenem	33 (67%)	16 (33%)
Imipenem	32 (65%)	17 (35%)
Minocycline	28 (57%)	21 (43%)
Tigecycline	35 (72%)	14 (28%)
Ciprofloxacin	29 (59%)	20 (41%)
Levofloxacin	36 (74%)	13 (26%)
Colistin	15 (39%)	30 (61%)

Table 6. Antibiotic resistance patterns in Critical and Non-critical areas

	MDR (n=1)	Non-MDR (n=48)
Critical areas (n=25)	1	24
Non-critical areas (n=24)	0	24
	XDR (n=13)	Non-XDR (n=36)
Critical areas (n=25)	9	16
Non-critical areas (n=24)	4	20

had features of pneumonia and empyema (16).

43/49 (87.75%) isolates were cultured from hospitalized patients and 6/49 (12%) from outpatient departments. 25/49 (51%) were isolated from patients admitted in ICUs and HDUs whereas the rest 18/49 (36.73%) from patients admitted in different wards. Community-acquired infections by *S. paucimobilis* are not uncommon and have been reported in studies by Toh et al. and Puca (13, 14). In fact, their study reported a higher percentage of community-acquired *S. paucimobilis* infections compared with other studies (17). The environmental presence of *S. paucimobilis* in water and soil and the demonstration of any association between community-acquired *S. paucimobilis* infection and environmental exposure warrants additional studies (18). Increased chances of isolation of *S. paucimobilis* from hospital settings

have also been reported in case studies by Goker T (2). In hospital settings, as was found in the current study, *S. paucimobilis* might have originated from devices such as indwelling catheters, ventilator and hemodialysis devices, nebulizer, sterile intravenous fluid, and contaminated hospital tap and distilled water (14).

Diabetes mellitus (22%), steroid usage (16%), and malignancy (8%) were the most common co-morbid conditions observed in our study (P value significant <0.05). In fact, a significant statistical association was found between the presence of underlying associated medical conditions and the isolation of *S. paucimobilis*. Similar findings have also been reported in a case study by Hardjo and a study by Toh (7, 14). Another case study by Puca also reports diabetes mellitus as the most commonly identified risk factor; advanced age, malignancy, immunosuppression, being the other attributing factors (14). The plausible reason for diabetes being a significant risk factor is that that infection results in inflammation along with activated innate immunity, which indirectly leads to insulin resistance. Also, malignancies lead to compromised immune system making patients more prone to transient infections by a nosocomial pathogen. (19, 20) *S. paucimobilis* has been acknowledged to cause infection in the immunocompromised host with an increased propensity to infect patients with underlying conditions, hence can potentially survive and thrive in hospital environment (11).

Third and fourth generation cephalosporins like ceftriaxone (81%) and cefepime (86%) were found to be the most susceptible drugs whereas 61% of isolates were resistant to colistin followed by 43% of isolates demonstrating resistance to minocycline. Barring colistin, >50% sensitivity of isolates was seen for the commonly used drugs for this infection however the increased resistance rates (41%) to drugs like aminoglycosides, aztreonam, piperacillin –tazobactam, and fluoroquinolones like ciprofloxacin cannot be ignored and reiterate the fact that this organism also has the capability to become multidrug resistant in the near future if the currently available drugs are not used judiciously. As there are no definitive guidelines for antibiotic treatment for *S. paucimobilis* infections, individualized antibiotic therapy is initiated according to the *in-vitro* susceptibility pattern of the clinical isolate (14, 21).

Generally, *S. paucimobilis* is susceptible to carbapenems, aminoglycosides, trimethoprim-sulfame-

thoxazole, and piperacillin/ tazobactam and resistant to penicillins and first-generation cephalosporins. The resistance to penicillins and first-generation cephalosporins is attributable to the production of chromosomally encoded beta-lactamase (7). A study by Toh has reported resistance to amikacin, ceftazidime, and fluoroquinolones, while in another study by ozdemir it was reported to be resistant to ceftaxime and ceftazidime (14, 21). In our study, 72% of isolates demonstrated a susceptible profile for ceftazidime. 90% of the sphingomonas isolates were Multidrug resistant (MDR) in a study from Ghana (22). Antimicrobial susceptibility variations have also been reported from many other research works wherein most strains were found to be resistant to beta-lactam drugs and the antimicrobial drugs like quinolones, carbapenems, beta-lactam/beta-lactamase inhibitors, and aminoglycosides were found to be effective (5, 11).

CONCLUSION

S. paucimobilis is an emerging infectious agent that is ubiquitous in natural environments but may also be isolated from the hospital milieu and holds importance in immunocompromised patients and those having other underlying comorbidities. Even in immune-competent patients it cannot be neglected. It can be an etiological agent for both nosocomial and community-acquired infections. Although prophylactic therapy can eliminate it, sensitivity patterns, however, should be categorically studied to establish an optimal therapy.

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