**Achromobacter spp. Surgical Site Infections: A Systematic Review of Case Reports and Case Series**

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Abstract: *Achromobacter* species are isolated from rare but severe healthcare-associated infections, including surgical site infections. They are considered to preferentially infect immunocompromised patients but so far with limited evidence. We conducted a systematic review on *Achromobacter* spp. surgical site infections (SSIs) to determine if such infections were indeed more commonly associated with immunocompromised patients. The secondary objective was to describe the characteristics of infected patients. Eligible articles had to be published before 30 September 2020 and to report *Achromobacter* spp. SSIs across all surgical specialties excluding ophthalmology. Analyses were performed on individual data without meta-analysis. Cases were divided into 2 subgroups: one group which had either prosthesis or implant and the other group which did not. A first selection led to a review of 94 articles, of which 37 were analyzed. All were case reports or case series and corresponded to 49 infected patients. Most of the patients were under 65 years of age and had undergone a heart or digestive surgery followed by deep infection with no co-infecting pathogens. Nine out of the 49 cases were immunocompromised, with similar distribution between the two subgroups (16.6% and 20%, respectively). This review suggests that *Achromobacter* spp. SSIs do not preferentially target immunocompromised patients.

Keywords: *Achromobacter* spp.; surgical site infection; immunocompetent; review

1. Introduction

Surgical Site Infections (SSIs) are a major cause of increased morbidity and mortality, prolonged hospital length of stay, hospital readmissions, and increased health care costs in surgical patients [1]. According to the results of the latest Nosocomial Infections National Prevalence Survey (NINPS), SSIs accounted for 20% of all the Healthcare-Associated Infections (HAIs) in 2017 in the metropolitan and the overseas regions of France and represented the second most common HAI after the urinary tract infections [2]. The bacteria commonly isolated in SSIs are *Staphylococcus aureus* and *Enterobacteriaceae*, but environmental bacteria such as *Pseudomonas aeruginosa* account for a significant proportion of the agents involved in such infections [3].

*Achromobacter* species, especially *A.xylosoxidans*, have also been isolated from rare but severe HAIs including SSIs [4–9]. Initially described as low-virulence and sporadic contaminants, these bacteria have been emerging in health care facilities for the past few decades. Knowledge about these microorganisms is continuously increasing [10] with some virulence factors identified [11] and some case reports describing severe infections with fatal outcomes [11–15]. Most authors present *Achromobacter* spp. as an opportunistic pathogen that preferentially infects immunocompromised patients, but so far with insufficient amounts of evidence [6,16–22].
We hypothesize that patients with *Achromobacter* SSIs are not predominantly immunocompromised. A preliminary search in MEDLINE via PubMed database and in PROSPERO registry showed the lack of systematic review on *Achromobacter* spp. surgical site infections, neither published, nor in development. To explore our hypothesis, we conducted a systematic review on *Achromobacter* spp. SSIs across all surgical specialties. Our primary objective was to determine if *Achromobacter* spp. SSIs preferentially target immunocompromised patients. The secondary objective was to describe the main demographic and clinical characteristics of infected patients.

2. Materials and Methods

This systematic review was conducted following the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) recommendation.

The research question was: do *Achromobacter* spp. mediated SSIs preferentially target immunocompromised patients?

2.1. Search Strategy

A comprehensive literature search was performed in the following databases, registries and search engines: MEDLINE via PubMed, Cochrane Library, Clinicaltrials.gov, GoogleScholar.com, Theses.fr. The search was completed by the analysis of “similar situations” on e-sin.sante publique france.fr, the French reporting platform for healthcare-associated infections, and by the examination of the discussion board of cpias-ile-de-france.fr, a French website for the prevention of healthcare-associated infections. The search covered all publications up to and, including 30 September 2020, with no start date specified. Search terms were defined by two independent researchers and adapted to each repository by combining vocabulary, relevant MeSH terms, and keywords such as “Achromobacter”, “Alcaligenes xylosoxidans”, “surgery”, “surgical site infection”, “wound infection”, “nosocomial infection”, “healthcare-associated infection”, “bacteraemia”, “endocarditis”, “meningitis”, “bacteraemia”, “ventriculitis”, “mediastinitis”, “abscess”, “peritonitis”, “burns”. When available, filters were applied to select studies in English and French languages and include those involving human subjects only. Additional studies were identified from the references provided by retrieved studies. The detailed search strategy adapted to each database or repository is provided as Supplementary File S1.

2.2. Eligibility Criteria

A study was eligible for inclusion if it described at least one case of either deep or superficial *Achromobacter* spp. SSI in patients across all ages and included documentation of clinical and microbiological criteria, regardless of the length of the time interval between surgery and infection. The eligibility included the SSIs occurring either in the surgical wounds, spaces, or organs, and/or on prosthetic materials or implants which were placed during surgery. All types of surgery were considered except for ophthalmic surgery.

