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Stenotrophomonas maltophilia Bacteraemia: Analysis of 33 Episodes Occurred in the ICU at the University Hospital in Sousse, Tunisia

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Abstract

Background: *Stenotrophomonas maltophilia* is a multidrug-resistant, Gram negative *bacillus* that has emerged as an opportunistic pathogen associated with high morbidity and mortality rates. Aim: The aim of this study is to describe the characteristics of patients with bloodstream infections due to *S. maltophilia*. Methods: A descriptive retrospective study was performed at the ICUs over seven-year period in a teaching hospital. Cases of SMB were identified through a review of clinical microbiology laboratory and patient's records were retrieved for analysis. Findings: There were 22 deaths (71%) 15 ± 12 days after the bactaeremia. In our study, more than half of patients (17/31) was exposed to broad-spectrum antibiotic specifically imipinem (IMP) before their positive culture. Antibiotic susceptibility testing revealed that isolates were most sensitive to ciprofloxacin (84%) and to trimethoprim-sulfamethoxazole (71%). A probable portal of entry was identified in 27.3% of cases and 57% were catheter-related. Conclusion: Our results were similar to those described by other authors reported in the literature in the last 20 years. Prevention of *S. maltophilia* acquisition and infection depends on higher emphasis on control of antimicrobial consumption and consideration of environmental reservoirs.

Keywords

***Stenotrophomonas* Maltophilia, Bacteraemia, ICU, Risk Factors, Mortality**

Subject Areas: **Epidemiology, Infectious Diseases**

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1. Introduction

Stenotrophomonas maltophilia is emerging as an opportunistic nosocomial pathogen which is widespread in the environment [1] [2]. Although not highly virulent, reports indicate that infection with this organism is associated with significant morbidity and mortality particularly in severely compromised patients [3] [4]. Infection with this pathogen commonly manifests as bacteraemia [5] [6], but it also may cause a wide range of other infections [7]-[9]. Progress has been made in identifying risk factors for the acquisition of severe *S. maltophilia* infections [10]. Thus, clinical manifestations due to this strain was usually related to previous exposure to broad-spectrum antibiotics, prolonged hospitalization, intensive care unit (ICU) stay, mechanical ventilation, the use of intravascular devices and tracheostomy [3] [8] [11]-[16]. Therapy for infections with this pathogen is challenging because of its intrinsic resistance to most antimicrobial agents and the debilitated state of patients [17] [18]. Control of antibiotic use has been identified as a cornerstone of prevention of *S. maltophilia* infections in hospitals [19] [20], in addition to avoidance of prolonged implantation of foreign devices and reinforcement of hygiene practices [16]. The aim of this study is to describe clinical, microbiological, and epidemiologic features of *S. maltophilia* bacteraemia (SMB) in the three ICU at the Sahloul Hospital in Sousse, Tunisia

2. Materials and Methods

2.1. Patient Source, Period of Study and Case Finding

The Sahloul university hospital is a 629-bed teaching hospital with specialty services including operating room and five intensive care units (ICU). A descriptive retrospective study was performed at the ICUs over seven-year period (January 2004-July 2011).

Cases of SMB were identified through review of clinical microbiology laboratory reports. When this organism was cultured from another body site in our patient group it wasn't recorded. For the Clinical data we've used information from the medical record of each patient. Patients with polymicrobial bacteraemia were included in the study.

An infection was defined nosocomial acquired in an ICU if it occurred more than 2 days after admission.

Patients were considered to have received previous antibiotic treatment if this took place in the week before the development of the bacteraemia, and if it was administered for at least 48 hours.

Considered as Broad spectrum antibiotic (BSA) molecules which are effective against a wide range of microorganisms such as carbapenems.

Antibiotic therapies were considered appropriate if they included at least one drug active *in vitro* against the isolates from blood culture.

2.2. Microbiological Data

The blood culture system was the "BacT ALERT 3D (BIOMERIEUX-FRANCE)".

