

## Effect of pre-operative and post-operative variables on postoperative hospitalization stay and infection in patients with osteoarthritis undergoing arthroplasty for hip and knee: A retrospective study

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Received: 04-11-2020 / Revised: 06-12-2020 / Accepted: 11-02-2021

### Abstract

**Background:** To evaluate the prevalence of preoperatively elevated serum inflammatory markers and to determine its association with periprosthetic joint infection (PJI) in patients with osteoarthritis (OA) undergoing arthroplasty of knee and hip. The study also evaluated the effect of the pre and postoperative factors associated with prolonged postoperative hospital stay. **Methods:** The study involved patients who underwent primary arthroplasty of knee and hip from May 2018 to September 2019. Patients with medical emergencies, open wounds, polytrauma with other system involvement and who had intra-articular steroid injection in last 2 months prior to surgery were excluded. Inflammatory markers were documented during preoperative evaluation. All necessary data were collected retrospectively and documented. The data were analysed using R software (version 3.6.1). **Results:** The study involved 52 patients with a male-to-female ratio of 0.625 and the mean age of 59.81 ± 11.67 years. Thirty-six (69%) patients had one or more preoperative comorbidities. High preoperative levels of CRP and/or ESR were found in thirty-seven (26.62%) patients. Two (3.85%) patients developed PJI and were treated successfully. Mean hospitalization time of patients was 13.38 ± 5.76 days. No other complications were noted. **Conclusion:** No significant link between high preoperative ESR and CRP and the occurrence of PJI was noted. Nevertheless, preoperative NLR, levels of alkaline phosphatase, and hemoglobin, and types of surgery performed were found to be helpful in assessing the length of postoperative hospital stay.

**Keywords:** erythrocyte sedimentation rate, C-reactive protein, NLR, periprosthetic joint infection, total knee arthroplasty, osteoarthritis

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### Introduction

Osteoarthritis has been identified as the second most common rheumatologic disease with a prevalence of 22% to 39% in India. Total knee arthroplasty (TKA) and total hip arthroplasty (THA) are reported to be effective in improving pain and physical function (PF) in patients with osteoarthritis. The risk of periprosthetic joint infection (PJI) and increased length of postoperative hospital stay have been identified as the two major limitations of arthroplasty. Although the incidence of PJI is reported to be only between 0.4%–2% post-surgery, literature studies have reported it as one of the most disastrous complications [2]. Different demographic factors and comorbidities are reported to play a major role in the development of PJI post-surgery [3–5]. Studies suggest Preoperative erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) as simple and inexpensive, markers for predicting potential postoperative PJI by several researchers [6,7]. The adoption of enhanced recovery after surgery (ERAS) program has helped in decreasing the length of postoperative hospital stay [8,9]. There is a dearth of information on the relation between prolonged length of hospital stay and factors like pain level, PJI, perioperative laboratory examination, surgical factors and procedures, and postoperative complications. Prolonged postoperative hospital stay, coupled with the expense of equipment, professionals, directly adds to the cost. Previous studies have determined that the mean length of hospital stay post-surgery as between 5 to 9.4 days [10–13]. Large surgical incisions, longer operat-

ive time, need for blood transfusion, difficulty in controlling pain and postoperative complications are some of the key factors influencing the length of the stay [14–16]. Proper management of these factors have been noted to reduce the length of hospital stay as well as cost of the treatment. The aim of this study was to identify the preoperative, perioperative, and postoperative factors associated with prolonged postoperative hospital stay. The role of elevated preoperative CRP and ESR and other preoperative variables in predicting postoperative PJI in patients after primary arthroplasty was also evaluated.

### Materials and methods

The study involved 52 patients who underwent arthroplasty for hip and knee between May 2018 and September 2019 at Sanjay Gandhi Institute of Trauma and Orthopedics, Bengaluru, Karnataka, India. Patients with medical emergencies, open wounds, polytrauma with other system involvement and who had intra-articular steroid injection in last 2 months prior to surgery were excluded. Variables like hemoglobin, total leucocyte count, neutrophil, lymphocyte, neutrophil lymphocyte ratio (NLR), eosinophil, monocyte, basophils, ESR, CRP, RA factor, alkaline phosphatase were documented during preoperative evaluation. All necessary data like demographic information and presence of comorbidities were collected retrospectively and documented.

