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Achromobacter species, an emerging cause of bacteremia in tertiary healthcare facilities in Egypt

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Abstract

During our laboratory routine, we detected Gram-negative, motile, aerobic, oxidase- and catalase-positive, lactose non-fermenting bacilli during microbial isolation from blood cultures of immune compromised patients. Our study investigates this phenomenon.

Blood culture results from 1000 samples were taken during febrile attacks in immune compromised patients in adult intensive care units (AICUs), pediatric and neonatal intensive care units (PICUs and NICUs, respectively), liver and kidney departments, and oncology and hematology departments in a tertiary healthcare facility in Cairo, Egypt. The blood cultures were processed in the microbiology laboratory and incubated in an automated system. An automated system was also used to identify the species in positive cultures and perform antimicrobial susceptibility testing. *Achromobacter* sp. were identified and isolated according to their morphological and biochemical characteristics.

Of one thousand blood cultures performed, 310 were positive (Gram-negative: 195, 63%; Gram-positive: 105, 34%; fungi: 10, 3%). Of these positive cultures, 16 (5.2%) were positive for *Achromobacter* sp., the most common being *Achromobacter xylosoxidans* (15/16, 93.75%), while *A. dentrificans* was identified in one case (6.25%). Among those affected, 37.5% were patients with hematological malignancies, 6.25% had organ transplants, 56.5% were in the ICUs (25% were in AICU, 18.8% in the PICU, and 12.5% in the NICU). *Achromobacter* sp. were resistant to cefepime, aminoglycosides, and fluoroquinolones. Central venous catheter infection occurred in 13 (81.25%) cases.

Our findings open discussion concerning *Achromobacter* sp. as an opportunistic pathogen in immune compromised patients and contribute to the development of future treatment approaches.

Keywords: *Achromobacter* sp; Bacteremia; Immune compromised; Central venous catheter; Antimicrobial susceptibility

1. Introduction

In 1923, the Committee of the Society of American Bacteriologists (today the American Society for Microbiology; ASM) first established Genus *Achromobacter* as a "non-pigment-forming, motile or non-motile Gram-negative bacteria, which was oxidase- and catalase-positive, occurring in water and soil" [1] Close resemblance of genus *Achromobacter* to genus *Alcaligenes*, both of which are members of the *Alcaligenaceae* family of the order *Burkholderiales*, prompted

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reassignment of several *Achromobacter species* to genus *Alcaligenes* and vice versa. Genus *Achromobacter* currently comprises 19 officially designated species, most of which were characterized within the last decade [2]

Fifteen species have been isolated from different clinical specimens, including *Achromobacter xylosoxidans, Achromobacter denitrificans, Achromobacter ruhlandii, Achromobacter piechaudii* [2], *Achromobacter animicus, Achromobacter mucicolens, Achromobacter pulmonis* [3], *Achromobacter insolitus, Achromobacter spanius Achromobacter deleyi* [4], *Achromobacter aegreficans, Achromobacter insuavis, Achromobacter anxifer, Achromobacter dolen* [3], and *Achromobacter marplatensis* [5].

Achromobacter causes infection specially to high risk patients, such as meningitis, urinary tract infections, abscesses, osteomyelitis, corneal ulcers, prosthetic valve endocarditis, peritonitis, and pneumonia [6]. Immunosuppressed patients, patients with cystic fibrosis [7] or underlying malignancy are particularly at risk for developing *Achromobacter* bacteremia, a rare but potentially life-threatening illness [8] Other risk factors include chronic renal failure, diabetes mellitus, cardiac disorders, immunosuppression, steroid treatment, and intravascular catheters [9].

Achromobacter infection is often acquired from exposure to contaminated solutions. This is due to its ability to survive in aqueous environment, producing a resistant biofilm. This allowed its recovery from hospital tap water, faucet aerators and disinfectant atomizers, as well as disinfectant solutions such as chlorhexidine gluconate, and ultrasound lubricating gel. [10, 11, 12] *Achromobacter* ia are multi-resistant opportunistic hydro-telluric pathogens. The two main intrinsic antimicrobial resistance mechanisms of *Achromobacter species* comprise multidrug efflux pumps and chromosomal, OXA-114-like lactamases. Extended spectrum β-lactamases (ESBLs), AmpC type β-lactamases, and metallo-β-lactamases (MBLs) have also been detected in *Achromobacter* isolates and appear to contribute to resistance to β-lactams, including carbapenems [13].