S. maltophilia isolates were identified in the clinical laboratory by biochemical tests and the Analytical Profile index procedure (API 20-NE-Biomérieux, France) supplemented by oxidase and DNase testing.

2.3. Antimicrobial Susceptibility Testing

A standardized disk diffusion method based on MH agar was performed by standardized methods recommended by the Comité de l' Antibiogramme de la Société Française de Microbiologie (CA-SFM) [21].

The inoculum suspension is prepared by selecting several morphologically similar colonies from overnight growth (16 - 24 h of incubation) on a non-selective medium with a sterile loop and suspending the colonies in sterile saline (0.85% NaCl w/v in water). The density of the suspension is adjusted to McFarland 0.5 standard (1 - 2*108 CFU/ml)

A sterile cotton swab is dipped into the inoculum suspension which is spread evenly over the entire surface of the agar plate by swabbing in three directions. Disks are applied firmly on the agar surface within 15 min of inoculation of the plates. It is important that zone diameters can be reliably measured Within 15 min of application of antimicrobial disks, the plates are inverted and incubated at 35, 1C for 16 - 20 h.

After incubation, inhibition zones are read at the point where no obvious growth is detected by the unaided eye when the plate is held about 30 cm from the eye. The inhibition zone diameters are measured to the nearest

millimeter with a ruler. Zone diameters are interpreted and categorized as susceptible, intermediate or resistant according to the CA-SFM clinical breakpoint tables [21].

2.4. Statistical Analysis

Descriptive statistics was used for all the studied variables. Satatistical analyses were performed using SPSS 17.0 Statistical package.

3. Results

From 2004 to 2011, 33 episodes of SMB were identified in 31 patients. All records were retrieved for analysis. Two patients had two episodes of bacteraemia separated respectively by 10 days and 35 days. Ninty three percent of these episodes were nosocomial acquired at the ICU. Based on microbiology laboratory data the annual frequency of *S. maltophilia* blood isolation remained constant during this period (endemic evolution) except two epidemic periods occurred in 2005 and in 2007, not investigated (**Figure 1**).

Thirty three episodes were collected via 31 patients. The mean duration of stay prior to SMB was 29 ± 23 days. There were 22 deaths in the 31 patients (71%). The mean time of death after the development of SMB was 15.6 ± 12 days (range from 3 to 44 days).

Among cases, 63.6% developed several nosocomial infections 20 ± 17 days prior to ICU-acquired SMB (bactereamia in 45.8% of the cases, urinary tract infection in 14.6% of the cases, lung infection in 20.8% of the cases). All These infections were microbiologically documented and related to strains other than *S. maltophilia* such us *A. baumannii* (25% (n = 11)), *E. cloacae*, *E. coli*, *K. pneumoniae* and other enterobacteriacae (41% (n = 18)).

More than half 51.6% (n = 16) of the patients had at least 1 surgical procedure during their hospitalization. Patient characteristics are presented in **Table 1**.

In our study, 30.3% (n = 10) of the episodes were polymicrobial and the additional isolates included *A. baumannii* (70%) imipinem resistant, *K. pneumoniae* Extended Spectrum Beta Lactamase (ESBL) and *Pseudomonas aeruginosa* (*P. aeruginosa*) Ceftazidime (CFZ) resistant. A probable portal of entry, with isolation from the site preceding SMB was identified in 27.3% (n = 9) of bacteraemic episodes. This included; CVCs (55.6% (n = 5)), urine and pleural fluid. In our series, 77.4% (n = 24) did not have a clinically apparent portal of entry but 91.7% of these individuals had a central catheter in place. Data regarding invasive procedures are summarized in **Table 2**. Nearly 77% (n = 24) of cases had received severel antibiotics prior to bactereamia caused by *S. maltophilia*, especially imipinem (IMP). Details are shown in **Table 3**.

Antimicrobial susceptibility data were derived from results of 33 isolates in 31 patients. All isolates were resistant to IMP. Approximately 85.4% were ciprofloxacin susceptible and 68.3% were susceptible to Trimethoprim-sulfamethoxazole (SXT). Resistances of *S. maltophilia* to CFZ and Fosfomycin (FOS) were 56% and 81.3% respectively. The antimicrobial susceptibility of blood isolates is shown in **Figure 2**.