*Achromobacter* spp. infection, either superficial or deep, was considered an SSI if it met the clinical and microbiological criteria specified by the Center for Disease Control [23]. With regard to the timing of onset, the French definition, which is more precise for this criterion, was preferred. An SSI was then defined as an HAI if it occurred within 30 days post-surgical procedure that did not involve an implant or prosthesis, and within one year when either implant or prosthesis was involved in the surgery process. Beyond this period, an SSI was considered a community-acquired infection unless authors established a clear link between surgery and infection [24].

All included articles had to provide sufficient information on the patients’ immune status. Unless the “immunocompetent” status was clearly announced, patients with at least one of the following criteria described in the NINPS protocol, i.e., solid tumor or hematological malignancy, organ transplantation, radiotherapy, chemotherapy, immunosuppressive therapy, high-dose prednisolone (>5 mg/kg/day) or prolonged (>30 days) use of corticosteroids or Human Immunodeficiency Virus infection with <500 CD4+ cells/mm³ [25] were
defined as immunocompromised. In contrast, co-morbidity factors (i.e., diabetes mellitus, obesity), which are known to predispose individuals to various infections [26], were not taken into account.

Articles dealing with fundamental science and general guidelines were excluded as well as those that described the surgical site colonization only.

2.3. Study Selection

Study selection was performed by two independent researchers using the Microsoft Excel software. Titles of potentially eligible studies were integrated into an Excel spreadsheet. By applying a color code and alphabetic classification, duplicates were eliminated and selection on titles and abstracts was performed online. The two independent researchers examined the selected full-text materials to ensure the accuracy and the eligibility of the criteria. In case of a disagreement between the two researchers, an opinion from a third researcher was requested. The case was discussed between the three researchers until a consensus was reached.

For recent studies (publication year > 2010), when the patient’s immune status or individual data were not provided, the authors of the studies were contacted for the missing data.

2.4. Data Collection Process and Items

Independent double extraction of data from eligible, full-text articles was performed by two researchers, each following the same extraction form. For each article, the following data were recorded: name of the first author, the year of publication, demographics (age and sex), immune status, surgical data (surgical specialty, date of surgery, surgical site), infection data (the time interval between surgery and diagnosis, depth, identification of Achromobacter spp., clinical criteria for diagnosis, associated microorganisms), treatments and outcome. The time period between surgery and diagnosis was defined as an interval between the surgery and the date of the first positive sample with Achromobacter spp..

Cases with some missing data were accepted as long as the information on the patient’s immune status was available.

2.5. Data Analysis

The analysis was carried out on the individual data file using the Microsoft Excel software. Categorical data were expressed as percentages (numbers). Quantitative data were expressed as a median [min-max] and means +/− standard deviation.

3. Results

3.1. Study Selection

PRISMA 2020 flow diagram (Figure 1) describes the different stages of study selection. A total of 820 records were identified by our literature search. Among these records, 94 were duplicates and therefore, removed. After examining the titles and abstracts, 548 records were excluded according to our eligibility criteria. Ninety four full-text materials were examined in their entirety. The authors from 5 cases were contacted for missing information but these authors were unresponsive. Finally, 37 articles were included in the analysis [4,6–8,12–14,16–22,27–49].
3.2. Study Characteristics

The extensive literature search led to the inclusion of case reports or case series only. These cases were published between 1960 and 2020. Thirty articles described isolated case reports; seven articles described clustered cases of infections i.e., liver abscesses, meningitis, skin and soft tissue infections, bacteremia, pediatric infections, and infections associated with medical devices [4,6,13,20,29–31]. SSIs were extracted from these cluster cases. Finally, a total of 49 different cases were included in the study.

According to Köppen’s climatic classification [50], 36 cases (73%) were from tropical, humid subtropical, or hot summer Mediterranean climates which are characterized by high heat and humidity.

The main characteristics of the final selections are shown in Table 1.

| Scheme 1. Surgical Procedures Including Prosthesis or Implant |
|---|---|---|---|---|
| Case Characteristics | Surgical Procedures |
| **Case no.** | **Author year (ref)** | **Country State/city Climate * ** | **Age (Y) Sex** | **Main Disease and Associated Pathologies** | **Immune Status** | **Type of Surgery** | **Description** |
| 1 | Derber 2011 [6] | USA Virginie Cfa | 54 F | Tetralogy of Fallot, Blalock-Taussig shunt as a child, total repair as a teenager | Comp | Heart | Bovine pulmonary valve replacement |
| 2 | Gelfand 2014 [28] | USA Tennessee Dfa | 29 F | Spina Bifida and placement of a ventriculo-peritoneal shunt in early childhood. | Comp | Neurological | Replacement of VP shunt |
Table 1. Cont.

