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Trends of C-reactive protein and erythrocytes sedimentation rate following total hip & knee arthroplasties and hemiarthroplasty in Western Rajasthan: A prospective study

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Abstract
Introduction: Primary diagnosis of infection can be made by serological inflammatory markers like erythrocytes sedimentation rate (ESR) and C-reactive protein (CRP). This study was planned to determine this normal temporal distribution of ESR and CRP in arthroplasty and hemiarthroplasty in Western Rajasthan.
Materials and Methods: This Hospital based Observational Analytical study was conducted in Tertiary care facility, Jodhpur from January 2022 to October 2022. The study population was patients undergoing Total Knee Arthroplasty (TKA) & Total Hip Replacement (THR) and Hemi Arthroplasty (HRA) operation with no history of inflammation, infection, chronic disease, and any autoimmune disease like rheumatoid arthritis. We have enrolled 52 uncomplicated cases. ESR and CRP was analysed over the time.
Results: The mean ESR and CRP value is maximum at day 3 in all three groups. The mean ESR value is highest in the THR group, and lowest in the Unilateral TKR group. Values of ESR continue to remain elevated at four weeks.

Keywords: CRP continues to be the best acute phase reactant in the early postoperative phase with a relatively typical pattern as compared to ESR

Introduction
Periprosthetic infection after hemi or total arthroplasty is a dreadful complication. Although it is rare in frequency, it results in substantial morbidity and compromised functional outcomes, which makes this area of interest [1]. Early diagnosis of infection requires higher clinical skills, while the serological investigation, diagnosing imaging and microbiological examination further add to the confirmation of diagnosis [1, 2].
Primary diagnosis of infection can be made by serological inflammatory markers like erythrocytes sedimentation rate (ESR) and C reactive protein (CRP) and these markers also help to monitor the effectiveness of treatment during the follow-up period. These tests are easily available, low-cost, and non-invasive [3-6].
The role of ESR and CRP as acute-phase reactants in the initial preoperative phase is well studied and documented [9-13]. ESR stays to raise for a longer duration in the postoperative period following surgery, while CRP trails a regular pattern with an immediate peak at 3rdnd postoperative days followed by a gradual decline over time [9, 12, 13].
Though, the period for normalization of CRP and ESR value in the postoperative phase is different in various studies over different populations [14, 15].
As per various literature, it seems that race and factors like public health and environment affect the process, hence the present study was conducted to determine this normal temporal distribution of ESR and CRP in arthroplasty and hemiarthroplasty in Western Rajasthan.

Materials and Methods
This Hospital based Observational Analytical study was conducted in the Department of Orthopaedics of Dr. SN Medical College, Jodhpur from January 2022 to October 2022.

The study population was patients undergoing Total Knee Arthroplasty (TKA) & Total Hip Replacement (THR) and Hemi Arthroplasty (HRA) operation with no history of inflammation, infection, chronic disease, and any autoimmune disease like rheumatoid arthritis. We studied 52 uncomplicated cases, out of them 20 patients have undergone THR, 12 patients have undergone Total knee replacement (TKR), and 20 patients have undergone HRA.

To prevent periprosthetic infection, a single dose of 1 gm ceftriaxone intravenous (I.V.) was given before starting the operation, and Piperacillin-tazobactam combination 4.5-gram I.V. three times a day and Injection of amikacin 500 mg I.V. twice a day after the antigen sensitivity test (AST). For prophylaxis of deep vein thrombosis, low molecular weight heparin 6000 International Unit was injected subcutaneously once a day for seven days.

Regional anesthesia was used in all cases. Blood samples were collected on the day before the operation and the 1st, 3rd, and 7th postoperative days. Further samples were also taken at the time of suture removal on the 14th day, and at the time of the first follow-up at the end of the 4th week. A total of 2 ml of a blood sample for each CRP and ESR analysis was collected. A quantitative CRP study was done by employing a testing kit that was based on the principle of immunoassay with a normal reference range of 0 to 5mg/l. ESR was done using the Wintrobes method with a normal reference range of 0 to 30mm/hr.

Results

The mean ESR value is maximum at day 3 in all three groups. The mean ESR value is highest in the THR group, followed by Bilateral TKR, Hemi Arthroplasty, and lowest in the Unilateral TKR group. Values of ESR continue to remain elevated at FOUR weeks. Distribution of CRP is almost like ESR values, maximum at day 3 in all groups. The mean CRP value is highest in the THR group and lowest in the Unilateral TKR group.