Definitive antimicrobial treatment was possible in the 33 episodes of SMB, 19 (57.6%) were treated with antibiotic therapy included an appropriate agent in the most cases (89.5%). A monotherapy was administrated in 8 cases (42.1%) and a biotherapy in 7 cases (36.8%). CIP were the most prescript (31.6%).

4. Discussion

The objective of our study is to describe clinical, microbiological, and epidemiologic features of SMB. Although,

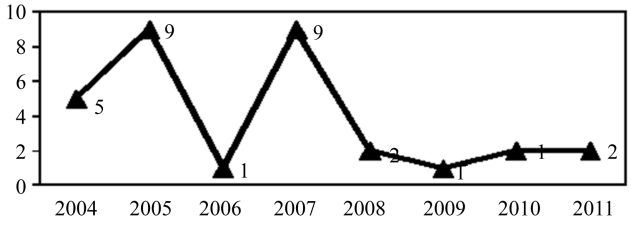

Figure 1. Distribution of *S. maltophilia* positive blood culture over seven years.

Table 1. Underlying characteristics of patients with bacteraemic episodes.

Characteristics n= 31 (*n= 33)	
Mean age mean ± SD [years] (range)	54 ± 16 (19 - 87)
Gender	
• Male	64.5% (20)
• Female	35.5% (11)
Cause of admission to ICU	
• Trauma	29% (9)
• Medical	45.2% (14)
• Urgent Surgery/Programmed surgery	25.8% (8)
Duration of stay in the ICU prior to SMB	29 ± 23 (5 - 108)
Past medical history	64.5% (20)
• Diabetes	55% (11)
✓ type 1 diabetes mellitus (ID)	45.5% (5)
✓ type 2 diabetes mellitus (NID)	54.5% (6)
• Hypertension	65% (13)
• Cancer	25% (5)
• Chemotherapy/ Radiotherapy	10% (2)
Other nosocomial infections before the bacteriemic episodes with *S. maltophilia**	63.6% (21)
Coexisting conditions	
• Major surgery	51.6% (n = 16)
• Purulent sputum	51.6% (16)
• Bronchopneumopathy	45.2% (14)
• Septic shock	12.9% (4)
• Visceral damage	12.9% (4)
• Respiratory failure	12.9% (4)
• Kidney failure	9.7% (3)
	9.7% (3)
Mechanical ventilation	74.2% (n = 23)
Central venous catheter	93.5% (n = 29)
Prior antibiotics therapy	77% (n = 24)
Surgical procedure	51.6% (n = 16)
Prior use of IMP	70.8% (17)
Polymicrobial bacteraemia	30.3% (n = 10)
Death	71% (22)

Table 2. Invasive procedure.

Invasive procedures n = 31 (n = 33)*	
Mechanical ventilation	74.2% (n = 23)
• Duration of mechanical ventilation	18.6 ± 9.6 (2 - 43) days/Median = 18
• Duration of mechanical ventilation prior to the bacteraemia*	10 ± 7 (0 - 22) days/Median = 8
Tracheostomy	25.8% (n = 8)
• Duration of Tracheostomy	36 ± 34 (1 - 88) days/Median = 32
• Duration of Tracheostomy prior to the bacteraemia*	15 ± 16 (0 - 48) days/Median = 9
Central venous catheter (CVC)	93.5% (n = 29)
✓ Subclavian vein*	19.4% (6)
✓ Internal jugular vein*	77.4% (24)
✓ Femoral vein*	3.2% (1)
• Duration of CVC	25 ± 19 (2 - 89) days/Median = 18
• Duration of CVC prior to the bacteraemia*	17 ± 17 (1 - 80) days/Median = 9
Central arterial catheter (CAC)	64.5% (n = 20)
✓ radial*	77.3% (17)
✓ Femoral*	22.7% (5)
• Duration of CAC	13.6 ± 6.6 (0 - 24) days/Median = 12.5
• Duration of CAC prior to the bacteraemia*	7.8 ± 6.4 (0 - 21) days/Median = 6
Urinary catheter	90.3% (n = 28)
• Duration of Catheterization	29 ± 21 (4 - 89) days/Median = 24.5
• Duration of Catheterization prior to the bacteraemia*	16 ± 16 (0 - 80) days/Median = 12.5

Table 3. Exposure to antimicrobial agent (n = 33).

