

# Economic Burden Of Prosthetic Joint Infection Following Primary Total Knee Replacement In Pakistan

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## Research article

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# Abstract

**BACKGROUND:** The financial burden of prosthetic joint infection after joint replacement in developed countries is well known. There is a need to evaluate the economic burden in developing countries like Pakistan. **MATERIALS AND**

**METHODS:** Cases performed during this study are divided into two groups. 1. Uneventful primary total knee arthroplasty. 2. Prosthetic joint infection treated with two stage revision. Categorical variables were compared through Chi-square and Fisher Exact test. Continuous variables were compared using Mann-Whitney test. Multivariable regression analysis was done to identify the variable that places major financial burden on patient economy.

**RESULTS:** The total cost of revision surgery for prosthetic joint infection considering twice hospitalization is found to be 7, 91, 353 ± 89,136 rupees. The total cost of uneventful arthroplasty is found to be 3, 50, 289± 32,123 rupees. We observed significant difference with respect to economic details between two groups.

**CONCLUSION:** Measures should be undertaken to reduce PJI by encouraging healthcare providers to consider evidence based protocols to prevent PJI and financial constraints associated with these events.

## Background:

Prosthetic joint infection (PJI) is one of the devastating complications after primary total knee arthroplasty (TKA) that actually increases financial burden to patient and affects quality of life as well [1] [2] [3] [4]. Despite modern modalities of preventing infection, incidence of prosthetic joint infection is 1–2% after knee replacement surgery [5] [6]. As the burden of lower limb arthroplasty procedure is frequently increasing in elderly population, the economic burden of prosthetic joint infection is steadily increasing as well [7]. The actual cost of treating patients with prosthetic joint infection is difficult to determine because it depends on multiple factors such as specific type of treatment given to patient, bacteria specific antibiotics and patient comorbidities as well. The spectrum of economic burden comprises of in-patient cost as well as out-patient cost which includes follow-up visits, rehabilitation and pharmacy etc. Prosthetic joint infection is one of the dilemma especially in developing countries like Pakistan. According to World banks classification, Pakistan belongs to lower middle income group [8]. The management of prosthetic joint infection varies from extended course of antibiotics to surgical debridement that places massive financial burden on health care system. The financial burden of prosthetic joint infection after joint replacement in developed countries is well known [9] [10]. There is a need to evaluate the economic burden in developing countries like Pakistan. The rationale of this study is to evaluate the existing economic burden of treating infected knee joint and to provide cost-effective policies in order to minimize financial burden.

Our purpose of this study is to evaluate in-hospital cost of treating infected joint after primary total knee replacement and compare them with uneventful total knee arthroplasty.

## Materials & Methods:

This was a single center retrospective case control study conducted at department of orthopedic surgery, Liaquat national hospital which is one of the private hospitals in Karachi, Pakistan. Patient enrolled for study were those who were operated between January 2014 to December 2018. All patients in this study bear full expenses as well. Cases performed during this period are divided into two groups. 1. Uneventful primary total knee arthroplasty. 2. Prosthetic joint infection treated with two stage revision. The first group with uneventful arthroplasty served as control. 1329 patients underwent for primary total knee arthroplasty during this period in our hospital. 32 patients diagnosed with prosthetic joint infection (PJI). Out of 32 patients, 27 patients had primary total knee arthroplasty somewhere else whereas 5 patients underwent for primary knee joint replacement in our hospital. According to center for disease control and prevention (CDC), periprosthetic joint infection (PJI) can be defined on laboratory and clinical grounds.

- Sinus tract that communicates with prosthesis [3]
- Two positive periprosthetic cultures with similar microorganism [3]
- Presence of three of following minor criteria [3]
  - Raised Erythrocyte sedimentation rate (ESR) >30mm/hr
  - Raised synovial fluid White cell count >10,000 cells/ $\mu$ L.
  - Raised synovial fluid neutrophil count >90%
  - Positive histological analysis of periprosthetic tissue (>5 neutrophils per high power field)
  - Single positive periprosthetic (tissue or fluid) culture

### Inclusion criteria:

- All patients diagnosed with prosthetic joint infection and underwent two stage revision surgery.
- Uneventful primary total knee arthroplasty (TKA).

### Exclusion criteria:

- Patients who underwent for debridement, antibiotics and implant retention (DAIR).
- Revision total knee arthroplasty (TKA) due to aseptic reasons
- Patients with persistent infection despite surgical debridement & antibiotics and require amputation as a last resort.
- Re-admission due to any reason in either group including prosthetic joint infection (PJI) after revision TKR.