### Surgical procedure

All patients who underwent primary TKA received 4.5 gm of injection of piperacillin + tazobactam within 1 hour of skin incision. Patients who were allergic to piperacillin + tazobactam received cephalosporins. At a tourniquet inflation pressure of 350 mmHg, a midline incision and medial para patellar approach knee arthroscopy were performed. Femoral and tibial bone incisions were made and respective components were fixed with gentamycin loaded bone

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cement. Deep fascia was sutured with no.1 Vicryl, subcutaneous tissue with Vicryl 2.0 and subsequently skin was stapled with knee in flexion position. Vacuum suction drain was regularly applied and was removed when daily output was <50 ml. The patients received post-operative antibiotics till drain removal. All patients who underwent THA received 4.5 gm of piperacillin + tazobactam injection and 500 mg of tranexamic acid injection within 1 hr of skin incision, and patients who were allergic received cephalosporins. Patients were operated in lateral position with affected hip on top. Using posterolateral approach, hip joint was exposed and femoral neck was excised. Serial acetabular reaming was done and acetabular component was fixed. Serial rasping of femoral canal was carried out and femoral stem fixed after trailing with appropriate implants. Capsule, short external rotators and TFL were sutured with Vicryl no.1 subcutaneous tissue with Vicryl 2-0 and skin was stapled by keeping the limb in hip abduction. Vacuum suction drain was applied regularly and removed when drain was < 50 ml in 24 hrs. Post-operative antibiotics were continued till drain removal.

**Statistical analysis**

Categorical variables were presented as numbers and percentages, continuous variables as means and standard deviation (SD), and non-continuous variables as median and range. Statistical significance between groups was determined using chi-square test for categorical variables, the ANOVA and t-test for continuous variables and Kruskal-Wallis test for non-continuous variables. Patients were categorised into the following three groups: normal CRP and ESR level group; either CRP or ESR level elevated group, and both CRP and ESR level elevated group. The corresponding elevated levels considered for ESR and CRP were >30 and >3. Multivariate

regression analysis was used for determining odds ratio (OR) and Wald test for significance testing. The variables that were found statistically significant in preliminary analysis, namely hypertension, haemoglobin, neutrophils, lymphocytes, ESR, CRP, alkaline phosphatase, occurrence of PJI and type of surgery, were considered for further analysis. The statistical tests evaluated odds ratio (OR) for postoperative hospitalization stay. P value <0.05 was considered as statistically significant. All the statistical analyses were performed with the statistical software packages R (<http://www.R-project.org>, The R Foundation, Vienna, Austria).

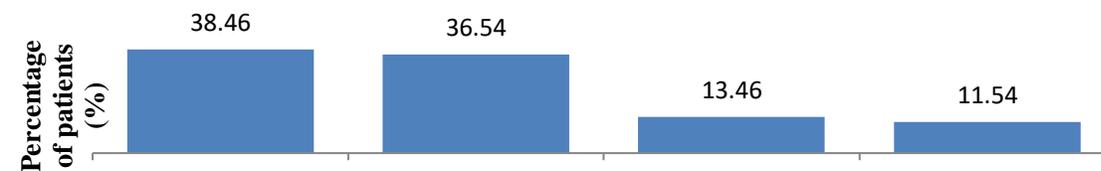
**Results**

The study considered 52 patients with a male-to-female ratio of 0.625 and mean age of 59.81±11.67 years. Demographic and preoperative laboratory information are summarized in table 1. Mean hospitalization of 52 patients was 13.38±5.76 days with minimum and maximum days of 5 and 37 respectively. The variables namely age, gender, diabetes, rheumatoid arthritis, other comorbidities, TLC, eosinophil, monocyte, basophils and RF factor did not differ statistically between the three groups (P>0.05). The mean CRP and ESR levels were significantly higher in the both CRP and ESR elevated and either CRP/ESR groups compared to normal CRP and ESR group (P<0.001). Other variables such as hypertension, neutrophils, leucocytes, and alkaline phosphatase significantly differed between the groups. t-test analysis of these variables revealed that the difference was only between both ESR and CRP elevated group and normal group. Overall prevalence of preoperatively elevated inflammatory ESR and CRP was 75%. Only two patients (4%) had PJI, one in normal group and another one in either high group.