Antibiotic	Cases % (no.)	Duration (days)	Duration of administration prior to the bacteraemia (days)
Amoxicillin-clavulanic acide (AMC)	45.8 (11)	4.4 ± 2.65 (2 - 10)	20.9 ± 22.62 (3 - 80)
Cefotaxim (CTX)	20.8 (5)	7.2 ± 2.95 (4 - 10)	8 ± 6.7 (1 - 19)
Imipenem (IMP)	70.8 (17)	22.9 ± 8.44 (8 - 40)	15.3 ± 13.93 (3 - 58)
Gentamicin (GM)	83.7 (20)	5.75 ± 3.37 (1 - 20)	15.55 ± 13.85 (1 - 65)
Ciprofloxacin (CIP)	16.7 (4)	10.5 ± 4.43 (6 - 16)	13.3 ± 14.2 (0 - 31)
Vancomycin (VA)	45.8 (11)	18.45 ± 5.78 (7 - 30)	13.45 ± 12.9 (0 - 65)
Colistine (CS)	12.5 (3)	18.3 ± 7.76 (12 - 27)	12.2 ± 9.4 (3 - 25)
Rifampicin (RA)	20.8 (5)	12.6 ± 8.84 (3 - 27)	9.2 ± 8.4 (1 - 24)

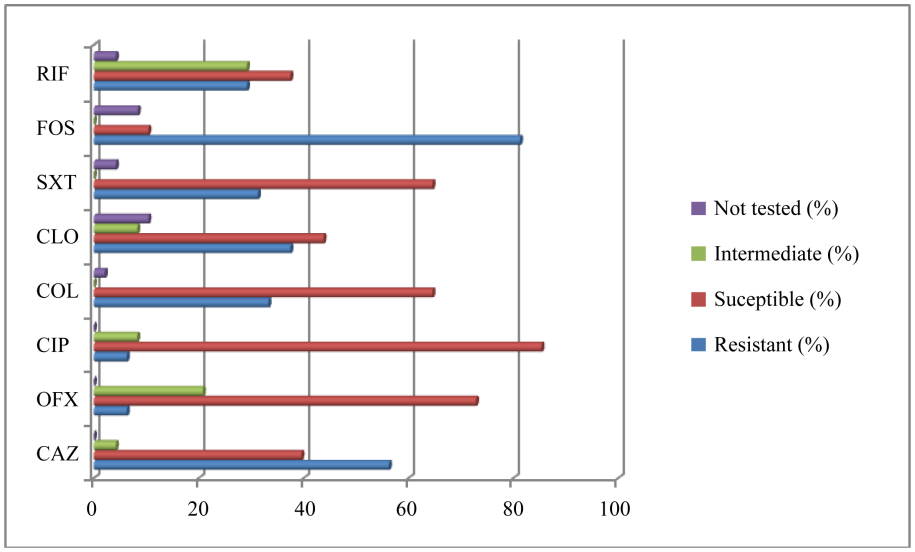

Figure 2. Antibiotic susceptibility of *S. maltophilia* for 33episodes of SMB *Rifampicin* (RIF), Fosfomycin (FOS), Trimethoprim-sulfamethoxazole (SXT); chloramphenicol (CLO); Colistine (COL) ciprofloxacin; (Cip); Ofloxacin (OFX), ceftazidime (CFZ)).

this study was restricted to the ICUs setting and had several limitations. First, the absence of a control group is a limitation recognised by the authors, and has previously been a valuable inclusion in studies of this kind [22] [23]. Second, we've included only 31 cases, indeed most previous studies had analysed a small population and have been mostly retrospective and only few of these included more than 35 patients [5] [11] [22] [24]. Finally, the heterogeneity of patients, lack of appropriate statistical analysis and lack of definition of nosocomial episodes of bacteraemia, lack of the criteria for attributing death to the bacteraemic episode were not specified, thus we had difficulties of determining a precise cause of death for our population who had multiple active co-morbidities. The characteristics in our population and those described by other authors are shown in **Table 4**.

