



Prosthetic Joint Infection Microorganism Pattern And Risk Factor Profile: A Single Center Study

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Abstract

Introduction: Prosthetic joint infection (PJI) is a serious complication especially following arthroplasty surgery. The outcomes of these cases are affected by the pattern of infection, causative microorganism and antibiotic resistance. This study was aimed to evaluate the prevalence of PJI, distribution of causative microorganism, antibiotic resistance, and risk factor profiling.

Methods: A retrospective review was performed by arthroplasty registry evaluation from 2008-2018, followed by medical record review and patient interview. Distribution of causative microorganisms, antibiotic resistance patterns, and onset of infection was extracted. Risk factor evaluation was performed by assessing preoperative (age, body mass index (BMI), comorbidities specifically type 2 diabetes) and perioperative parameters (duration of surgery, number of previous surgeries, interval between those surgeries).

Results: Seventeen patients were diagnosed with PJI (13 hip and 4 knee), with the prevalence of 1.56% and 1.77% respectively. The most common causative organism was *Staphylococcus aureus* and *Escherichia coli* with multiple antibiotic resistance patterns. These infections mostly occurred in patients with the age of 40-60 years, and BMI > 30kg/m². Perioperative risk factor was duration of surgery more than 3 hours, have undergone more than 3 surgeries with an average surgical interval of 2 months.

Conclusions: The prevalence of PJI in this series was 1.56% in hip and 1.77% in knee. Risk factor profile showed that most cases have high BMI, prolonged duration of surgery, and high number of previous surgeries within a short interval.

Keywords: *Prosthetic Joint Infection, Microorganism, Arthroplasty, Hip Knee, Risk Factor*

Level of Evidence: IV



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Introduction

Patients with severe hip and knee pathology typically underwent joint arthroplasty to restore function and improving their quality of life.¹ One of the most challenging complications of joint arthroplasty is periprosthetic joint infection (PJI), which occurs in 0.78 to 2% of cases.^{2,3} The risk of PJI is known to increase in elderly patients, patients with morbid obesity (BMI >30kg/m²), underweight (BMI <18.5), pre-operative health conditions (such as immunity, diabetes, smoking), bilateral arthroplasty, allogenic transfusion, myocardial infarction, urinary tract infection, post-operative atrial fibrillation, and longer hospitalization.^{1,3} A study in the UK revealed that the rates of PJI in both underweight and obese patients doubles the rates of normal patients.³ The morbidities caused by PJI may span from mild discomfort, pain, impaired mobility, psychological detriments, extended hospitalization, to long-term disability or even death especially in the frail and elderly population.⁴ The risk of mortality in patients who underwent joint arthroplasty surgery is increased by 2.5-7 fold if the patients developed PJI.⁵ In addition, PJI is also recognized as a leading cause for revision surgery accounting for up to 23-25% of revisions in the USA and UK.^{3,6}

The causative pathogens in PJI are mostly consisted of gram positive bacteria, which account for 60.1% of knee arthroplasty. The most frequent organism is methicillin-resistant *Staphylococcus aureus*, followed by methicillin-sensitive *Staphylococcus aureus* and *Staphylococcus epidermidis*.⁷ Common gram negative pathogens found in PJI are *Escherichia coli* and *Klebsiella pneumoniae*. It should be noted that some patients may develop polymicrobial infection, albeit in rare cases.^{1,7} The distribution of pathogens also follow certain predilections depending on geographical areas and surgical sites.⁸ For instance, anaerobic pathogens comprise of only 3-6% of PJIs but *Propionibacterium acnes* was found in nearly 25% of shoulder arthroplasty infections.^{9,10} Understanding the common pathogens associated with a given PJI is important as the type of pathogens in a given PJI is known to influence clinical outcomes and prognoses.¹¹ One study showed that PJIs caused by methicillin-resistant *Staphylococcus aureus* are associated with

a higher risk of surgical failure and poor prognoses.¹¹ Currently, there are limited studies regarding PJIs in Indonesia, necessitating more studies in this field to provide better information to clinicians. This study aims to describe the distribution of infection and identifying the risk factors associated with PJI following hip and knee arthroplasty in our center.