**Table 1: Baseline characteristics of the patients**

Parameters	Total (n=52)	Group based on ESR and CRP levels			P- Value*
		Both normal (n=13)	either high (n=17)	both high (n=22)	
AGE	59.81±11.67	58.46±11.41	60.71±13.47	59.91±10.78	0.8752
Male	20(38.46)	7	6	7	0.4102
Female	32(61.54)	6	11	15	
Diabetes	8(15.39)	2(15.39)	2(11.77)	4(18.18)	0.911
Hypertension	13(25.00)	4(30.77)	5(29.41)	4(18.18)	<b>0.0184</b>
Rheumatoid Arthritis	5(9.62)	0	3(17.65)	2(9.09)	0.2655
Others	10(19.23)	3(23.08)	4(23.53)	3(13.64)	0.6808
Haemoglobin	11.37±1.5	12.3±1.1	11.36±1.48	10.83±1.49	<b>0.0161</b>
Total Leucocyte Count	7500±2465.54	6338.46±1139.84	7373.53±2277.55	8284.09±2928.52	<b>0.0735</b>
Neutrophil	68.75±9.41	64.15±11.72	67.12±7.09	72.73±8.16	<b>0.0198</b>
Lymphocyte	26.38±9.49	31.08±11.13	27.76±7.87	22.55±8.37	<b>0.0249</b>
Neutrophil lymphocyte ratio	3.26±2.06	2.56±1.64	2.84±1.69	4.01±2.35	<b>0.074</b>
Eosinophil	2.54±1.04	2.31±1.03	2.71±1.1	2.55±1.01	0.5858
Monocyte	2.19±1.66	2±1.29	2.47±1.7	2.09±1.85	0.7004
Basophils	0.12±0.32	0.15±0.38	0.12±0.33	0.09±0.29	0.8691
ESR	53.4±27.81	19.85±8.14	51.29±17	74.86±20.89	<b>&lt;0.001</b>
CRP	3.25±2.66	1.25±0.59	1.66±1.01	5.67±2.36	<b>&lt;0.001</b>
RA Factor	30.25±31.35	28±23.93	39.59±38.58	24.36±28.57	0.3145
Alkaline Phosphatase	115.85±171.87	73.08±33.59	157.76±293.33	108.73±54.12	<b>0.02613</b>

\*P value< 0.05 is considered statistically significant



**Fig 1: Distribution of patients based on the type of surgery**

Out of 52 patients, 20(38.46%),19(36.54%),7(13.46%), 6(11.4.6%), underwent left TKA, right TKA, left THA and right THA surgeries respectively. It was found that both the patients who had PJI postoperative had undergone left THR. About 28.57% of the patients who underwent left THR had PJI (2 out of 7). Therefore, PJI and types of surgery performed were also considered for multivariate regression analysis along with the significant variables such as

ESR,CRP,hypertension,hemoglobin,neutrophil,leucocyte,alkaline phosphatase. OR along with lower and upper bond at 95% confidence interval for each variable on length postoperative hospital stay is summarised in table 2 . Increased likelihood for longer post-operative hospital stay was noted in patients with preoperative lower hemoglobin, higher alkaline phosphatase, and occurrence of PJI.