Risk factors for acquiring *S. maltophilia* infection especially in the ICU are associated with a severely compromised health status and underlying disease, a long-term hospitalization or ICU stay, medical treatment involving indwelling devices such as intravascular catheters and exposure to broad-spectrum antimicrobials [1] [2] [13].

Usually *S. maltophilia* primarily affects patients with co-morbid illness such as immunosuppression, cystic fibrosis, malignancies, neutropenia, corticotherapy, chronic disease and severe trauma [3] [31]. Comorbid medical conditions in our patients were dissimilar to other studies [4] [17] [31] [33]. Most of comorbidities cited previously were uncommon in our population. Third of our patients 29% (9) had major trauma among them 6 were died (66.7%) and 64.5% (n = 20) of patients had chronic disease. In this group 15/20 (75%) were died versus 7/11 (63.6%) in the other group. The difference was not statistically significant (P = 0.7) by chi-square

Table 4. Baseline characteristics of the patients in comparison with selected previously reported studies.

Authors	No. of cases /episodes	Age	Duration of hospitalization (days)	Previous Imipinem	Intubation	CVC	Death
Our study	33	54 ± 16	19 ± 17	71% (17)	74% (n = 23)	93% (n = 29)	71%
Lai *et al.* (2004) [1]	84	62 ± 2	24 (3 - 100)	42%	36%	83%	33%
Senol *et al.* (2002) [2]	30	46	11 ± 18	33% (n = 10)	13%	80% (n = 24)	27%
Friedman *et al.* (2002) [5]	45	54	19	40% (18)	48% (21)	84% (38)	18% (n = 8)
Apisarnthanarak 2003 [6]	13	ND	14	54% (n = 7)	ND	61% (n = 8)	ND
Muder *et al.* (1996) [11]	91	ND	ND	ND	20%	82%	21%
Araoka H *et al.* (2010) [18]	53	57	ND	31%	ND	57% (30)	51%
Micozzi *et al.* (2000) [22]	37	29	29	ND	ND	86% (32)	24%
Victor *et al.* 1994 [23]	14	34 (7 - 68)	23	50%	ND	100%	92%
Elting *et al.* 1990 [24]	60	51	13	50%	ND	88%	38%
Wang *et al.* (2004) [25]	50	28 - 94	36	56%	40%	60%	62%
Cheong *et al.* (2008) [26]	109	53 ± 15	>30.	ND	16%	76% (n = 83)	ND
Nseir 2006 [27]	38	63 ± 12	14 ± 11	15% (n = 6)	84%	92% (35)	60%
Metan G *et al.* 2005 [28]	41	51	24	75%	27%	90.2%	4%
Ubeda P *et al.* 1998 [29]	26	40	ND	25%	50%	73% (n = 19)	20%
Villarino *et al.* 1992 [30]	45	46	23	38% (n = 17)	84%	ND	33% (n = 15)
Ansari S. *et al.* 2007 [31]	54	55	16	46%	ND	ND	22%
Gopalakrishnan. 1999 [32]	143	60	13	7%	82%%	ND	47%

test. A higher incidence of diabetes was demonstrated in our study when compared with other reported series [2] [24] [32].

A number of studies have pointed to an association between ICU stays and the subsequent increasing of incidence, mortality and morbidity due to *S. maltophilia* [11] [25] [31].

