Non-elective and Revision Arthroplasty Are Independently Associated With Hip and Knee Prosthetic Joint Infection Caused by Acinetobacter Baumannii: a Brazilian Single Center Observational Cohort Study of 98 Patients

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Research Article

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**Abstract**

**Background:** Prosthetic joint infection (PJI) caused by *Acinetobacter baumannii* (*Ab*) has become a growing concern due to its overwhelming ability to express resistance to antibiotics and produce biofilm.

**Aim:** This study aimed to identify independent risk factors (RFs) associated with *Ab*-PJI and its role in the treatment outcome.

**Methods:** Single-center retrospective, cohort study of PJI patients diagnosed between January 2014 and July 2018. PJI diagnosis was based upon MSIS 2018 criterium. To estimate RFs associated with *Ab*-PJI, multivariate analyses with level of significance of $p < 0.05$ was performed. To evaluate treatment failure, the Kaplan–Meier (KM) analysis and log-rank test was performed.

**Results:** Overall, 98 PJI cases were assessed, including 33 with *Ab*-PJI and 65 with PJI due to other microorganisms (Non-*Ab*-PJI). Independent RFs associated with *Ab*-PJI were revision arthroplasty (odds ratio [OR] = 3.01; 95% confidence interval [95% CI] = 1.15–7.90, $p = 0.025$) and non-elective arthroplasty (OR = 2.65; 95% CI = 1.01–7.01, $p = 0.049$). *Ab*-PJI was also more likely to be classified as a chronic late infection (OR = 5.81; 95% CI = 2.1–16.07, $p = 0.001$) than Non-*Ab*-PJI. *Ab*-PJI was not associated with treatment failure ($p = 0.557$).

**Conclusions:** Late chronic infections, surgical revision, and non-elective arthroplasty are well-known predictors of PJI, but were also independently associated with *Ab*-PJI. High selective pressure imposed by misuse of antibiotics is likely to have played a role. Infections caused by *Ab* and surgical treatment with DAIR were not associated with PJI treatment failure.

**Trial registration:** Study data supporting our results were registered at an open access virtual platform for registration of studies on humans performed in Brazil. The Brazilian Registry of Clinical Trials (ReBEC) http://www.ensaiosclinicos.gov.br/rg/RBR-6ft5yb/

**Register Number:** RBR-6ft5yb

**Introduction**

Worldwide, an increasing number of individuals have undergone joint replacement surgeries particularly at the hip and knee, either for elective reasons or following sustained trauma. Among the possible complications, prosthetic joint infection (PJI) is the most feared despite the low incidence ranging between 1–2% [1, 2] for primary and up to 4% for revision surgeries [3, 4], but with high morbidity and mortality rates. Gram-positive cocci (GPC), such as *Staphylococcus aureus* and coagulase-negative *Staphylococci* are the major PJI-related microorganisms followed by gram-negative bacilli (GNB), with prevalence ranging from 5–23% [4–6]. In some case series, PJI due to GNB have been reported at rates greater than 40%. [7, 8]

*Acinetobacter* is a genus of gram-negative bacteria comprising 31 different species. Due to its ability to spread in healthcare environments, *Acinetobacter baumannii* (*Ab*) is currently the most difficult species to
control and eradicate.[9] This microorganism is ubiquitous in the environment [9] and has become one of the most successful pathogens associated with healthcare-related infections due to its ability to express a variety of antimicrobial resistance mechanisms and to form biofilms on both biotic and abiotic surfaces. [10] On a global scale, approximately 50% of Ab strains have been identified as multidrug-resistant (MDR). The World Health Organization (WHO) has declared carbapenem-resistant Ab to be one of the most important species among the group of bacteria termed ESKAPE (Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, A. baumannii, Pseudomonas aeruginosa, and Enterobacter species), which are considered priority pathogens due to the threat they pose to global public health, requiring urgent actions and the development of new antibiotics to combat them.[11, 12] Unfortunately, among several Latin American countries, Ab strains have shown resistance to virtually all classes of antibiotics, including carbapenems. This worrisome microbial epidemiology has been identified at some Brazilian hospitals, where 77% of these isolates have exhibited resistance to carbapenems.[13] The production of oxacillin-hydrolysing carbapenemase (carbapenem-hydrolysing class D enzymes) has been identified as the most common antibiotic resistance mechanism, and the global dissemination of OXA-type clones, including OXA-23, OXA-72, and OXA-58, is regarded as the most common mechanism of antibiotic resistance [13, 14].