2. Material and methods

The study was conducted at Maadi Armed Forces Medical Compound; a tertiary healthcare facility in Cairo, Egypt, over a period of two years, and included patients admitted to the following services: Medical Intensive Care Units, Pediatric intensive Care Units, Neonatal Intensive Care Units, Oncology and Hematology Departments.

Febrile patients were subjected to clinical assessment, and categorized according to age, sex, presenting symptoms, presence or absence of an underlying malignancy, chronic medical conditions such as Diabetes mellitus, Chronic respiratory disease, renal insufficiency, as well as history of solid organ transplantation.

Blood culture samples were collected from two venipuncture sites. Additional blood sample was obtained from central venous line (if present). Specimens were aseptically inoculated into Bact/ALERT 3D bottles and were incubated in BacT/ALERT 3D system (bioMérieux, Marcy L'Etoile, France) for 7 days at 37℃. Blood culture bottles with positive signals were sub-cultured on blood, chocolate and MacConkey agar plates and further incubated at 37℃. Isolates were identified systemically by microscopic examination of Gram stained smears, and their biological activities were identified using VITEK-2 system (bioMérieux) with Gram positive (GP) and Gram negative (GN) identification cards. VITEK-2 system was also used for antimicrobial susceptibility testing to determine minimal inhibitory concentrations (MICs), according to the guidelines provided by Clinical Laboratory Standards Institute (CLSI). Information regarding biological characteristics of the microbial isolates, their phenotypic drug resistance, and their MICs against various antimicrobial agents were collected from the VITEK-2 Compact database (bioMérieux). Data were statistically analyzed using SSPS ver.26 (IBM).

3. Results and discussion

The study group comprised 16 patients with equal sex distribution and a mean age of 33.5. The clinical assessment revealed underlying medical conditions summarized in table 1. All patients had central venous catheters inserted, and central line-associated blood stream infection (CLABSI) was documented in 13 out of the 16 patients enrolled (81.25%).

Most isolates occurred in patients from ICUs (56.25%), followed by Hematology (37.5%) and Nephrology Services (6.25%).

Table 1 Clinical assessment results for patients enrolled in the study

Clinical Condition	**Number (%)**
Malignancies	7 (43.75)
Hematological malignancies	6 (37.5)
Solid organ tumors	1 (6.25)
Concurrent Medical Conditions	9 (56.25)
Diabetes Mellitus	1 (6.25)
Congestive Heart Disease	1 (6.25)
Chronic Renal Insufficiency	1 (6.25)
Chronic Respiratory Impairment	3 (18.7)
Chronic Gastrointestinal Conditions	2 (12.5)
Chronic CNS lesions	1 (6.25)

Microbial growth was observed in 310 out of 1000 blood samples collected. Of these 310 positive blood cultures, 195 isolates were Gram-positive bacteria, while 105 were Gram-negative bacteria, and the remaining 10 blood cultures yielded fungal isolates (See Fig. 1).