Methods

Patients Selection

A retrospective descriptive study was conducted by collecting data from our institutional arthroplasty registry. The study protocol was approved by our institutional review board and informed consent was waived since the patients were not recalled for this study. We identified 1060 arthroplasty surgeries (834 hip and 226 knee) were performed between January 2008 and December 2018. From this registry, all PJI cases was consecutively enrolled. The inclusion criteria of this study were patients diagnosed with hip or knee PJI based on the diagnostic criteria for PJI. (Table 1)¹² The exclusion criteria were as follows: incomplete microbiology data, refusal to participate or unable to be contacted. Medical record review and phone call interview was performed to obtain detailed information of the patients.

Data Extraction and Analysis

The data extracted from medical records were: onset of infection to determine the classification of PJI (acute or chronic), microorganism involved, and antibiotic resistance pattern. Patient demographics data were also obtained from the medical record, such as age, gender, body mass index (BMI) and comorbidities (specifically type 2 Diabetes Mellitus). Furthermore, perioperative data (number of previous surgeries, interval between surgeries and the duration of latest surgery before the PJI was diagnosed) was also obtained from the medical record or by interview if the data was not found in the record. Previous surgery was defined as the surgeries on the hip or knee that was performed before the infection occurred (it may span from an open reduction internal fixation surgery, arthroplasty or even earlier revision arthroplasty due to various reasons).

The type of PJI was determined based on onset of PJI after surgery, with acute PJIs occurring <3 months after surgery.¹³ Antibiotic pattern resistance is identified using the criteria by Magiorakos et al (Table 2).¹⁴ Data analysis was performed using SPSS version 21. The data obtained would be evaluated for their frequencies, mean values, and standard deviation, if the data distribution were normal according to the Shapiro-Wilk normality test, with $p>0.05$. If not, median and minimal to maximal data were displayed.

Results

Patient Demographics

A total of 17 cases of hip PJI (13 cases) and knee PJI cases (4 cases) were included in this study, which made the prevalence of hip and knee PJI in our institution were 1.56% and 1.77%, respectively. Patient characteristics are presented in Table 3 and Table 4. The mean age of patients with knee PJI was higher than the hip PJI cases. The mean BMI was comparable between both groups. Number of previous surgeries and duration of latest surgery were higher in patients with hip PJI, whereas the knee PJI patients had longer interval between surgeries. Nine patients (52.9%) also had diabetes mellitus as their comorbidity.

Type of PJI

Most of hip PJI (9 out of 13) cases have delayed/chronic onset, with a mean onset of 5.69 ± 3.83 months. Acute hip PJI had the onset of 2.3 ± 0.96 months; meanwhile the chronic one was averaged 7.22 ± 3.63 months.

As for knee PJI, the proportion of acute and chronic PJI was comparable (2 cases in each type), with the mean onset of 3.5 ± 1.29 months (2.5 ± 0.71 in acute and 4.5 ± 0.71 in chronic PJI).

Microorganism and Antibiotic Resistance Pattern

Culture of PJI samples revealed that Gram positive pathogens predominated in the THA group (5 cases). However, there were more Gram-negative pathogens in the TKA group (2 cases). Negative culture results were also found in both hip and knee PJI.

In both hip and knee PJI, MDR pathogens were the most common findings. A smaller number of cases were infected by XDR pathogens. Fortunately, there were no PDR pathogens identified in the cases this study.

Discussion

PJI is a common and serious post-operative complication in hip and knee arthroplasty. Existing literature has shown that numerous risk factors associated with PJI. The type of pathogen responsible for the infection is also known to affect clinical outcomes and prognosis. Recognizing the risk factors that influence the incidence of this complication, as well as the most common type of pathogens culpable may better inform clinicians to take preventive measures. As mentioned before, this study was aimed to describe the distribution of infection and identified the risk factors associated.

The prevalence of our study was comparable with other studies.^{2,3} The annual incidence rate of PJI ranged at about 1.99-2.18% for the hip and 2.05-2.18% for the knee, with there being slightly higher percentage for the knee, which is similar to our findings.¹⁵ The number the hip PJI cases were larger than the knee, which was caused by the inclusion of both hemiarthroplasty and total hip replacement cases in our series. However, the exact prevalence of PJI in our series was unable to be extracted. We included all PJI cases that were treated in our institution regardless of where the index surgery was performed.