The emergence of musculoskeletal surgical site infections (SSIs) and orthopaedic implant-associated infections caused by Ab has become a matter of urgent concern for healthcare providers due to the limited therapeutic arsenal available, particularly against carbapenem-resistant strains.[15] Moreover, treatment of PJI caused by MDR and extensively drug-resistant (XDR) GNB, particularly Ab, is hampered by its ability to be encased within biofilms. The resistance of Ab against virtually all antimicrobials and its intrinsic capacity for biofilm formation may be associated to lower cure rates and increase disease morbidity, since treatment usually requires a combination of highly toxic systemic antibiotics [16, 17] Despite this challenge, to our knowledge, no published studies investigated independent risk factors (RFs) for the Ab-PJI. Indeed, few previous publications on Ab-PJI attempted to describe in case-series report format, aspects of surgical and antibiotic therapy [15, 18, 19]. Therefore, this study aimed to identify the independent RFs for Ab-PJI and assess the role of Ab on the treatment outcome.

**Materials And Methods**

**Study design**

This study was performed as an observational, single-centre, retrospective, cohort study using data obtained from 2,672 patients undergoing arthroplasties between January 2014 and July 2018, at a Brazilian orthopaedic referral center. All patients diagnosed with PJI, either due to Ab (Ab-PJI) and other microorganisms (Non-Ab-PJI), were identified from clinical and microbiological records and surgical description sheets. The primary study endpoint was the identification of independent predisposing factors associated with PJI caused by Ab and secondary endpoint was to access if the Ab-PJI have influence on treatment outcome. The study included individuals aged 18 years or older who met the diagnosis criteria for PJI according to the Musculoskeletal Infection Society (MSIS) [20]. Inclusion criteria also required the same identified pathogen yielding in at least two peri-prosthetic tissue samples, and prospective follow-up
period of a minimum one-year period. Patients who underwent arthroplasty at an institution other than ours, did not meet the criteria for PJI as defined by the MSIS or had culture-negative results were excluded. The study was reviewed and approved by the local ethics committee (approval no. 2,610,914 on April 20, 2018).

**Definitions**

The PJI onset date was defined according to the date of the first observation of typical infectious signs and symptoms. MDR-Ab was defined as the nonsusceptibility of the identified pathogen to at least one antimicrobial agent from three or more different antimicrobial classes (e.g., aminoglycosides, cephalosporins with an anti-Pseudomonas effect, carbapenems, fluoroquinolones, penicillin + β-lactamase inhibitors, monobactams and polymyxin). Ab that were extensively drug-resistant (XDR) to multiple antibiotics were defined as those lacking susceptibility to at least one antimicrobial agent from all but two classes of antimicrobials [21]

Early-onset PJI was defined as those cases occurring < 3 months after the index surgery, whereas late PJI was defined as those cases in which the diagnosis occurred more than 3 months after the index surgery. The remission of infection was defined as the absence of clinical, laboratory, or radiological symptoms at the last medical follow-up (with a minimum follow-up time of one year). Therapeutic failure was defined as infection recurrence at a previously controlled site; requirement for new surgery, a second course of antimicrobial therapy, chronic antibiotic suppression, excision arthroplasty, or limb amputation; or death within the follow-up period [22, 23]