Demographic data and clinical record of patients which include duration of stay in orthopedic ward or intensive care unit retrieved from hospital record. Administrative and economic data retrieved from non-medical person that were blinded to patient diagnosis and outcome. Outpatient visits such as follow-up visits and rehabilitation cost were not included in this study. On admission, the medical condition of all

the patients were assessed and classified according to American society of Anaesthesiologists (ASA) grade [11]. All patients underwent two stage revision after diagnosing Prosthetic joint infection (PJI). We used 3 gm vancomycin as a cement spacer in all cases. Pus and deep tissue sent for routine microbiological culture and sensitivity along with histological examination of infected tissue. Tissue samples were obtained from five standard surgical sites such as synovium, medullary canal of femur and tibia [12]. In patients with prosthetic joint infection, causative organism and its antibiotic susceptibility, date of diagnosis and its treatment retrieved from hospital records. Infectious disease team was kept on board. Patients kept on intravenous antibiotics (IV) for 6 weeks. Some patients require two antibiotics depending on organism susceptibility to particular antibiotic. Re-aspiration was performed two weeks after stopping antibiotics. Revision surgery performed at 3 to 4 months after 1st stage.

In order to calculate final cost, we divide total hospital cost into two groups. Hospital stay cost and operating room cost.

Hospital stay - ward or Intensive care unit cost- maintenance, meals and accommodation cost. Diagnostic test- cost for imaging, microbiology and blood tests. Medication cost- with or without antibiotics. The duration of stay in ward and ICU was retrieved from hospital records. The diagnostic test performed in uneventful arthroplasty was complete blood counts (CBC), urea creatinine and electrolytes, coagulation profile, urine microbiology culture and sensitivity, Hepatitis B and C profile, X-rays (pre-operative and post-operative) and standing scannogram. The diagnostic test performed in revision total knee replacement considering twice hospitalizations was also similar with addition of C-Reactive protein, erythrocyte sedimentation rate (ESR) along with cultures and histopathology (HP). Hepatitis profile was performed on first admission in revision cases.

Operating room- costs of equipment, general and clinical support specific for surgery along with surgeon & anesthetist fees. This includes cost of operating room and recovery room charges, epidural and medications used by anaesthetist as well as surgical drapes. Cost of clinical materials used such as cement spacer during first stage and implants used during revision surgery such as constrained condylar knee (CCK), rotating hinge knee (RHK) with or without metaphyseal sleeves, metal augments or wedges were considered

With all these variables in mind, average cost for each of differentiated groups is reported in rupee which is then converted into US dollar (\$). Cost of implant and other consumable remain same throughout study period. These prices convert to US dollar (\$) with market exchange rate at the end of study period. The data was analyzed statistically using statistics version 20.0. Categorical variables were compared through Chi-square and Fisher Exact test. Continuous variables were compared using Mann-Whitney test. Multivariable regression analysis was done to identify the variable that places major financial burden on patient economy. The level of significance was set at P value < 0.05.

## Results:

During study period, 32 patients were diagnosed with prosthetic joint infection (PJI). We are unable to find economic data in three cases and two patients were lost to follow-up after first stage so ultimately 27 patients are included in this study and served as cases. We obtained record of 27 patients during the study period who underwent for primary arthroplasty and are considered as control. Patient with uneventful primary total knee arthroplasty was selected randomly, whereas 27 patients suffered with PJI were evaluated in terms of economic burden.

All patients with prosthetic joint infection underwent two stage revision surgery in this study. Basic demographic data and clinical data of cohort are found in Table 1. There was no statistical difference between cases and control with respect to age, ASA score and gender. However, we observed significant difference between two groups in terms of length of stay in ward and ICU (intensive care unit) and time in operating room with P value < 0.05.