The mean duration of stay in our study prior to SMB was 19 ± 17 similar to other reports [1] [5] [23] [28] [30] [31] [34], who reported a duration ranged between 16 and 23 days. Whereas some authors found more extended duration of stay (>29 days) [22] [25] [26]. Others [2] [6] [24] [27] [32], have reported a less extended duration ranged between 11 and 14 days. In addition, in a case control study dealing with 53 cancer patients by Ansari *et al*. [31], ICU stay within 30 days before the isolation of *S. maltophilia* was found to be significantly associated with the emergence of Multi-Drug Resistant (MDR) *S. maltophilia* and had the highest OR of all the risk factors. Micozzi *et al*. [22] included in his study a control group of patients with bacteraemia due to *P. aeruginosa*. He observed that more cases of SMB are developed during hospitalization but he didn't find any statistical significant difference between a control group and his population with SMB. In addition, Metan *et al*. [28] had found that the patients who died within 30 days after the onset of SMB had a higher rate of intensive care unit stay. The importance of intravascular devices exposure in the pathogenesis of SMB is, however, becoming increasingly recognized such as mechanical ventilation, tracheostomy [4] [11] [12] [23] [24].

The majority of patients in our study have had indwelling intravascular devices related to the fact that our cases was exclusively collected from ICU and patients had characteristics that indicated significantly worse underlying severity of illness. The presence of an indwelling CVC has been previously reported for 78% - 86% of patients [23] [24] [35] [36]. This range is lower than the proportion in our figure which was 93.5%. Wang [25] in his univariate analysis revealed that CVC and mechanical ventilation were significantly associated with a high crude mortality rate. This also tallied with several other studies who implicated CVC [17] [30] and mechanical ventilation [11] [17] [23] [24].

The portal of entry of *S. maltophilia* infection is frequently unknown. Our results highlight the fact that Central-venous lines are the most common source of SMB (SMB was attributed to a CVC infection in almost 55.6% of our patients). This finding is consistent with those of other reports [5] [10] [11] [22] [33] [37] [38].

In cases where there is no obvious source of infection it has been suggested that these devices may be the primary source [16]. Muder *et al*. [11] reported that in their series 56% of cases with SMB did not have a clinically apparent portal of entry but 84% of these individuals had a CVC in place. Senol [2] found that 30% of cases had no apparent primary source of infection, but all had CVCs in place. In our study 77.4% didn't have a clinically apparent portal of entry. As 91.7% of these patients had a CVC in place, it is likely that the catheter was the ultimate source of infection in many of these patients.

Most studies on risk factors for the emergence of *S. maltophilia* have revealed that Selective pressure caused by the overuse of broad-spectrum antibiotics, especially carbapenems, predispose to infection or colonization with *S. maltophilia* [13] [31] [32]. In the present study, we found a high frequency in IMP prescription prior to SMB, which is consistent with previous reports, in which between 25% and 43% of patients received this antibiotic [5] [11] [23] [35]. The use of carbapenems has also been established as the primary risk factor for *S. maltophilia* infections [31] [39]. Prior therapy with IMP was 10 times more frequent amongst cases of *S. maltophilia* than in matched controls in a previous case-control study conducted at the University of Texas [12]. Many other studies, used multi-variate analysis, found carbapenem use before admission to the ICU to be an independent risk factor [12] [27] [30] [40] [41].

An association between the emergence of this strain and the broad-spectrum antibiotics other than IMP, such as aminoglycosides, fluoroquinolones, and extended-spectrum cephalosporins, has been previously documented [2] [15] [42]. Meyer [40], in his univariate analysis, added strength to this findings by demonstrating a significant correlation between carbapenems, other broad-spectrum antibiotics and total antibiotic consumption with the incidence density of *S. maltophilia*.

Susceptibility study among the strains isolated from the 33 episodes of SMB showed that the most effective antibiotics *in vitro* were CIP (85.4%), SXT (68.3%), C (43.9%) and CFZ (43.9%). These observations coupled with other reports from different institution [1] [2] [11] [5] [12] [42]-[45] (**Table 5**).

The major problem which challenges the laboratorians and clinicians is the emergence of resistance to SXT. Indeed, SXT remains the most effective drug for the treatment of *S. maltophilia* infections despite the view that this drug is only bacteriostatic for most isolates [11] [7] [23] [16] [43] [46]-[49].