**Microbiological analysis**

In the surgical ward, a minimal of three different periprosthetic tissue samples and synovial fluid were collected and processed for microbiology. Synovial fluid sample were aseptically inoculated into aerobic standard blood culture bottles. Tissue samples were homogenised in 3 ml of brain-heart infusion (BHI) broth for 1 min and inoculated onto aerobic sheep blood agar, chocolate agar, and anaerobic blood agar and into thioglycolate broth (BD Diagnostic Systems, Sparks, MD). The time limit for processing samples was 6 hours. Aerobic were incubated aerobically at 35–37°C in 5–7% CO$_2$ for 7 days, and anaerobic plates were incubated at 37°C for 14 days. Additionally, 0.5 ml of tissue homogenate was inoculated in thioglycolate broth, incubated for 14 days, and sub-cultured on blood agar plates when the broth became cloudy. Colonies of microorganisms growing on plates were identified, and their susceptibilities to antibiotics were tested according to standard microbiological techniques. The bacteria were identified by conventional biochemical and metabolic tests in accordance with the international standards and definitions established by the European Committee on Antimicrobial Susceptibility Testing (EUCAST) [24]. Sensitivity tests were performed using the disk diffusion technique, and the determination of minimum inhibitory concentrations (MICs) was performed by automated means or by the e-test method, the results of which are presented according to standardised microbiological techniques.

**Potential risk factors**
Variables associated with the patient, surgery, and postoperative procedures were identified by reviewing the medical, intraoperative, and microbiological records to identify potential RFs for Ab-PJI. Demographic variables (sex and age), comorbidities (the presence and number of comorbidities, alcoholism, and smoking habits), the American Society of Anaesthesiologists (ASA) physical status classification, previous use of antibiotics during the past three months, and previous orthopaedic infections were assessed. Associated surgical aspects included the arthroplasty site (hip vs knee), total or partial arthroplasty, primary or revision surgery, and post-traumatic arthroplasty or elective arthroplasty. The factors related to the postoperative period that were considered included postoperative hematoma, the presence of sepsis at the time of diagnosis, concomitant infections diagnosed at different sites, and early or late infection. The surgical strategies, including debridement, antibiotics, and implant retention (DAIR) or any prosthesis removal (Non-DAIR), were assessed for survival and outcome analyses.

**Statistical analysis**

For the overall study population and the groups defined as Ab-PJI and Non-Ab-PJI, qualitative variables are reported as the mean and percentage, and quantitative variables are presented as the median and standard deviation (SD). Associations between qualitative variables were analysed using the Chi-square test and Fisher's exact test, as indicated. The associations between quantitative variables were assessed by logistic regression. The risk estimate was calculated for the associated variables and reported as the odds ratio (OR) with a 95% confidence interval (CI). The logistic regression model was used to select significant variables from among those identified as significant in univariate analyses. Only variables with significance less than 0.20 (p < 0.20) were included in the logistic regression. Variables with significance less than 0.05 (p < 0.05) in the multiple regression were included in the final model. To estimate the probability of survival as a function of time, Kaplan-Meier (KM) analyses were performed, and the resulting curves were compared using the log-rank method. All data were analysed using SPSS, version 23 (IBM-SPSS Inc., Chicago, IL, USA).

**Results**

A total of 115 PJI cases were assessed for inclusion in the study, of which, 14 cases that did not meet the MSIS criteria for infection and 3 cases with less than two or negative tissue cultures were excluded. Therefore, 98 PJI cases were analysed, 33 in the Ab-PJI group and 65 in the Non-Ab-PJI group.