Risk factor profile was identified in the demographic data. Older age, higher BMI, increased number of surgeries and shorter interval between them has been proven as the risk factor of PJI.^{15,16,17} Previous studies has shown that in older patients, PJI is more frequent and occurred earlier than in younger people.¹⁶ This finding is concurrent with our series, which showed that a majority of our patients had a relatively advanced age especially in the knee group and these patients also experienced an earlier onset of infection (acute). Interestingly, *the average age of hip PJI cases was quite young. The fact, that many hip arthroplasties were actually performed in younger patients (e.g. avascular necrosis, early arthritis due to dysplasia), may be a plausible explanation for our findings.*

BMI is also recognized as another risk factor to PJI, as delineated by the study by Wagner et al which showed that obese patients (BMI >30kg/m²) experienced an increased rate of post-operative infection.¹⁷ One study by Lubbeke et al asserted several explanations for this correlation, namely the underdosing of antibiotics due to increased body mass, thickness of subcutaneous adipose tissue at site of operation thereby increasing predisposition to infection due to poorer perfusion and lower oxygen tension, enhanced risk of hematoma and higher mechanical tension in wound which may lead to dehiscence.¹⁸ Moreover, obese patients may experience more soft tissue damage and prolonged surgery.¹⁸ From an immunological perspective, it is established that adipose tissue produces mediators that may potentially impair the immune system.¹⁹ Most of our PJI cases (12 out of 17 cases) occurred in obese patients with a mean BMI of 30.07 ± 1.10 in the hip PJI group and 31.34 ± 0.14 in the knee PJI group.

Type II diabetes is a recognized comorbid disease that predisposes a post-operative patient to PJI. A meta-analysis of 14 studies by Zhu et al demonstrated that across eight studies, concurrent type II diabetes proved to be a statistically significant predictor of PJI.²⁰ This is consistent with our findings which showed more than half (9 out of 17 patients) with PJI also had type II diabetes as a comorbid. The same meta-analysis also identified several surgery-related risk factors for PJI including prolonged surgical duration and previous surgeries. The analysis of the sample studies in this meta-analysis stated that the odds ratio (OR) of prolonged surgical duration and previous surgeries were 2.18 and 3.15 and with p value of 0.001 and 0.003 respectively.²⁰ All cases in our series has a history of previous surgery. Among them, 13 out of 17 patients had a surgery in less than 6 months prior to their last procedure. Although there were no data regarding the interval between previous surgeries, we believe shortened interval between the surgeries will increase the risk of infection. Further investigation is needed in this topic.

It is known that the most frequently found microorganisms in PJI are gram positive organisms, this is thought to be due to their predominance in the normal flora of human skin.²¹ With regards to hip infections, it is thought that the causative pathogens are usually normal flora

of the genitals due to their proximity.²¹ Despite the popular notion that most infections are due to the monomicrobial infection of gram positive pathogens, particularly *Staphylococcus aureus*, one study by Peel et al debunked this finding, with results that state that majority of joint infections comprise of mixed gram positive-negative organisms.²²

The widespread indiscriminate use of antibiotics in many healthcare facilities has led to the rise of prophylactic failure in post-operative patients.²¹ A study by Tornero et al found that methicillin resistance accounted for up to 9% of PJIs due *S. aureus*, and 60% due to *S. epidermidis*, and fluoroquinolone resistance was made up of 16% *S. aureus* and 35% *S. epidermidis* infections respectively.²³ Another study by Martinez et al showed that up to 85% of *E. coli* isolated from PJIs produced beta lactamases.²⁴ It is also important to note that these patterns vary based on the frequency and type of antibiotics abused in different hospitals.²¹ Recognizing the common microorganism patterns in PJI is also important to guide clinicians in forming empirical antibiotic regimens and possibly preventing PJIs entirely.

There are several limitations in our study. Due to its retrospective design, our study is susceptible to recall bias. The number of negative culture results was also relatively high compared to other studies. This may be due to the fact that antibiotic regimens were not halted prior to culture examination, which may decrease the concentration of the causative microorganism in the sample. And as mentioned before, our prevalence may be inaccurate as not all PJI cases in this series were originally treated in our institution. Low number of positive PJI cases was also a limitation of this study. However, considering this was a single center study and the prevalence was proportionate with previous studies, multicenter collaboration was needed to improve the analysis. Despite these limitations, the strength of our study was the involvement of microbiology data and its resistance pattern that was not commonly reported in other similar studies.