| Case no. | Author year (ref) | Country State/city Climate * | Age (Y) | Sex | Main Disease and Associated Pathologies | Immune Status | Type of Surgery | Description |
|----------|-------------------|-------------------------------|---------|-----|----------------------------------------|---------------|----------------|-------------|
| 3        | Gupta 2012 [17]   | India Lucknow Csa            | 65      | M   | Small paraumbilical hernia             | Comp          | Digestive      | Open mesh repair |
| 4        | Van Hal 2008 [18] | Australia Sydney Cfa         | 37      | M   | Native valve endocarditis, intravenous drug user | Comp          | Heart          | Aortic valve replacement |
| 5        | Olson 1981 [14]   | USA California Csa           | 35      | M   | Dissection of the aortic root, aortic stenosis, and insufficiency | Comp          | Heart          | Aortic resection and Daflon tube graft insertion |
| 6        | Santeufemia 2014 [30] | Spain Madrid Csa           | 0.16    | F   | Congenital hydrocephalus               | Comp          | Neurological   | Reducer cranioplasty and VP shunt |
| 7        | Sawant 2013 [19]  | USA California Csa           | 62      | F   | Chronic heart failure, chronic obstructive pulmonary disease, chronic kidney disease | Comp          | Heart          | Bioprosthetic aortic valve replacement and placement of pace-maker |
| 8        | Shigeta 1978 [31] | Japan Fukushima Cfa         | 9       | F   | Arachnoid cyst                         | Comp          | Neurological   | Arachnoid cyst and VP shunt |
| 9        | Shigeta 1978 [31] | Japan Fukushima Cfa         | 8       | M   | Thalamic tumor                         | Supp          | Neurological   | VP shunt |
| 10       | Tena 2014 [32]    | Spain Guadalajara Csa       | 57      | F   | No underlying disease                  | Comp          | Orthopedic     | Total knee arthroplasty |
| 11       | Ahn 2004 [21]     | Korea Iksan Dfa              | 35      | M   | Chronic heart failure                  | Comp          | Heart          | Pacemaker placement |
| 12       | Padmaja 2013 [8]  | India Hyderabad Aw           | 17      | M   | Congenital aortic stenosis             | Comp          | Heart          | Prosthetic aortic valve replacement |
| 13       | Rafael 2014 [35]  | USA Ohio Dfa                 | 50      | F   | Splenomegaly, pancytopenia, ventricular septal defect | Supp          | Heart          | Ventricular septal defect repair |
| 14       | Linde 1960 [44]   | USA California Csa           | 20      | M   | Tetralogy of Fallot                    | Comp          | Heart          | Definitive repair using Ivalon patch |
| 15       | Tokuyasu 2012 [36] | Japan Tottori Cfa           | 86      | F   | Chronic heart disease                  | Comp          | Heart          | Prosthetic aortic valve replacement |
| 16       | Taylor 1991 [37]  | USA Missouri Dfa             | 53      | F   | Rheumatoid arthritis                   | Supp          | Orthopedic     | Prosthetic knee replacement |
| 17       | Bhattarai 2016 [22] | USA Illinois Dfa            | 37      | F   | Chronic heart disease, intravenous drug user | Comp          | Heart          | Mitral valve replacement |
| 18       | Marion-Sanchez 2018 [12] | Martinique Fort-de-France AM | 81      | M   | Chronic heart disease                  | Comp          | Heart          | Mitral valve replacement |
| 19       | Marion Sanchez 2019 [4] | Martinique Fort-de-France AM | 58      | M   | Digestive ulcer                        | Comp          | Thoracic       | Esophageal stent placement |
| 20       | Marion Sanchez 2019 [4] | Martinique Fort-de-France AM | 41      | M   | Biliary stenosis                       | Comp          | Digestive      | PEG tube placement |
Table 1. Cont.

| Scheme 1. Surgical Procedures Including Prosthesis or Implant | Surgical Procedures |
|---------------------------------------------------------------|---------------------|
| **Case Characteristics** | **Main Disease and Associated Pathologies** | **Immune Status** | **Type of Surgery** | **Description** |
| Case no. | Author year (ref) | Country State/city Climate | Age (Y) | Sex | | | |
| 21 | Lofgren 1981 [42] | USA Minneapolis Dfa | 77 | F | Rheumatic aortic stenosis | Comp | Heart | Prosthetic aortic valve replacement |
| 22 | Tripathi 2020 [41] | USA Lexington Cfa | 65 | M | Distal common bile duct stone, chronic alcoholism, tonsillar adenocarcinoma | Supp | Digestive | PEG tube placement |
| 23 | McKinley 1989 [45] | UK Aylesbury Cfb | 28 | M | Aortic valve regurgitation | Comp | Heart | Aortic valve replacement |
| 24 | Lee 2014 [46] | Korea Seoul Dwa | 52 | M | Osteoarthritis | Comp | Orthopedic | Total knee arthroplasty |