Nevertheless, the emergence of resistance to this agent [42] [47] [50], and allergic reactions or more accurately, hypersensitivity reactions, which are not uncommon, leads to further limitation of available treatment options [16] [47].

We've noted in our study 31.7% of resistance and this value is alarming. Several reports have shown that the prevalence of strains that are resistant to SXT is increasing and a widely variation in resistance to SXT was documented [22] [16] [51] [49] [52]. Indeed, in Spain, Canada and Latin America, authors reported that 2% of isolates of *S. maltophilia* were resistant to SXT [53] [54] [49], 10% in Europe [49]. Whereas an Italian study reported the highest levels of resistance reached 80.9% of the isolates [55].

Table 5. Antibiotic susceptibility characteristics of our population in comparison with selected previously reported studies (n = 33).

	Ceftazidime (CFZ)	Ciprofloxacine (CIP)	Sulfamethoxazole (SXT)	Chloramphenicol (C)
Our study	44 %	85%	68%	44%
Lai *et al.* (2004) [1]	60%	83%	76%	71%
Looney W. *et al.* (2009) [3]	5% - 53%	0% - 82%	0% - 100%	1% - 80%
Morrison *et al.* (1986) [4]	4%	ND	100%	ND
Friedmann *et al.* (2002) [5]	65%	60%	80%	76%
Muder *et al.* (1996) [11]	56%	62%	91%	ND
Micozzi *et al.* (2000) [22]	27%	19%	42%	ND
Wang *et al.* (2004) [25]	44%	36%	60%	42%
Ubeda P. *et al.* (1998) [29]	62%	60%	90%	ND
Tsai *et al.* (2006) [34]	62%	43%	14%	ND
Betriu *et al.* (2001) [43]	50%	15%	95%	33%
Safdar *et al.* (2007) [44]	15% - 24%	16% - 61%	75% - 98%	0%

Betriu [43] showed that resistance to SXT decreased significantly from 16.8% in 1995-1996 to 4.7% in 2001 ($P < 0.005$). He also observed an increasing trend in the rates of resistance to ciprofloxacin ($P < 0.05$) from 54% in 1993-1994 to 68.7% in 2001. These patterns of susceptibility reflected the development the antibiotic prophylaxis practices in the hospitals according to some authors [1] [42] [56].

It is clear that infections caused by *S. maltophilia* are particularly difficult to manage and should be approached with caution because of many features of resistance of clinical isolates. The concept of "appropriate" therapy for *S. maltophilia* is challenging. There is ongoing debate, regarding the optimal treatment of *S. maltophilia* infection, about the use of monotherapy versus combination therapy [16] [11] [25] [57] [42] [47]. In our study, among patients 57.6% were treated with an appropriate agent. Several studies have reported a significant association between survival and administration of appropriate antimicrobial therapy [22] [23] [11] [35]. We did not find such association, most likely because therapy was not controlled in our study. Interest in antibiotic combinations has led to numerous studies of *in vitro* synergy [30] [5] [43] [58]. The potential benefits of combination antibiotic therapy are well recognised. They include a broadened and more reliable spectrum of activity, enhanced antibacterial activity due to any synergistic or additive effect allowing lower doses of toxic agents to be given, and prevention of the emergence of resistance [3] [11] [46].

About the management of Infection by other means than antimicrobial agents, several investigators have stressed the importance of removing infected CVC [1] [24] [18] [38] [45] [59]. Boktour *et al*. [33], found that prompt removal of the catheter in cancer patients, in whom Catheter-related SMB was occurred, was found to be associated with a better prognosis. However, Muder and al. [11] reported the successful management of CVC-related bacteraemia without removal of the device and concluded that there was no standardized protocol for catheter removal and culture.