We also evaluate in-hospital economic data of 27 cases with prosthetic joint infection (PJI). Economic calculations are expressed in Table 2. The total cost of revision surgery for prosthetic joint infection (PJI) considering twice hospitalization is found to be 17, 80,222 ± 313686 rupees (12277 +/- 2163 \$). The total cost of uneventful arthroplasty is found to be 3,90,172 ± 51,460 rupees (2690 +/- 354.9\$).. The total cost is the sum of two variables such as cost of hospital stay and operating room cost. We observed significant difference with respect to economic details between two groups with P value < 0.05. We further divide ward stay into two variables such as semi-private room and private room. The cost of semi-private room in our hospital is 6800 rupees/day (47 \$) whereas cost of private room is 8900 rupees/day (65 \$). The mean duration of stay of patient with uneventful arthroplasty was 5 ± 1 days whereas it was 11 ± 3 days with revision total knee replacement (P value < 0.05). The diagnostic test further divided into blood test, imaging and microbiology. The total cost of blood test including inflammatory markers was 12,290 rupees (85 \$). Imaging or x-rays of unilateral knee cost is 2220 rupees (15 \$) whereas bilateral knee x-ray cost was 4440 rupees (31\$). The cost of microbiology (histopathology and cultures) is 5000 rupees (35\$). Diagnostic test also found to be statistically significant in both groups (P value < 0.05). Antibiotics were given intra-venous (IV) for six weeks according to culture and sensitivity. We mostly encountered MRSA (Methicillin resistant staphylococcus aureus), MSSA (methicillin sensitive staphylococcus aureus), pseudomonas and streptococcus during study period. We used vancomycin for MRSA, Amoxiclav for MSSA, Piperacillin/Tazobactam for pseudomonas and penicillin or Cephalosporins for streptococcus. One vial of vancomycin costs 1331 rupees (9 \$), tazocin 870 rupees( 6\$), amoxiclav 670 rupees(4.6\$ ) and cephalosporin 165 rupees (1.2 \$). Organisms and their antibiotics sensitivity are found in Table 3. The total cost of stay in ICU in our hospital is 13,500 rupees / day (89.66 \$). None of the Patients with primary arthroplasty stayed at ICU whereas patients with prosthetic joint infection had mean ICU stay was 3 ± 1 days (P value < 0.05). The cost of operating room is 15,500 rupees (107 \$), recovery room 10,000 rupees ( 69 \$), epidural kit 15,000 rupees ( 107 \$), surgical drapes 7500 rupees( 52 \$) and medications used by anesthetist is 10,000 rupees (69 \$). The average operation room (OR) cost after uneventful primary arthroplasty was 58,247 ± 4,223 (3160 +/- 29.12 \$) whereas it was 98,394 ± 9286 (6785 +/-64.04\$) after revision total knee replacement (P value < 0.05). The average cost of implants used during primary total knee arthroplasty was 202345 ± 12734 (1395.5 +/- 88\$), whereas it was

1374763 ± 242567 (9481+/- 1672 \$) after revision knee replacement. The cost of specific implant used during revision surgery is mentioned in Table 2. Surgeon & Anesthetist fees for primary & revision knee arthroplasty cases are also mentioned in Table 2.

Multivariable regression analysis was done to identify the variable that places major financial burden on patient economy. We found that ward cost, diagnostic tests, antibiotics, clinical materials, surgeon and anesthetist fees has major impact on patient economy after diagnosing prosthetic joint infection (PJI). The detailed results are shown in Table 3.

Table 1  
DESCRIPTIVE STATISTICS OF DEMOGRAPHIC FEATURES BETWEEN TWO GROUPS:

VARIABLE	PRIMARY ARTHROPLASTY (control n = 27)	PROSTHETIC JOINT INFECTION (PJI) (cases n = 27)	P value
Age	58.4 ± 4.9	61.3 ± 5.9	0.08
Length of stay in ward (Days)	5 ± 1	11 ± 3	0.004°
Length of stay in ICU (Days)	0	2 ± 1	0.001°
ASA score	10	05	0.07
Class 1	17	15	
Class 2		07	
Class 3			
Class 4			
Time in operating room (OR)	58 ± 5.6	118 ± 8.9	0.003°
Gender	17	17	0.08
Male	10	10	
Female			
P value°<0.05 considered significant			

Table 2  
IN-HOSPITAL ECONOMIC DATA OF 27 PJI cases:

VARIABLE	PRIMARY ARTHROPLASTY (n = 27) (PRICE IN PKR FOR ONE PRIMARY TKR)	PROSTHETIC JOINT INFECTION (n = 27) (PRICE IN PKR FOR ONE REVISION TKR)	P VALUE
HOSPITAL STAY	42,539 ± 8346 (294+/-58 \$)	89,345 ±	0.001
Ward cost	13,425 ± 1892 (92.5 +/-13 \$)	12,346(616+/-85.14\$)	0.000
Diagnostic test		29,456 ± 2572 (	0.09
Medications excluding antibiotics	11,242 ± 1792 (77.5+/-12.3\$)	203+/-17.7\$)	0.001
Antibiotics	9,245 ± 636 (63.35 +/-4.24\$)	12,941 ± 2041 (89.24+/-14.07\$)	0.003
ICU stay	0	68,925 ± 13,942 (475 +/-96.1\$)	0.004
Total cost	76511+/- 12666 (527.6+/-87.35\$)	26789+/-12623( 185+/- 87 \$) 227456+/-43524 ( 5054.6+/-300.2 \$)	
OPERATING ROOM	58,247 ± 4,223 (3160 +/-29.12\$)	98,394 ± 9286 (678.5 +/-64.04\$)	0.004
OR cost (Epidural plus medications)	202345 ± 12734 ( 1395.5 +/-88\$)	1374763 ± 242567 (9481+/-1672 \$)	0.003
Clinical materials including implant	19,4325 ± 12326	498000+/-22347	0.000
Average cost	33425+/- 7524 (230 +/-51.9 \$)	998000+/- 24786	0.001
- PS/CR	19644+/-1987 (135.47 +/-13.7\$)	1610000+/- 74269	
- TC3 FIXED BEARING	313661+/-38794 (2163+/-267.5 \$)	93000+/- 11000	
- TC3 WITH MBT		54623+/- 12897 ( 376\$ +/-88.94 \$)	
- RHK		24986+/-5412	
- Metaphyseal Augment		(172.3+/-37.32 \$)	
SURGEON FEES		1552766+/- 270162	
ANESTHESIA FEES		(10708+/- 1856\$)	
Total cost: (Sum of OR cost + average cost of implant)			

P value°<0.05 considered significant
OR- Operating Room
ICU- intensive care unit
CS- cruciate substituting
CCK- constrained condylar knee
RHK- rotating hinge knee
TC3- Total condylar

VARIABLE	PRIMARY ARTHROPLASTY (n = 27) (PRICE IN PKR FOR ONE PRIMARY TKR)	PROSTHETIC JOINT INFECTION (n = 27) (PRICE IN PKR FOR ONE REVISION TKR)	P VALUE
TOTAL COST (in rupees) (Total Hospital stay + operating room cost)	390172+/-51460 (2690+/-354.9\$)	1780222+/-313686 ( 12277+/-2163 \$)	0.002
P value°<0.05 considered significant			
OR- Operating Room			
ICU- intensive care unit			
CS- cruciate substituting			
CCK- constrained condylar knee			
RHK- rotating hinge knee			
TC3- Total condylar			

Table 3  
MULTIVARIABLE ANALYSIS:

VARIABLE	ODDS RATIO	95% CI	P VALUE
Ward cost	9.452	1.020–1.462	0.004
Diagnostic test	4.824	1.069–1.331	0.001
Medications excluding antibiotics	1.283	1.248–1.756	0.064
Antibiotics	19.826	0.842–1.214	0.014°
ICU stay	2.142	1.123–1.134	0.031
OR cost	1.183	1.148–1.556	0.064
Clinical materials including prosthesis	17.826	0.842–1.214	0.011°
P value°<0.05 considered significant			
CI- confidence interval			

## Discussion:

It is with no surprise that management of prosthetic joint infection (PJI) represents a massive economic burden on health care systems, hospital and patients as well. There are only few papers available that address this issue in well developed countries but there is a need to evaluate the impact of management of prosthetic joint infection over patient economy in developing countries like Pakistan. To the best of our knowledge, this report is first from single centre of Karachi, Pakistan regarding the economic burden of prosthetic joint infection (PJI) following primary total knee replacement (TKR). The total financial burden of management of prosthetic joint infection (PJI) over patient economy is much more than the sum of all available data that can be objectively ascertained. In the current study, we only reported the in-hospital cost and we are unable to report the out-patient cost such as follow-up visits and rehabilitation cost. We are also unable to assess indirect cost as well such as productivity loss and absenteeism from work of patient and his caregivers. It is also very difficult to compare our economic burden after management of prosthetic joint infection (PJI) with other developing countries due to difference in the health-care system and economic standard of particular nation.

Kapadia et al [13] in his study compares 21 infected primary total knee replacement with 21 non-infected patients who underwent uneventful total knee replacements. He found that patients with prosthetic joint infection had significantly prolonged hospitalizations. The total cost for patients with prosthetic joint infection was \$116,383 USD (range, \$44,416 to \$269,914) which was significantly more than uneventful primary knee arthroplasty \$28,249 USD (range, \$20,454 to \$47,957). This study was conducted in Sinai Hospital which is one of the renowned private American hospitals. We are unable to compare our economic burden with the results presented by Kapadia et al in his study due to difference in health care system and economic standard between two countries. In our study, patients with prosthetic joint infection (PJI) had more prolonged stay as well considering both hospitalizations that actually impose a major impact on patients and his family economy ( P value < 0.05) as shown in Table 1 and Table 3. In our study, ICU care was decided on the basis of ASA score and post-operative evaluation in recovery room. 22 (81.4%) patients with prosthetic joint infection had ASA score of 3 and 4 and warrant ICU admission for further monitoring as per decided by anaesthesia team. Patients with uneventful arthroplasty had ASA score of 1 and 2 and didn't require ICU admission post-operatively.