Subgroup 2—Surgical Procedures without Prosthesis or Implant

| Case Characteristics | Surgical Procedures |
|---------------------------------------------------------------|---------------------|
| **Case no.** | **Author Year (Ref)** | **Country State/City Climate** | Age (Y) | Sex | **Main Disease and Associated Pathologies** | **Immune Status** | **Type of Surgery** | **Description** |
| 25 | Ferroir 1988 [27] | France Paris Cfb | 54 | F | Pneumocephalus, Hodgkin disease | Supp | Thoracic | Lobectomy |
| 26 | Holmes 1977 [29] | UK London Cfb | 38 | F | Breast Carcinoma, steroid, and hormonal therapy, chemo and radiotherapy. | Supp | Gynecological | Mastectomy |
| 27 | Ozer 2009 [16] | Turkey Hatay Csa | 38 | M | Traffic accident, central facial paralysis | Comp | Neurological | Removal of arachnoid cyst by craniotomy |
| 28 | Santaeufemia 2014 [30] | Spain Madrid Csa | 13 | M | Traffic accident, open fracture of the proximal left tibia and fibula | Comp | Orthopedic | Osteosynthesis |
| 29 | Shigeta 1978 [31] | Japan, Fukushima Cfa | 49 | M | Meningioma | Supp | Neurological | Meningioma resection by craniotomy |
| 30 | Tena 2014 [32] | Spain Guadalajara Csa | 47 | F | Mandibular abscess | Comp | Stomatological | Submandibular abscess debridement |
| 31 | Tena 2014 [32] | Spain Guadalajara Csa | 18 | H | Pilonidal cyst | Comp | Digestive | Cyst removal |
| 32 | Tsay 2005 [20] | Taiwan Changhua Cfa | 46 | M | Empyema | Comp | Thoracic | Decortication of empyema |
| 33 | D’Amato 1988 [33] | USA New York Db | 14 | M | Totally transected spinal cord after gunshot to the chest | Comp | Thoracic | Ligation of bleeding vessels and repair of lung laceration |
| 34 | Asano 2005 [13] | Japan Kumamoto Cfa | 52 | F | Cholecystolithiasis | Comp | Digestive | Cholecystectomy |
| 35 | Asano 2005 [13] | Japan Kumamoto Cfa | 57 | M | Cholecystolithiasis | Comp | Digestive | Cholecystectomy |
| 36 | Asano 2005 [13] | Japan Kumamoto Cfa | 52 | M | Cholecystolithiasis | Comp | Digestive | Cholecystectomy |
### Table 1. Cont.

| Case no. | Author year (ref) | Country State/city Climate * | Age (Y) | Sex | Main Disease and Associated Pathologies | Immune Status | Type of Surgery | Description |
|----------|-------------------|-----------------------------|---------|-----|----------------------------------------|---------------|-----------------|-------------|
| 37       | Vinod 2013 [7]    | India Kerala AM            | 51      | M   | Simple renal cyst                      | Comp          | Neurological    | Laparoscopic deroofing of a simple renal cyst |
| 38       | Teng 2009 [34]    | Taiwan Taipei Cfa          | 27      | M   | Cholecystolithiasis                    | Comp          | Digestive       | Cholecystectomy |
| 39       | CPIAS 2003 [38]   | France Paris Cfb           | 36      | M   | Achilles tendon rupture                | Comp          | Orthopedic      | Achilles tendon |
| 40       | Rotter 2020 [39]  | USA Minnesota Dfb          | 70      | M   | Mucocele                               | Comp          | Neurological    | Resection of left frontal sinus and zygomatico-maxillary mucocele |
| 41       | Sari 2018 [40]    | Turkey Yozgat Dsb          | 56      | M   | Kidney stone                           | Comp          | Nephrological   | Intrarenal surgery for kidney stone |
| 42       | MarionSanchez 2019 [4] | Martinique Fort-de-France AM | 74      | M   | History of colorectal Adenocarcinoma, Peritonitis | Supp | Digestive | Exploratory laparotomy |
| 43       | MarionSanchez 2019 [4] | Martinique Fort-de-France AM | 63      | F   | Chronic heart disease                  | Comp          | Heart           | Double coronary bypass |
| 44       | MarionSanchez 2019 [4] | Martinique Fort-de-France AM | 65      | F   | Arteritis                              | Comp          | Vascular        | Femorofemoral bypass |
| 45       | Linde 1960 [44]   | USA California Csa         | 4       | M   | Defect of interventricular septum      | Comp          | Heart           | Direct closure |
| 46       | Zhi Yang 2014 [43] | Singapore Af               | 46      | F   | Extensive thermal burns (41.5% of the total body) | Supp | Reconstructive | Burn excision and staged, free and cadaveric skin grafting |
| 47       | Revati 2019 [47]  | India Kerala AM            | 40      | F   | Cholelithiasis                         | Comp          | Digestive       | Cholecystectomy |
| 48       | Appelbaum 1980 [46] | USA Pennsylvania Cfa       | 75      | M   | Cholecystitis                          | Comp          | Digestive       | Laparotomy |
| 49       | Demirel 2015 [49] | Turkey Istanbul Csa        | 59      | F   | Bladder tumor                          | Supp          | Urological      | Transurethral tumorectomy |

* According to Köppen climate classification: Y: years; Comp: immunocompetent; Supp: immunosuppressed; M: male; F: female; VP: ventriculo-peritoneal.