**Study population:**

The demographic and clinical characteristics of the study population are summarized in Additional file 1. Most PJI patients were females (58.16%), with a mean age of 67.3 years (SD ± 13.2). Interestingly, hip arthroplasty was the most frequent procedure (83.7%). Over 70% of patients had at least one comorbidity, among which hypertension (61.2%) and diabetes mellitus (20.4%) were the most common. Arthroplasty was primary surgery in 57.1% (56/98) of cases and due to fractures (non-elective) in 39.8% (39/98). PJI was classified as early in 69.4% (68/98) and 19.4% (19/98) had a previous PJI (Additional file 1)

**Microbiology**
Among 33 patients with Ab-PJI, 27 strains were classified as Ab-XDR, 4 as Ab-MDR, and only 2 Ab strains were sensitive to multiple antibiotics (Ab-MS). Although the susceptibility to carbapenem was below 6%, all isolates were 100% susceptible to colistin (Table 1).

| Antibiotics | SPT | CIP | AMP/S | IMP | MER | PITA | CFP | AK | GM | CAZ | CO |
|-------------|-----|-----|-------|-----|-----|------|-----|----|----|-----|----|
| Ab \(a\). N (%) | 8 | 1 | 5 | 1 | 2 | 1 | 0 | 15 | 5 | 0 | 33 |
| | 24.24 | 3.03 | 15.15 | 3.03 | 6.06 | 3.03 | 0 | 45.45 | 15.15 | 0 | 100 |

SPT; co-trimoxazole, AMP/S; Ampicillin-sulbactam CIP; ciprofloxacin, IMP; imipenem, MER; meropenem, PITA; piperacillin/tazobactam; CFP; cefepime, AK; amikacin, GM; gentamicin, CAZ; ceftazidime, CO; colistin

Culture yielded in the Non-Ab-PJI group were mainly *S. aureus*, *Enterobacter aerogenes*, and *Pseudomonas aeruginosa*. The MRSA rate was 7.0% (additional file 2).

**Outcomes and potential risk factors for Acinetobacter baumannii-associated PJI**

On the univariate analysis, RFs associated with patient characteristics, surgery, and the postoperative period were investigated for possible associations with Ab-PJI, as shown in Table 2. Compared with PJI caused by other microorganisms, Ab-PJI was significantly associated with the previous use of antibiotics during the last three months (51.5% vs 30.8%; \(p = 0.045\)), previous orthopaedic infections (36.4% vs 12.3%; \(p = 0.005\)), revision arthroplasty (60.6% vs 33.8%; \(p = 0.011\)), and post-traumatic/non-elective arthroplasty (54.4% vs 32.3%; \(p = 0.034\)). Ab-PJI patients received more blood transfusions than patients with PJI due to other microorganisms (36.4% vs 10.8%; \(p = 0.002\)). Early infections occurred in 48.5% (16/33) of patients with Ab-PJI, and 81.5% (53/65) of patients with Non-Ab-PJI (\(p = 0.001\)). Following an infectious diagnosis, DAIR was the surgical strategy chosen for 57.6% of the Ab-PJI cases (\(p = 0.047\), (Table 2). The factors that remained independently associated with Ab-PJI upon multiple logistic regression were revision arthroplasty (OR = 3.01; 95% CI = 1.15–7.90, \(p = 0.025\)) and non-elective arthroplasty (OR = 2.65; 95% CI = 1.01–7.01, \(p = 0.049\)). In addition, Ab-PJI was more likely to be classified as a late chronic infection (OR = 5.81; 95% CI = 2.1–16.07, \(p = 0.001\) than Non-Ab-PJI. (Table 3)
Table 2
Univariate analysis of risk factors associated with Ab-PJI\textsuperscript{a}.