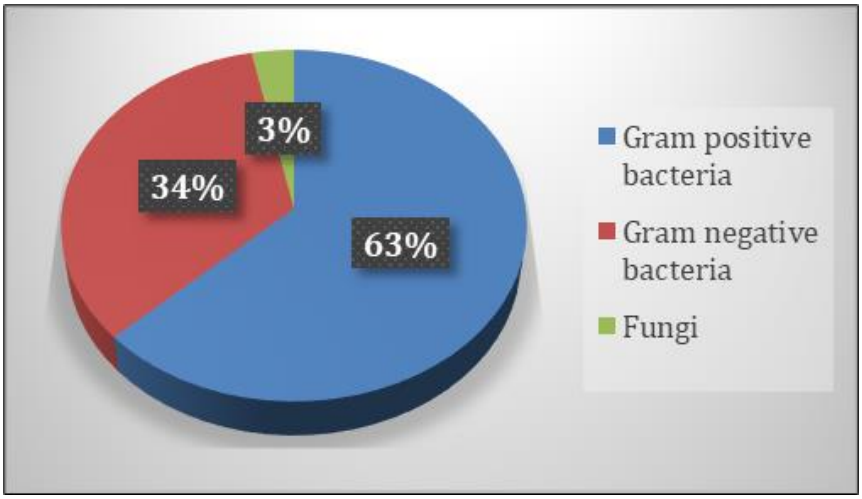

Figure 1 Distribution of Positive Microbial Isolates

Distribution of Microorganisms isolated from positive blood culture is shown in table 2. The most common Gram-negative pathogen isolated was *Klebsiella pneumoniae* (23%) followed by *Acinetobacter baumannii* (9%), while the least encountered was *Serratia Marcescens* and *Salmonella spp.* (each comprising 0.3%). The most common Gram-positive pathogen isolated was *Staphylococcus hemolyticus* (27.8%). The most common fungal isolate was *Candida albicans* (1.3%).

Achromobacter was encountered in 16 cultures out of the positive 310, which constitutes about 5.2%. The species isolated included *Achromobacter xylosoxidans* (15 isolates; 4.8%) and *Achromobacter denitrificans* (1 isolate; 0.3%).

The Antimicrobial susceptibility patterns of *Achromobacter species* isolates were analyzed according to the MICs of various antimicrobial agents. The results of antimicrobial susceptibility are depicted in table 3.

Table 2 Distribution of Microbial Isolates

Isolated pathogens	**Number (%)**
Gram-negative bacteria	195 (63)
Klebsiella pneumoniae	71 (23)
Acinetobacter baumannii	28 (9)
Escherichia coli	27 (8.7)
Pseudomonas aeruginosa	24 (7.7)
Achromobacter spp.	16 (5.2)
Enterobacter cloacae	14 (4.5)
Stenotrophomonas maltophilia	13 (4.2)
Serratia marcescens	1 (0.3)
Salmonella sp.	1 (0.3)
Gram-positive bacteria	105 (33.8)
Staphylococcus haemolyticus	27 (8.7)
Staphylococcus epidermidis	26 (8.5)
Staphylococcus hominis	26 (8.5)
Staphylococcus aureus	13 (4.2)
Enterococcus faecium	4 (1.3)
Enterococcus faecalis	3 (1)
Staphylococcus warneri	3 (1)
Staphylococcus lentus	2 (0.6)
Staphylococcus lugdunensis	1 (0.3)
Fungi	10 (3.2)
Candida albicans	4 (1.3)
Candida parapsilosis	2 (0.6)
Candida glabrata	1 (0.3)
Candida krusei	1 (0.3)
Candida famata	1 (0.3)
Cryptococcus laurentii	1 (0.3)
Total	310

Achromobacter sp. were recently isolated and reported as laboratory pathogens in developing countries [9, 10]. The principal reason behind the increased identification and reporting of *Achromobacter* sp. is the use of automated identification and sensitivity methods. The previously used manual identification methods led to the misidentification of *Achromobacter* sp. as *Pseudomonas aeruginosa*, *Burkholderia cepacia* complex bacteria, and *Stenotrophomonas maltophilia*, particularly in laboratories that were unable to perform specialized assessments [4]. The underestimation and misdiagnosis of *A. xylosoxidans* infection lead to inappropriate treatment [11]. Patients with cancer, patients undergoing hematopoietic and organ transplantation, patients with HIV infection/AIDS, and premature infants are all at increased risk, and in such individuals, *Achromobacter* sp. infections occasionally present as life-threatening illnesses.

Because most *Achromobacter* sp. infections are nosocomial, a common source can be frequently traced. Possible sources include intravascular catheters, contaminated dialysis fluid, deionized water, mechanical ventilators, chlorhexidine solution, and incubators, as well as normal stool matter colonized by *Achromobacter species* [14].