### 3.3. Descriptive Analysis of Included Cases

Since our final selection was limited to cases and cluster cases with significant methodological heterogeneity, it was not possible to carry out a meta-analysis. Therefore, results will be presented in narrative form. For descriptive analysis, two subgroups were defined according to the presence (subgroup 1, \( n = 24 \)) or absence (subgroup 2, \( n = 25 \)) of either prosthesis or implant (Table 1). Because of the small sample size, no statistical comparisons were performed on these two subgroups.
3.3.1. Demographics

The median and mean ages were similar between subgroup 1 (45.5 years [min: 0.16, max: 86]; mean = 44 +/- 23.4) and subgroup 2 (47 years [min: 4, max: 74]; mean = 45.3 +/- 19); Forty of the 49 patients included (81.6%) were under 65 years of age. The M/F sex ratios were 13/11 in subgroup 1 and 16/9 in subgroup 2 (Table 1).

3.3.2. The Patients’ Immune Status

Only 9 of the 49 recorded cases (18.3%) were immunocompromised, with similar distribution between the two subgroups (16.6% and 20%, respectively) (Table 1). Five patients had solid tumors, 1 patient had Hodgkin’s lymphoma, 1 patient had rheumatoid arthritis, 1 patient had undergone splenectomy and 1 patient was a burn victim. Therefore, the remaining 81.7% of the cases were immunocompetent patients.

3.3.3. Surgical Data and Infections

Surgical data are provided in Table 2. The main pathologies leading to surgery were heart diseases (30.6%, n = 15), digestive pathologies (22.4%, n = 11) and neurological impairments (14.3%, n = 7). The 80% of total cases presented were deep infections.

Table 2. Infection topographies, treatments, and outcomes.

| Subgroup 1—Surgical Procedures Including Prosthesis or Implant | Infections Topographies | Treatments and Outcomes |
|---------------------------------------------------------------|-------------------------|-------------------------|
| Case no. | Infection, Depth | Delay (Days) | Identified Species/Associated Bacteria | Suspected Origin of Infection | Treatments | Outcomes |
|---|---|---|---|---|---|---|
| 1 | Endocarditis, deep | 120 | Ax subsp. denitrificans/ No | Ukn | Piperacillin/Tazobactam, Imipenem/Cilastatin/ Levofloxacin | Recov |
| 2 | Ventriculitis, deep | 30 | Ax/No | Ukn | Doripenem | Recov |
| 3 | Abscess, deep | Ukn | Ax/No | Mesh | Ceftriaxone, Levofloxacin | Recov |
| 4 | Endocarditis deep | 180 | Ax/No | Duckpond water used to solubilize drugs for injection | Meropenem | Recov |
| 5 | Mediastinitis, deep | 180 | Ax/No | Ukn | Carbenicillin/ Cotrimoxazole/Rifampin, Moxalactam/Rifampin, Azlocillin/Rifampin | Death |
| 6 | Ventriculitis, deep | 20 | Ax/No | Ukn | Ceftazidime/Meropenem | Recov |
| 7 | Endocarditis, deep | 90 | Ax/No | Exposing leg ulcers to water outdoors | Piperacillin/Tazobactam, Meropenem/Cotrimoxazole, Meropenem/Rifampin/ Amikacin | Recov |
| 8 | Ventriculitis, deep | 12 | Ax/No | Aqueous Chlorhexidine solution diluted with non-sterile tap water. | Chloramphenicol | Recov |
| 9 | Ventriculitis, deep | 30 | Ax/Serratia marcescens | Aqueous Chlorhexidine solution diluted with non-sterile tap water. | Chloramphenicol | Recov |
| 10 | Wound infection, superficial | Ukn | Ax/No | Ukn | Ukn | Ukn | Recov |
| 11 | Endocarditis, deep | 2920 | Ax/No | Scaling and root planning at local dental clinic | Ceftazidime/Piperacillin | Recov |
Table 2. Cont.

### Subgroup 1—Surgical Procedures Including Prosthesis or Implant

| Case no. | Infection, Depth | Delay (Days) | Identified Species/Associated Bacteria | Suspected Origin of Infection | Treatments | Outcomes |
|----------|-----------------|--------------|----------------------------------------|------------------------------|------------|----------|
| 12       | Endocarditis, deep | 150          | *Ax* subsp. *denitrificans*/No         | Ukn                          | Meropenem/Levofloxacin, Meropenem/Cotrimoxazole | Recov     |
| 13       | Intracardiac abscess, deep | 10,585 | *Ax*/No                                  | Ukn                          | Piperacillin/Tazobactam/Cotrimoxazole            | Recov     |
| 14       | Endocarditis, deep | 3            | *Achromobacter* spp./No                 | Contamination of extracorporal heart pump | Chloramphenicol/Sulfonamides                     | Death     |
| 15       | Endocarditis, deep | 1825         | *Ax*/No                                  | Ukn                          | Meropenem                                         | Death     |
| 16       | Abscess, deep    | Ukn           | *Ax*/No                                  | Ukn                          | Cefazidime, Imipenem/Cotrimoxazole               | Recov     |
| 17       | Endocarditis, deep | Ukn          | *Ax*/No                                  | Cocaine mixed with stored tap water | Meropenem                                         | Recov     |
| 18       | Mediastinitis, deep | 20           | *Ax*/Staphylococcus* aureus             | Water leaks in the ceiling in intensive care unit | Piperacillin/Tazobactam, Meropenem/Vancomycin, Ceftazidime | Death     |
| 19       | Mediastinitis, deep | 10           | *Achromobacter* spp./No                 | Ukn                          | Meropenem/Vancomycin                              | Recov     |
| 20       | Abscess, deep    | 90           | *Achromobacter* spp/No                  | Ukn                          | Tazobactam                                         | Recov     |
| 21       | Endocarditis, deep | 120          | *Ax*/No                                  | Ukn                          | Cotrimoxazole/Moxalactam                         | Death     |
| 22       | Peritonitis, deep | 16           | *Achromobacter* spp./No                 | Ukn                          | Piperacillin/Tazobactam, Meropenem/Vancomycin     | Death     |
| 23       | Endocarditis, deep | 135          | *Achromobacter* Group B/No              | Ukn                          | Cefuroxime/Gentamycin                             | Recov     |
| 24       | Prosthetic infection deep | 395 | *Ax*/No                                 | Ukn                          | Cefazolin Ciprofloxacin Imipenem                  | Recov     |