| Variables                        | Ab-PJI\textsuperscript{a} | NON-Ab-PJI\textsuperscript{b} | P-value\# |
|----------------------------------|----------------------------|--------------------------------|-----------|
|                                  | No. (%)                    | No. (%)                        |           |
| Demographic data                 |                            |                                |           |
| Age (median [variation]) (years) | 71.0 (48–88)               | 69.0 (30–92)                   | 0.626***  |
| Females                          | 16 (48.5)                  | 41 (63.0)                      | 0.166*    |
| Patient-related variables        |                            |                                |           |
| Alcoholism                       | 7 (21.2)                   | 7 (10.77)                      | 0.222*    |
| Smoking                          | 4 (12.1)                   | 9 (13.8)                       | 1.000*    |
| Comorbidities (yes)              | 25 (75.8)                  | 46 (70.8)                      | 0.601**   |
| SAH\textsuperscript{c}          | 20 (60.6)                  | 40 (61.5)                      | 0.929**   |
| DM\textsuperscript{d}           | 8 (24.2)                   | 12 (18.5)                      | 0.502**   |
| Malnutrition                     | 4 (12.1)                   | 4 (6.2)                        | 0.436**   |
| Anemia                           | 2 (6.1)                    | 0 (0.0)                        | 0.111**   |
| Cancer                           | 0 (0.0)                    | 1 (1.5)                        | 1.000**   |
| Lung disease                     | 0 (0.0)                    | 5 (7.7)                        | 0.122**   |
| Metabolic syndrome               | 5 (15.2)                   | 13 (20.0)                      | 0.558*    |
| Cardiovascular disease           | 2 (6.1)                    | 3 (4.6)                        | 1.000**   |
| Other comorbidities\textsuperscript{e} | 3 (9.1)                   | 8 (12.3)                      | 0.746**   |
| ASA score\textsuperscript{f,*}  |                            |                                |           |
| ASA 1                            | 2 (6.1)                    | 19 (29.2)                      | 0.009**   |
| ASA 2                            | 22 (66.7)                  | 25 (38.5)                      |           |
| ASA 3                            | 8 (24.2)                   | 21 (32.3)                      |           |

Ab-PJI\textsuperscript{a}; Prosthetic joint infection caused by \textit{Acinetobacter baumannii}, NON-Ab-PJI\textsuperscript{b}; non-\textit{Acinetobacter} species causing prosthetic joint infection, SAH\textsuperscript{c}; Systemic arterial hypertension, DM\textsuperscript{d}; diabetes Mellitus; Other comorbidities\textsuperscript{e}; rheumatoid arthritis, hypothyroidism, hyperthyroidism, depression; ASA\textsuperscript{f}; American Anesthesiology Association, DAIR\textsuperscript{g}; debridement, antibiotics and implant retention

Significance probabilities refer to the Chi-squared test (*), Fisher's exact test (**), and Student's t-test (***)P values\# < 0.05 were considered statistically significant.
| Variables                                      | Ab-PJI\(^a\) | NON-Ab-PJI\(^b\) | P-value\(^#\) |
|-----------------------------------------------|---------------|------------------|---------------|
|                                               | No. (%)       | No. (%)          |               |
|                                               | N = 33        | N = 65           |               |
| ASA 4                                         | 1 (3.0)       | 0 (0.0)          |               |
| **Use of antimicrobials**\(^*\)               |               |                  |               |
| Previous use                                  | 17 (51.5)     | 20 (30.8)        | 0.045\(^*\)  |
| Single antimicrobial                          | 6 (18.2)      | 5 (7.7)          | 0.104\(^**\) |
| Antimicrobial combination                     | 11 (33.3)     | 15 (23.1)        |               |
| Previous PJI                                  | 12 (36.4)     | 8 (12.3)         | 0.005\(^*\)  |
| **Variables related to the surgical procedure**\(^*\) | | | |
| Arthroplasty                                  |               |                  |               |
| Total                                         | 24 (72.7)     | 51 (78.5)        | 0.527\(^*\)  |
| Revision                                      | 20 (60.6)     | 22 (33.8)        | 0.011\(^*\)  |
| Non-elective                                  | 18 (54.4)     | 21 (32.3)        | 0.034\(^*\)  |
| Duration of the procedure > 2.5 hours         | 3 (9.1)       | 12 (18.5)        | 0.223\(^*\)  |
| Blood transfusion                             | 12 (36.4)     | 7 (10.8)         | 0.002\(^*\)  |
| **Variables related to the postoperative period**\(^*\) | | | |
| Infection-related sepsis                      | 2 (6.1)       | 0 (0)            | 0.111\(^**\) |
| Concomitant non-orthopedic infection          | 18.2 (6)      | 10.8 (7)         | 0.352\(^*\)  |
| Surgical wound complications                  | 42.4 (14)     | 26.6 (16)        | 0.071\(^*\)  |
| Early infection                               | 48.5 (16)     | 81.5 (53)        | 0.001\(^*\)  |
| DAIR\(^g\)                                    | 57.6 (19)     | 76.9 (50)        | 0.047\(^*\)  |