In our series there was a crude mortality percentage 71% of *S. maltophilia* bactereamia suggesting that SMB itself serves as a marker of serious pathology. This is higher than reported mortality rates in earlier studies, which ranged from 22% to 69% [2] [23] [11] [25] [26] [30] [32] [34]-[36]. Direct attributable mortality is weak, and seems to depend on the severity of the underlying disease. There have been some studies on mortality of *S. maltophilia* bactereamia, but most studies included only small numbers of patients [5] [22]. Furthermore, data regarding risk factors for mortality of *S. maltophilia* bactereamia are limited and the criteria for attributing death to the bacteremic episode were not specified [26].

Polymicrobial SMB is a frequent occurrence and there was a significant debate about the association of this common characteristic with the mortality rate [24]. Indeed, according to some investigators, the acute mortality rate associated with these polymicrobial bacteraemias is not significantly different from that associated with SMB alone [12] [53]. In our study Polymicrobial bacteraemia occurred in 10 of the 33 cases and the mortality rate was as high as 60% versus 78.3% in monomicrobial cases ($P = 0.4$). These percentages were similar to previous studies [1] [23] [11] [35] [6] [10] [18] [25] [29]. The main additional isolate was *A. baumannii* (70%, n = 7) similar to prior report from Lai [1], who explained that the increased isolation of *Acinectobacter* spp. may have been due to antibiotic selective pressure (**Table 6**).

Table 6. Polymicrobial characteristics of our population in comparison with selected previously reported studies (n = 33).

	Frequency of polymicrobial episodes	Additional isolates
Our study	30% (n = 10)	*A baumannii* (n = 7), *K. pneumoniae* (*n* = 1), *P. aeruginosa* (*n* = 1), *Alcaligenes* spp. (*n* = 1)
Lai *et al.* (2004) [1]	27% (n = 23)	Enterobacteriaceae (n = 10), *Acinetobacter* spp. (n = 6), *SARM* (n = 6), *Enterococcus* spp.
Morrison *et al.* (1986) [4]	64% (n = 63)	*Enterobacter* (n = 14), *P. aeruginosa* (*n* = 12), *S. aureus* (*n* = 10), *E. coli* (*n* = 8), *K. pneumoniae* (*n* = 7), *Candida* (n = 7), *A baumannii* (n = 4)
Muder *et al.* (1996) [11]	40% (n = 36)	*Coagulase-negative staphylococci* (*CoNS*) (n = 10 isolates), other Non fermentative Gram-negative bacilli (NF-GNB) (n = 10), Enterobacteriaceae (n = 9), *Enterococcus* spp. (7), *Candida spp* (n = 3)
Araoka *et al.* (2010) [18]	38% (20/53)	*Enterococcus* spp. (n = 13), *Staphylococcus epidermidis* (n = 5), *P. aeruginosa* (n = 4), *E. cloacae* (n = 3), Methicillin-resistant *Staphylococcus aureus* (MRSA) (n = 3), *Enterobacter aerogenes* (n = 1), *Burkholderia cepacia* (n = 1), *K. pneumoniae* (n = 1), *Bacteroides fragilis* (n = 1)
Micozzi *et al.* (2000) [22]	16% (6/37)	Cocci Gram positif
Wang *et al.* (2004) [25]	16% (8/50)	*A. baumannii* (n = 3) *Enterobacter aerogenes* (n = 2) *E. coli* (n = 2), *Candida albicans* (n = 1)

5. Conclusion

Data in our study and the current status of knowledge show that SMB in ICU is a cause of concern. This problematic opportunist is closely related to debilitated host, long-term stay in ICU, indwelling devices and prior exposure to broad-spectrum antibiotics. Therapy for this infection is increasingly challenging for the high level of intrinsic resistance, uncertainties about the value of *in-vitro* susceptibility testing, and the emergence of resistance to antimicrobials such as SXT and TCC, which are recommended for empirical treatment. Effective control strategies are needed to prevent the spread of this micro-organism. These strategies must emphasize the importance of continued local surveillance of *S. maltophilia* isolation, in addition, the implantation of a multidisciplinary, education-based, antibiotic-resistance management approach and reinforcement of hygiene practices.

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Conflicts of Interest

We declare that we have no conflicts of interest.

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