### Subgroup 2—Surgical Procedures without Prosthesis or Implant

| Case no. | Infection, Depth | Delay (Days) | Identified Species/Associated Bacteria | Suspected Origin of Infection | Treatments | Outcomes |
|----------|-----------------|--------------|----------------------------------------|------------------------------|------------|----------|
| 25       | Meningitis, deep | 15           | *Ax*/No                                  | Aerosol                      | Metronidazole/Imipenem                           | Recov     |
| 26       | Wound infection, superficial | 270 | *Ax*/No                                  | Ukn                          | Ukn        | Ukn      |
| 27       | Meningitis, deep | 3            | *Ax*/No                                  | Ukn                          | Meropenem                                         | Recov     |
| 28       | Wound infection, superficial | 11 | *Ax*/No                                 | Ukn                          | Imipenem, Vancomycin                              | Recov     |
| 29       | Ventriculitis, deep | 6            | *Ax*/No                                 | Aqueous Chlorhexidine solution diluted with non-sterile tap water. | Ukn        | Recov     |
| 30       | Cervical abscess, superficial | Ukn | *Ax*/Candida albicans                   | Ukn                          | Ciprofloxacin                                      | Recov     |
| 31       | Gluteal abscess, superficial | Ukn | *Ax*/No                                 | Ukn                          | Cotrimoxazole                                     | Recov     |
| 32       | Wound infection, superficial | Ukn | *Ax*/No                                 | Ukn                          | Cefepime                                           | Recov     |
| 33       | Meningitis, deep | 15           | *Ax*/No                                  | Gunshot                      | Cotrimoxazole/Ceftazidime                         | Recov     |
| 34       | Liver abscess, deep | 150         | *Ax*/No                                  | Ukn                          | Ukn        | Ukn      |
| 35       | Liver abscess, deep | 1140        | *Ax*/No                                  | Ukn                          | Ukn        | Death    |
### Table 2. Cont.

| Case no. | Infection, Depth | Delay (Days) | Identified Species/Associated Bacteria | Suspected Origin of Infection | Treatments | Outcomes |
|----------|------------------|--------------|----------------------------------------|------------------------------|------------|----------|
| 36       | Liver abscess, deep | 660          | Ax/No                                  | Ukn                          | Levofoxacin/Cotrimoxazole, Cefoperazone/Sulbactam, Levofoxacin/Cotrimoxazole | Death     |
| 37       | Perinephric abscess, deep | 730          | Ax/No                                  | Ukn                          | Levofloxacin/Cotrimoxazole, Cefoperazone/Sulbactam, Levofoxacin/Cotrimoxazole | Recov     |
| 38       | Liver abscess, deep | 16           | Ax/Escherichia coli                    | Ukn                          | Cefpirome, Colistin           | Recov     |
| 39       | Wound infection, superficial | 75           | Achromobacter subsp. Denitrificans, Escherichia coli, Morganella morganii | Ukn                          | Myambutol/Ciprofoxacin/Clarithromycin | Recov     |
| 40       | Abscess, deep      | 3650         | Achromobacter spp./S.epidermidis, S. salivarius, Mycobacterium avium | Spread via the auditory canal | Ertapenem, Ceftriazone/Cotrimoxazole/Meropenem | Recov     |
| 41       | Urinary tract infection, deep | Ukn          | Ax/No                                  | Ukn                          | Ciprofoxacin/Ceftriazone/Methenamine hippurate | Recov     |
| 42       | Abscess, deep      | 14           | Achromobacter spp./Stenotrophomonas maltophilia, Candida albicans | Ukn                          | Tazobactam/Aminicain           | Death     |
| 43       | Mediastinitis, deep | 9            | Achromobacter spp./E coli              | Ukn                          | Tazobactam/Aminicain, Cefotaxime/Aminicain, Cefotaxime/Fosfomycin | Recov     |
| 44       | Wound infection, superficial | 53           | Achromobacter spp./No                  | Ukn                          | No antibiotic therapy          | Recov     |
| 45       | Endocarditis, deep | 2            | Achromobacter spp./No                  | Contamination of the heart-lung machine | Chloramphenicol/Streptomycin/Sulfadiazine | Recov     |
| 46       | Wound infection, superficial | 11           | Achromobacter baumannii                | Ukn                          | Piperacillin/Tazobactam Polymixin B | Recov     |
| 47       | Abscess deep       | Ukn          | Achromobacter spp./No                  | Endogenous via biliary tract  | Piperacillin/Tazobactam       | Recov     |
| 48       | Abscess deep       | Ukn          | Achromobacter Group Vd biovar 1/No     | Ukn                          | Cefazolin Gentamycin          | Death     |
| 49       | Urosepsis deep     | 30           | Ax/No                                  | Ukn                          | Cefuroxime Meropenem/Cotrimoxazole | Recov     |