Ab-PJI\(^a\); Prosthetic joint infection caused by *Acinetobacter baumannii*, NON-Ab-PJI\(^b\); non-*Acinetobacter* species causing prosthetic joint infection, SAH\(^c\); Systemic arterial hypertension, DM\(^d\); diabetes Mellitus; Other comorbidities\(^e\); rheumatoid arthritis, hypothyroidism, hyperthyroidism, depression; ASA\(^f\); American Anesthesiology Association, DAIR\(^g\); debridement, antibiotics and implant retention
Significance probabilities refer to the Chi-squared test \((*)\), Fisher’s exact test \((**)\), and Student’s t-test \((***)\)
P values\(^#\) < 0.05 were considered statistically significant.
### Table 3
Predisposing factors independently associated to Acinetobacter baumannii PJI – multivariate analysis

| Variables              | A. baumannii<sup>a</sup> | Other bacteria | Odds Ratio (OR) | 95% CI | P-value<sup>a</sup> |
|------------------------|---------------------------|----------------|-----------------|--------|---------------------|
| Revision arthroplasty  | 20 (60.6)                 | 22 (33.8)      | 3.01 (1.15–7.90)| 0.025  |
| Non-elective arthroplasty | 18 (54.5)                | 21 (32.3)      | 2.65 (1.01–7.01)| 0.049  |
| Late infection         | 17 (51.5)                 | 12 (18.5)      | 5.81 (2.1-16.07)| 0.001  |

<sup>a</sup> A. baumannii<sup>a</sup>: PJI caused by *Acinetobacter baumannii*; CI: confidence interval

On the KM survival curve, infection by *Ab* was not identified as an RF for treatment failure (p = 0.557, Fig. 1), and no increase in the failure rate was observed for the Ab-PJI group that underwent DAIR compared with the non Ab-PJI that underwent DAIR (p = 0.530, Fig. 2).

### Discussion

To our knowledge, this is the first study attempting to investigate predisposing factors associated *Ab*-PJI. Interestingly the well-known predictors of PJI, revision surgeries, non-elective arthroplasties and late infections (PJI diagnosed after 3 months of index surgery) were independently associated with *A. baumannii* infection. This likely reflects the particular epidemiology of a Brazilian orthopaedic referral center, on which, the rates of nosocomial SSI caused by MDR-GNB is high [25, 26]. In addition, high selective pressure imposed by misuse of empirical broad-spectrum antibiotics is likely to have played a major role [27]. Since then, a local antimicrobial stewardship program has been implemented as a tool towards the appropriateness of antibiotics prescription.

In the microbiological sample, a higher frequency (81.8%) of *Ab* strains causing PJI was XDR, whereas 12.1% were MDR and only 6.1% were MS. Susceptibility to carbapenems was worryingly low, with only 3% of cases sensitive to imipenem and 6% sensitive to meropenem. The higher prevalence of *Ab*-PJI at our institution was not assumed to represent an outbreak, but this is rather an endemic nosocomial pathogen typically identified in the intensive care unit (ICU) environment, which presents an overwhelming ability to colonise the human skin. Furthermore, before 2018 the immediate postoperative care for patients who undergo arthroplasty in our hospital was usually performed at ICU, which is likely to have increased the rate of skin colonisation by *Ab* strains.