Conclusions

In conclusion, the overall prevalence of PJI in our study is relatively rare (1.56% for hip PJI and 1.77% for knee PJI). Our study population had a predilection for several characteristics known to

predispose a patient to PJI including old age, BMI>30kg/m², type 2 diabetes, increased duration of surgery, short interval with previous surgery, and a prolonged operative time. Gram-positive microbes were more common in PJI patients that underwent hip arthroplasty, whereas gram-negative microbes were more frequent for the knee arthroplasty. Future multicenter collaboration study with bigger sample was needed to obtain better analysis.

Conflict of Interest

The authors affirm no conflict of interest in this study

Acknowledgement

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Table 1. Diagnostic Criteria for PJI¹²

PJI is present when one of the Major Criteria Exists or Three out of Five Minor Criteria Exist	
Major Criteria	1. Two positive periprosthetic cultures with phenotypically identical organisms 2. A sinus tract communicating with the joint
Minor Criteria	1. Elevated serum C-reactive protein (CRP) AND erythrocyte sedimentation rate (ESR) 2. Elevated synovial fluid white blood cell (WBC) count OR ++ change on leukocyte esterase test strip 3. Elevated synovial fluid polymorphonuclear neutrophil percentage (PMN%) 4. Positive histological analysis of periprosthetic tissue 5. A single positive culture

Table 3. Patient Demographics

	Hip PJI (n=13)	Knee PJI (n=4)
Age	48.85 ± 19.76	71 ± 13.09
Gender		
□ Male	9	2
□ Female	4	2
BMI	30.07 ± 1.10	31.34 ± 0.14
Number of Previous Surgeries	3 (1-5)	1 (1-2)
Interval Between Previous two Surgeries (month)	3.77 ± 2.17	6.25 ± 4.03
Duration of Latest Surgery (minute)	194 ± 27.24	145 ± 46.55

Table 2. Antibiotic Resistance Pattern Criteria

Criteria	Definition
MDR (Multidrug-resistance)	The isolate is non-susceptible to at least 1 agent in more than 3 antimicrobial category
XDR (Extensively drug-resistance)	The isolate is non-susceptible to at least 1 agent in all but 2 or fewer antimicrobial category
PDR (Pandrug-resistance)	Non-susceptibility to all agents in all antimicrobial category

Table 4. Summary of Patient Data

Initials	Age	Gender	BMI	Comorbidities	Number of Previous Surgeries	Surgeries Interval (Months)	Last Surgery Duration (minutes)	Onset of Infection	Microorganism Found	Antibiotic Resistance Pattern
Hip PJI										
RD	63	M	31,56	Type II diabetes	2	2	180	3	Escherichia coli	XDRO
RB	52	F	37.91	Type II diabetes	3	6	230	14	Acinetobacter baumannii	XDRO
DS	53	M	34.89	N/A	4	5	180	6	Negative	N/A
SW	46	M	29,67	N/A	3	5	210	7	Negative	N/A
SET	30	F	30,42	N/A	1	0	170	2	Staphylococcus epidermidis	MDRO
SIR	25	M	30,23	N/A	2	6	180	5	Staphylococcus epidermidis	MDRO
AA	53	M	33.56	Type II diabetes	3	4	150	12	Negative	N/A
ZA	64	M	26.12	N/A	1	0	170	6	Negative	N/A
RS	29	M	30.25	Type II diabetes	5	3	240	1	Staphylococcus aureus	MDRO
SA	71	M	28,56	Type II diabetes	4	4	200	3	Staphylococcus aureus	XDRO
RS	89	F	29,54	Type II diabetes	2	7	180	8	Escherichia coli	MDRO
R	36	M	31,57	Type II diabetes	4	3	230	3	Staphylococcus aureus	MDRO
DUD	24	F	28,98	N/A	3	4	200	4	Acinetobacter baumannii	MDRO
Knee PJI										
IY	76	M	31,24	Type II diabetes	2	4	160	2	Escherichia coli	XDRO
ES	54	M	31,45	N/A	1	3	200	4	Pseudomonas Aeruginosa	MDRO
RZ	69	F	37.46	N/A	1	12	90	5	Negative	N/A
P	85	F	34.63	Type II diabetes	1	6	130	3	Staphylococcus epidermidis	MDRO