Ax: Achromobacter xylosoxidans.

In subgroup 1, the most represented surgery was cardiac surgery (54.1%, n = 13); 95.9% (n = 23) of SSIs were deep infections and occurred mainly after thoracotomy (9 endocarditis, 3 mediastinitis, and 2 abscesses). Only one superficial wound infection was described after total knee arthroplasty (case no 10). The time of onset was recorded for 21 out of 24 SSIs and 16 (76.2%) met the criteria for nosocomial infection. In other words, only 5 infections occurred more than one year after surgery.

In subgroup 2, the most represented surgery was digestive surgery (32%, n = 8); 68% (n = 17) of SSIs were deep infections and occurred mainly after digestive surgery (1 peritonitis and 7 abscesses). The time of onset was described for 19 out of 25 SSIs and 9 (47.3%) occurred within one month of surgery, thus meeting the criteria for a nosocomial infection.

### 3.3.4. Isolated Strains

The species responsible for the infection was identified as *Achromobacter xylosoxidans* in 84.4% of the included cases (n = 38) (Table 2). For the 11 other cases, identification led to
Achromobacter spp. (n = 9), Achromobacter Group B (n = 1) and Achromobacter Group Vd Biovar (n = 1). The method of strain identification was indicated in 51% of cases (n = 25) only. The most commonly used method was culture and biochemical tests (n = 17). Only 4 studies involving a total of 8 cases including our previous case report utilized molecular detection methods. Of these studies, only one case described the detection and identification via nrdA gene sequencing [12].

Most cases in both subgroup 1 (91.6%, n = 22) and 2 (72%, n = 18) were not co-infected. The main co-infecting microorganisms detected in both subgroups belonged to the family of Enterobacteriaceae.

### 3.3.5. Treatments and Outcomes

Detailed information about antibiotic therapy was available for 87.7% of cases (n = 43) (Table 2). For 27 of these 43 cases (62.7%), an empirical antibiotic therapy was initiated. Antibiotic sensitivity of isolated strains was provided for 41 cases out of 49. Based on available data, a total of 30 out of 41 cases had an antibiotic therapy adapted to strain sensitivity (73.2%). Carbapenems (Imipenem, Meropenem and Ertapenem) were the most prescribed drugs (n = 18), followed by Cotrimoxazole® (n = 8), Quinolones (n = 6) and Tazocillin® (n = 7).

Outcome was indicated for 49 cases. Ten patients died. Global mortality rate was 20.4% with 25% (n = 6) for subgroup 1 and 16% (n = 4) for subgroup 2. Only 2 out of 9 immunocompromised patients died (22.2%).

In subgroup 1, 12 patients (50%) underwent surgical revision involving the removal of prosthetic material and all 12 patients survived. Conversely, 50% of the remaining patients (n = 6) who did not undergo such removal died. In this subgroup, 19 out of 24 (79.1%) patients received an antibiotic therapy adapted to sensitivity but 5 of these treated patients died with implanted materials still in place.

### 3.3.6. Origin of Infection

A possible origin of infection was proposed for 14 cases. The most suspected sources were contaminated waters (Table 2). Three cases were extracted from an outbreak associated with 6 Achromobacter spp. cerebral ventriculitis in the neurosurgical ward and the source was confirmed as a contaminated aqueous chlorhexidine solution [31]. For other suspected environmental sources, no analysis was performed.

### 4. Discussion

This review supports our hypothesis stating that Achromobacter spp. SSIs do not preferentially target immunocompromised patients. To our knowledge, this is the first systematic review of post-surgical infections associated with this bacterium. It provides an overview of reported cases over a period of 60 years showing that the majority of published cases on Achromobacter spp. involve individuals under the age of 65 who mainly develop deep infections after a heart surgery involving either prosthesis or implant or after a digestive surgery that did not involve prosthetic materials. As we have previously suggested [4], these infections seem to preferentially affect patients living in warm and humid environments. However, this observation needs to be confirmed by further studies.