Orthopaedic implant-associated infections have traditionally been considered a difficult-to-treat disease due to the formation of bacterial biofilms on the implant surface, and the low levels of antibiotic penetration into bone tissue and biofilms.[28, 29] In addition, the higher levels of bacterial resistance
commonly expressed by *Ab*, makes treatment even more challenging due to the scarcity of available drugs and to antibiotic-related toxicity.[30] Although *Ab* is ubiquitous in nature and colonises the skin of healthy individuals, most human infections are healthcare-associated. A systematic review by Falagas et al.,[31] which included 55 articles describing *Ab* infections, associated *Ab* infections with prolonged hospital stays, intensive care unit treatments, and the use of invasive devices.

Despite the poor availability of studies specifically describing *Ab*-PJI, the number of osteomyelitis and fracture-related infections caused by *Ab* seems to be on the rise worldwide, especially those associated with high-kinetic energy trauma and open fractures.[32] Many studies have described a strong association between complex traumatic gunshot wounds resulting in fracture-related infections or osteomyelitis with *Ab* in various conflict-affected regions, such as Iraq, Afghanistan, and Yemen.[32–35] However, whether *Ab* is acquired during the injury itself from primary contamination, or is hospital-acquired during the trauma care and subsequent surgical procedures remains unclear. In addition to reports from Middle Eastern countries, a study by Vanegas et al.[36] from Colombia addressed osteomyelitis, skin and soft tissue infections and reported an increased number of infections caused by *Ab*, and strong association with recent hospitalisation or surgery, and previous use of antimicrobials in the past six months. Despite the increased risk of PJI following revision surgeries [37–39], the association between revision arthroplasty and *Ab*-PJI has not yet been reported in the literature. However, we are aware that implant contamination during surgery is a primary source of infection, and patients previously colonised with *Ab* may be at increased risk for PJI.

In our study, a 2.6-fold increase in the risk of *Ab*-PJI was identified among patients undergoing emergency arthroplasties, which suggests that similar to fracture-related infections, post-traumatic arthroplasties may be a predisposing factor to *Ab*-PJI. The reasons underlying the association between trauma and *Ab* infection were not elucidated in this study and require further investigation. In addition, we were unable to identify any independent associations between *Ab*-PJI with closed proximal femoral fractures in the elderly population, the recent hospitalisation history, or recent use of antibiotics. However, non-elective arthroplasties may require longer preoperative hospital stays due to the mandatory propaedeutic for assessing preoperative risks and the need to compensate for clinical comorbidities prior to performing the surgical procedure, which might increase the risk of colonisation by *Ab*.[40] However, the length of preoperative hospital stays, which could validate this hypothesis, was not a variable that was assessed in the present study.

In our study late PJI was independently associated with *Ab* infection, and a possible explanation may rely upon the lower level of virulence expression when bacteria expresses multiple antibiotic-resistant mechanisms. Several mechanisms associated with antimicrobial resistance, including pump efflux and biofilm organisation abilities, also decrease the bacterial replicative capacity.[41] This stationary phase, associated with biofilm formation and maturation, is likely to cause *Ab* infections to develop more slowly, increasing the likelihood of being diagnosed as late PJI.[42, 43] Neither *Ab* infections nor the surgical strategy used after the infectious diagnosis was independently associated with final outcomes or risks of treatment failure. Few studies have assessed the prognostic factors associated with *Ab*-PJI development,
although some reported high rates of therapeutic failure in Ab-PJI, such as Vasso et al., [19] which described a 33.3% failure rate for Ab-PJI. However, that study was underpowered, assessing only nine patients in a group containing a mix of infections associated with both Ab and P. aeruginosa. Another study that assessed the outcomes of PJI caused by BGN-MDR reported that infections caused by MDR/XDR BGN were associated with high-therapeutic failure rates when DAIR (52.2%) was performed compared with non-DAIR strategies (23.4%) [44]. However, only 3 patients had Ab-PJI in this study, which is not a representative sample.