**Table 2: ODD ratio of different parameters on time of hospitalization**

Parameters		Odds ratio(CI)	Wald test- P value
PJI (Yes)		33957340(0- 3.466259E+37)	<0.0001
Hypertension (Yes)		0.25(29245.34- 39428530000)	0.3877
Hemoglobin		0.32(0.01-6.2)	<b>0.04405</b>
Neutrophil		1.09(0.1-0.97)	0.80741
Leucocyte		1.06(0.52-2.3)	0.88391
ESR		0.98(0.5-2.25)	0.61906
CRP		1.07(0.91-1.06)	0.84103
Alkaline Phosphatase		1.01(0.55 -2.08)	<b>0.00265</b>
Type of surgery	Left TKA	1.17(1-1.02)	0.93813
	Right THR	0.17(0.02-71.32)	0.52138
	Right TKR	0.49(0-42.88)	0.74147

\*P value< 0.05 is considered statistically significant

### Discussion

The current study considered the usefulness of preoperative elevated ESR and CRP levels in evaluating the occurrence of PJI in patients who underwent arthroplasty. The study has noted no significant difference between the 3 groups (normal CRP and ESR level group; either CRP or ESR elevated group, and both CRP and ESR elevated group) with respect to the incidence of PJI. These findings are in line with that of Khamis *et al.*, (2019) who have reported that there was no significant link between elevated preoperative ESR and CRP and prevalence of PJI. In contrast, Xu *et al.*, (2018) have reported higher prevalence of PJI in elevated CRP and ESR level group compared to normal CRP and ESR level group and either CRP or ESR level elevated group. The overall prevalence of PJI noted was 4% and 2% for normal CRP and ESR level group and either CRP or ESR level elevated group respectively. However, no case of PJI was reported in both CRP and ESR elevated group. Nevertheless, variables like ESR, CRP, hypertension, NLR and alkaline phosphatase were found to be significantly elevated in both CRP and ESR level elevated group compared to the other two groups. The level of hemoglobin was found to be reduced in both CRP and ESR level elevated group compared to other two groups. Difference of all these factors were statistically significant at  $P < 0.05$ . Previous studies have reported preoperative patient characteristics pain level, preoperative knee function, perioperative laboratory examination, surgical factors, and postoperative complications as important factors affecting the length of postoperative hospital stay [14,16]. Subsequent analysis evaluated the effect of significant factors like ESR, CRP, hypertension, hemoglobin, neutrophil, leucocyte and alkaline phosphatase along with types of surgery performed and PJI on the length of postoperative hospital stay. Multivariate regression analysis was performed to obtain the OR for these variables. Patients with preoperative lower hemoglobin, higher alkaline phosphatase, occurrence of PJI had increased likelihood for prolonged post-operative hospital stay. The average length of post-operative hospital stay reported by various studies was between 5 to 9 days.<sup>10-13</sup> The mean length of hospitalization noted by the current study of 52 patients was much higher (13.38±5.76 days) than earlier reported in

the literature. Nevertheless, in the current study, the minimum time of hospital stay was as low as 5 days. This study findings show that the increase in mean length of hospital could be mainly attributed to PJI and this association was obvious in patients who had average 30 days of postoperative hospital stay. Hence, it could be inferred that PJI is a major postoperative complication that directly contribute to the length of hospital stay in patients undergoing arthroplasty [13]. In addition, the previous reports of prolonged stay due to the need of blood transfusion is in line with the observation of preoperative low hemoglobin level noted in the current study [17]. Despite the effective implementation of enhanced recovery after surgery program, early discharge is not possible in certain cases due to various reasons [14]. The present study highlights the significance of recognizing all such factors and their effective management to optimize the care of patients for early discharge. The retrospective nature and smaller sample size were the major limitations of the study. A prospective study would have provided some more additional information regarding the factors influencing the length of hospital stay. Moreover, the sample size was very small to draw valid conclusion on the effects of age, gender, and BMI. Further studies involving larger sample size are warranted to corroborate the association between PJI and length of postoperative hospital stay.

### Conclusion

In conclusion, preoperative elevated alkaline phosphatase level, reduced hemoglobin level and PJI are the major factors influencing prolonged length of postoperative hospital stay. Effective management of these factors leads to reduced length of postoperative hospital stay and make arthroplasty a cost-effective technology for the treatment of knee osteoarthritis. Further studies are needed to corroborate the potential of preoperative CRP and ESR levels in predicting postoperative outcome.

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**Conflict of Interest: Nil**

**Source of support: Nil**