The very low rate of immunocompromised patients is consistent with our hypothesis and also with a recent publication demonstrating that both immunosuppressed and immunocompetent populations can be potential targets for Achromobacter spp. healthcare-associated infections [51]. These findings also strengthen our previous finding showing a higher rate (56.1%) of such infections occurring in immunocompetent patients [4]. In addition, a thorough examination of the articles revealed that while the link between immunosuppression and Achromobacter spp. infections is initially proposed by almost all the studies either in the introduction or in the discussion section, the data presented in these studies suggest otherwise [6,16–22]. In our study, we consider actual immunosuppression (defined in the NINPS protocol), not the weakening of the immune system due to chronic illness,
implanted devices, even hospitalization or surgery itself; such criteria favor any type of infection related to any microorganism, especially opportunistic ones [26]. Studying such a relationship would not have been of interest since it is already known.

The majority of the cases included are said to be infected with *Achromobacter xylosidans*. However, the validity of such a level of identification remains questionable. To our knowledge, the nrdA gene sequencing is the only method that allows identification of *Achromobacter* isolates down to species level [52] and so far, there is only one study (authored by this group) that utilized this method of detection [12]. On another hand, it is important to note that many of the studies included in this review predate the time when molecular and genetic methods of bacterial identifications were available.

Lack of a greater number of series, heterogeneity of available evidence base, and publication bias are potential limitations of this study and these limitations may preclude us from reaching definitive conclusions. Moreover, we did not conduct the assessment of the methodological quality of each included finding, which may result in confounding, selection, and information bias. The lower rate of immunocompromised patients could be interpreted as being related to the extreme scarcity of *Achromobacter* spp. infections among immunocompetent patients, leading to more frequent publications of these rare cases. But on the other hand, *Achromobacter* spp SSIs are sufficiently rare to be reported regardless of the immune status of patients.

Similarly, our study shows higher death rates among the reported cases (26.1% for subgroup 1 and 14.3% for subgroup 2) than those associated with other SSI-causing microorganisms (from 2.5 to 6% depending on the study) [33]. Surprisingly, the death rate was not higher among immunocompromised patients. The high mortality rates may be related to publication bias with a majority of severe cases being published at the expense of mild cases. Fifty percent of these deaths can be explained by the pathology itself, i.e., severe cardiac damage requiring implants or artificial valves and leading to mediastinitis or endocarditis. On the other hand, deaths following cholecystectomy in patients without other comorbidity are more questionable. Retrospective studies on *Achromobacter* spp. HAI’s report death rates of 22% [34] and 15% populations [9] which are similar rates to those observed in the present study. The hypothesis of high mortality rates being associated specifically with *Achromobacter* spp. itself, therefore, cannot be fully ruled out.

Some of the delays between the surgery and the infection were extremely lengthy. The lengthiest was an intra-cardiac abscess occurring 29 years after surgery [35]. Either a greater number of extremely late infections have been published because of their impressive character, or there is a specific cause of delayed infection. Perhaps *Achromobacter* spp. deep SSIs develop very slowly over time while remaining in transient dormancy and most likely in biofilm communities; delayed diagnosis may also be responsible for the prolonged onset because of misidentification or mild, nonspecific clinical signs at initial diagnosis [14,17,29]; finally, delayed *Achromobacter* infections are more likely due to delayed acquisition in the hospital environment.

Prevention and treatment of SSI itself present significant challenges and it can be further exacerbated by the intrinsic nature of bacteria causing the infection such as seen in many SSI cases associated with *Achromobacter* spp. First, this bacterium was shown to acquire resistance to the antiseptic solutions used for skin preparation. Three cases were concerned by the growth of this microorganism inside aqueous chlorhexidine solutions [31]. Second, *Achromobacter* spp. is able to grow in sterile distilled water [55]. We previously isolated this organism from a patient who was treated with V.A.C. therapy associated with sterile water irrigation. It is plausible that this treatment may have supported the growth of this microorganism [12] and therefore worsened the existing infection. Third, *Achromobacter* spp is known to form biofilms [55,56] which favor the transfer of resistance genes as well as the development of bacterial tolerance to antimicrobial agents. Biofilm growth may explain a higher rate of deep infections observed in patients with prostheses or implants and subsequent challenges these patients encountered during antibiotic therapy. Although
many of the patients seem to have benefited from adapted antibiotic therapy, the removal of implanted materials appears to be the only treatment that ensured survival. In accordance with the literature, Carbapenem were the most prescribed antibiotics regardless of the presence or absence of foreign materials in patients’ bodies. Unfortunately, frequent and widespread usage of these molecules has favored the increase in acquired resistance [57]. New therapeutics against carbapenem-resistant Gram-negative non-fermenters are emerging; Cefiderocol, a new generation cephalosporin, has recently been shown efficacious in the treatment of Achromobacter post-operative osteomyelitis [57].

5. Conclusions

This review suggests that Achromobacter spp. surgical site infections can affect patients independent of their immune status. Patients living in hot and humid climates may be at a greater risk of acquiring Achromobacter spp. SSIs but effective preventive measures can be proposed only when the source of such infections are clearly identified. The association between Achromobacter spp. infections and climate needs to be thoroughly investigated. Future studies including a greater number of case series and similar reviews extended to all types of healthcare-associated infections caused by Achromobacter spp. are recommended.

Supplementary Materials: The following are available online at https://www.mdpi.com/article/10.3390/microorganisms9122471/s1; Supplementary File S1: Detailed search strategy.

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