J.Garrido-Gomez et al [14] performs a descriptive analysis of economic cost of patients with prosthetic joint infection in public health system of Andalusia (Spain). They presented results of prosthetic joint infection on basis of occurrence. The mean cost per patient was 24,980 \$ (19,270.80 €) for patients with early PJI and rise to 78,111 \$ (60,257 €) for those with late PJI. Our study excludes those patients who present early and underwent DAIR (debridement, antibiotics and implant retention) procedure. He also concludes that hospital stay followed by cost of surgical implants puts major impact on patient economy. Fernandez-Fairen et al [15] performed a systematic review and found that revision knee arthroplasty was 2–4 times more expensive than uneventful primary knee arthroplasty. We found that management of prosthetic joint infection is 4.5 times more expensive than patient who underwent primary uneventful knee arthroplasty. We also observed that ward cost, diagnostic test, antibiotics, clinical materials including prosthesis and surgeon and anesthetist fees used during revision surgery

have significant impact on economic status of patient presented with prosthetic joint infection (PJI) as shown in Table 3.

The economic burden of prosthetic joint infection (PJI) can be reduced by making health policies as well as implementation of preventive measures to attenuate the risk of prosthetic joint infection (PJI). Knowledge of the cost related to prosthetic joint infection is necessary to optimize existing health resources in developing countries like Pakistan. Although, there are treatment protocols and guideline exist to prevent the incidence of prosthetic joint infection (PJI) following joint replacement procedure, a more pro-active and individualized approach may be necessary to sort out this issue [16] [17]. There is a need to identify high risk patients with proactive implementation of pre and post-operative protocols in order to prevent this devastating complication thereby reducing financial burden. Previous studies reported number of evidence based protocols that have proven to be effective in reducing prosthetic joint infection (PJI) such as use of prophylactic antibiotics and negative pressure wound therapy (NPWT) on surgical incisions [18] [19]. According to data from OECD (organization for economic co-operation and development), the U.S. spent 17.8% of its gross domestic product (GDP) on health care, while the average spending level among all high-income countries is 11.5 percent of gross domestic product (GDP) [20]. On other hand, the share of total public health expenditure in Pakistan as percentage of GDP (Gross domestic product) is only 0.7 percent. The current indicators of economic burden in Pakistan demonstrate the overall poor picture of expenditures on health. The increase in the expenditure as percentage of GDP on health besides other social expenditures should be strongly emphasized.

The major limitation of this study is that we mainly focused on in-hospital cost and exclude outpatient cost such as follow-up visits and rehabilitation cost so that exact economic burden can't be determined. Although this small retrospective case-control study manifest some important conclusions. Another drawback is that this was a single centre study.

## **Conclusion:**

The finding of this study shows that prosthetic joint infection (PJI) following total knee replacement (TKR) imposes a major economic burden on patient and his family.

## **List Of Abbreviations**

TKA- Total knee arthroplasty

PJI- Prosthetic joint infection

CDC- Centre for disease control and prevention

ESR- Erythrocyte sedimentation rate

DAIR- Debridement, antibiotics and implant retention

ASA- American society of Anaesthesiologists.

IV- intravenous antibiotics

CBC- complete blood counts

HP- Histopathology

CCK-Constrained condylar knee

RHK-Rotating hinge knee

MRSA- Methicillin resistant staphylococcus aureus

MSSA- Methicillin sensitive staphylococcus aureus

OR- Operation room

NPWT- Negative pressure wound therapy

GDP- Gross domestic product

## **Declarations**

### **ETHICS APPROVAL & CONSENT TO PARTICIPATE:**

The study was approved by ethical review board (ERB) committee of Liaquat national hospital. (0111-2018)

### **CONSENT FOR PUBLICATION:**

Consent for publication has been taken.

### **AVAILABILITY OF DATA AND MATERIAL:**

Provided in methodology.

### **COMPETING INTERESTS:**

The Authors declare no conflict of Interest.

### **FUNDING:**

The Authors declare that no funding was involved in this study.

### **AUTHORS CONTRIBUTION:**

All authors contribute equally.

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