The present study has potential limitations. First, it was performed as a retrospective study, conducted at a single centre, located in a major city in a developing country, which offers specialised orthopaedic care for the regional population. Consequently, the results obtained at our hospital may not apply to other hospitals. In addition, the identification and sensitivity tests were performed using non-automated methods, and no molecular or genotypic analyses were performed to identify clonal variants or similar patterns of resistance mechanisms. Furthermore, no pairing was performed between the Ab-PJI and Non-Ab-PJI groups to control for preoperative hospitalisation times or the preoperative colonisation by Ab, which could support the hypothesis that PJI contamination occurred intraoperatively. However, this study explored the previously unexamined issue of PJI-predisposing factors and relied on the largest number of Ab infection cases described to date, with a high frequency of MDR/ XDR strains.

**Conclusions**

The findings suggest that non-elective and revision arthroplasties that were primarily performed due to trauma, and PJI diagnosed after three months of index surgery were independently associated with Ab-PJI. In addition, PJI caused by Ab was not associated with treatment failure, and no difference between the DAIR in Ab-PJI versus NON-Ab PJI was identified for disease-free survival rate. The present study added relevant data to the rising field of MDR-GNB PJI cases, but multicentre cohort studies with larger sample size is still needed.

**List Of Abbreviations**

- Ab - Acinetobacter baumannii
- ASA - American Society of Anesthesiologists
- BHI - brain-heart infusion
- CI. - confidence interval
- DAIR - (debridement, antibiotics, and implant retention)
- EUCAST - European Committee on Antimicrobial Susceptibility Testing
- GNB - gram-negative bacilli
- GPC - Gram-positive cocci
- ICU - intensive care unit
- KM - Kaplan–Meier
• OR- odds ratio
• OXA- oxacillin-hydrolysing
• MRSA- methicillin-resistant *Staphylococcus aureus*
• MIC- minimum inhibitory concentrations
• MDR- multidrug-resistant
• MSIS- Musculoskeletal Infection Society
• PJI- Prosthetic joint infection
• RF- risk factors
• SD- standard deviation
• SSI- surgical site infections
• WHO- World Health Organization
• XDR - extensively drug-resistant

**Declarations**

**Ethics approval and consent to participate**

The study was conducted according to the guidelines of the Declaration of Helsinki and approved by Ethics Committee) of Fundação Hospitalar São Francisco de Assis (no. 2,610,914 on April 20, 2018)

**Informed Consent Statement**

Patient consent was waived due the research involves no more than minimal risk to the subject because is a retrospect observational study without any intervention. Informed Consent Statement was waived by ethics committee of Fundação Hospitalar São Francisco de Assis. Rua Itamaracá, 535, coordprojetos@saofrancisco.org.br

**Consent for publication**

Not applicable

**Availability of data and materials**

The datasets generated and/or analysed during the current study are available in the http://www.ensaiosclinicos.gov.br/rg/RBR-6ft5yb/

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**Competing interests**

The authors declare no conflict of interest
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Authors’ contributions

Conceptualization, RBS. and MJCS.; methodology, RBS. and MJCS; validation, MJCS., formal analysis, MJCS.; investigation RBS and ROA.; data curation, RBS.; writing—original draft preparation, RBS and MJCS.; writing—review and editing, MJCS and ROA; visualization, MJCS.; supervision, MJCS.; project administration, RBS. All authors have read and agreed to the published version of the manuscript

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Figures

Figure 1

Kaplan-Meier survival curve for death/recurrence considering PJI caused by Acinetobacter baumannii
Figure 2

Kaplan-Meier survival curve for death/recurrence considering PJI by A. baumannii PJI DAIR versus Non-Ab-PJI DAIR

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