Table 3 Antimicrobial Susceptibility Testing for *Achromobacter* isolates

Antimicrobial Agent	**No. of Susceptible Isolates (%)**
Piperacillin-tazobactam	14 (87.5)
Ceftazidime	13 (81.25)
Meropenem	12 (75)
Trimethoprim-sulfamethoxazole	12 (75)
Tobramycin	3 (18.75)
Levofloxacin	3 (18.75)
Ampicillin-sulbactam	3 (18.75)
Tigecycline	3 (18.75)
Moxifloxacin	2 (12.5)
Imipenem	2 (12.5)
Sulbactam-cefoperazone	1 (6.25)
Ertapenem	1 (6.25)
Cefepime	1 (6.25)
Ciprofloxacin	0 (0)
Gentamycin	0 (0)
Ampicillin	0 (0)
Amikacin	0 (0)
Cefazolin	0 (0)
Cefoxitin	0 (0)
Ceftriaxone	0 (0)
Nitrofurantoin	0 (0)
Cefuroxime	0 (0)
Cefotaxime	0 (0)

Our study results revealed *Achromobacter* sp. as an emerging nosocomial pathogen, representing 5.2% of positive blood culture results. *A. xylosoxidans* was the most frequently isolated *Achromobacter species* (93.75%), which agreed with Aisenberg et al. [7], who reported that *A. xylosoxidans* was isolated in 94% of bacteremia cases. Although *A. denitrificans* was isolated in 6.25% of our cases, the percentage of *A. xylosoxidans* bacteremia in patients with cancer, particularly those with underlying hematologic malignancies, was 37.5%. A Spanish single-center study reported *A. xylosoxidans* bacteremia in 39% of patients with cancer [13]. *A. xylosoxidans* bacteremia is almost always a nosocomial infection that is related to intravascular catheters and is frequently reported in patients with underlying malignancies [2]. Another report [11] revealed that malignancies and CVC implants were the most common underlying conditions, which correspond with our study findings.

All the patients in our study had intravascular catheters, and CVC's were a source of infection in 13/16 patients (81.3%). This finding corresponded to Stutzman et al. [15], who reported catheter-related infections in 82% of cases. Other case series have reported rates of catheter-related bacteremia of 19% [6], 25% [16], 55% [17], and 65% [18]. The higher

rate of catheter-related infections in our study might reflect the higher frequency of use of intravascular catheters in our patients.

Achromobacter sp. is typically is resistant to various antibiotics, including ampicillin, aztreonam, aminoglycosides, first- and second-generation cephalosporins, tetracyclines, and rifampicin. Although most show in vitro sensitivity to trimethoprim/sulfamethoxazole, imipenem, and, in some cases, ceftazidime, piperacillin, and cefoperazone, the antimicrobial susceptibility profile for each case must be considered to determine appropriate therapy [19]. Regarding the in vitro antimicrobial susceptibility of the isolates in our study, they were susceptible to piperacillin/tazobactam (87.5%), ceftazidime (81.25%), trimethoprim/sulfamethoxazole (75%), and meropenem (75%), and most were resistant to ampicillin, most cephalosporins, aminoglycosides, and fluoroquinolones. These results are in agreement with Pandey et al. [20], Shie et al. [17], De Fernandez et al. [21], and other reports [6, 18, 22, and 23]. Thus, antimicrobial susceptibility information is crucial when making therapeutic decisions, especially for IC and critically ill patients.

4. Conclusion

It is essential to keep a close watch on *Achromobacter sp.* as an emerging nosocomial pathogen, and the advent and widespread use of automated methods has made this possible. Regular analysis of the patterns of antimicrobial drug resistance will aid in determining appropriate changes in treatment modalities and preventive measures over time. Careful modification of hospitals' antibiotic policy with focus on such emerging pathogens would greatly aid in containing the spread of these organisms and thus help in preventing multi-drug resistance patterns.

Compliance with ethical standards

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Disclosure of conflict of interest

There is no conflict of interest.

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