Table 1: Mean value of ESR at different time intervals in patients undergoing different surgeries

	Pre-operative	Day 1	Day 3	Day 7	Day 14	Week 4th
Bilateral TKR	21.53±4.16	48.28±5.05	89.73±6.15	68.36±6.28	53.56±5.20	30.87±4.57
Unilateral TKR	20.56±5.07	43.37±4.44	81.31±4.82	68.00±4.61	50.00±6.31	34.81±3.98
Total Hip Replacement	19±3.54	49.51±5.87	93.25±6.40	68.61±4.83	54.07±5.33	39.48±4.03
Hemi Arthroplasty	18.52±4.12	46.78±4.89	88.46±5.89	68.45±4.70	53.21±5.01	37.39±4.21

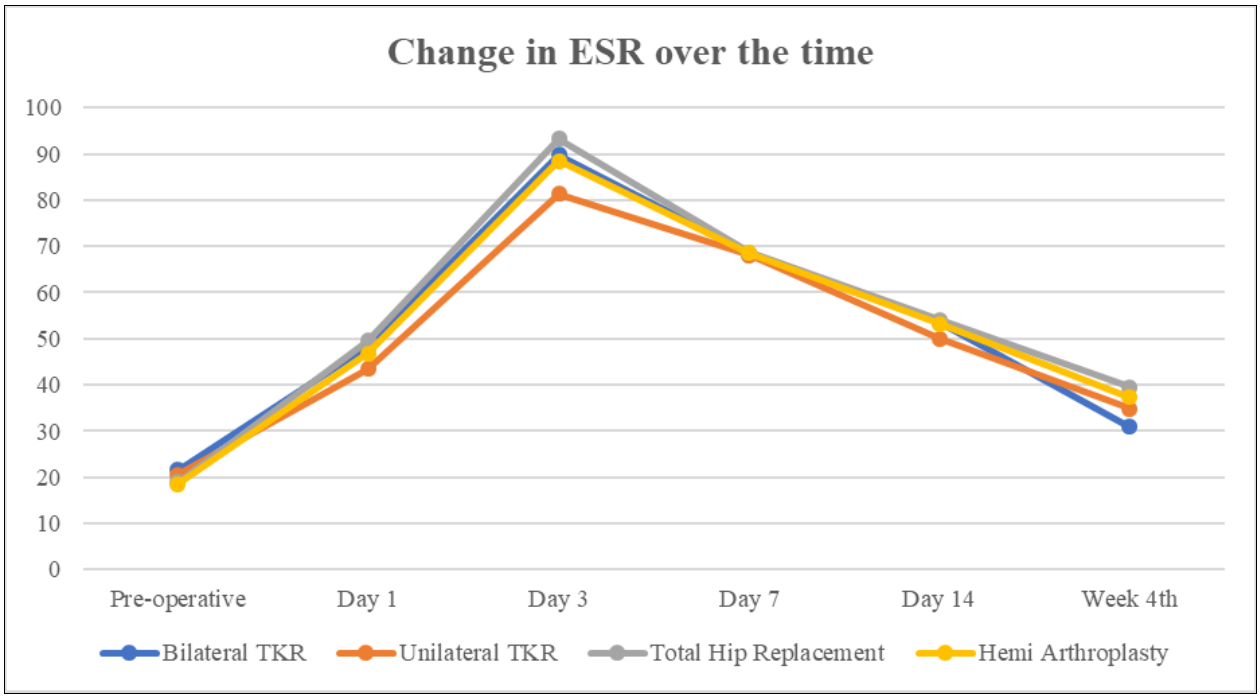

Fig 1: Change in ESR value over time in patients undergoing different surgeries

Table 2: Mean value of CRP at different time intervals in patients undergoing different surgeries

	Pre-operative	Day 1	Day 3	Day 7	Day 14	Week 4th
BL TKR	3.49±1.08	105.30±22.99	150.76±57.25	70.15±14.15	13.08±5.52	5.22±2.25
UL TKR	3.19±1.55	70.76±23.63	99.03±36.08	48.76±12.96	10.33±2.57	4.79±2.42
THR	4.10±1.46	107.37±28.51	142.85±67.30	64.14±13.33	11.62±2.61	5.12±2.05
HRA	3.80±1.12	86.78±20.89	122.36±45.89	57.45±14.70	10.21±2.01	4.39±2.21

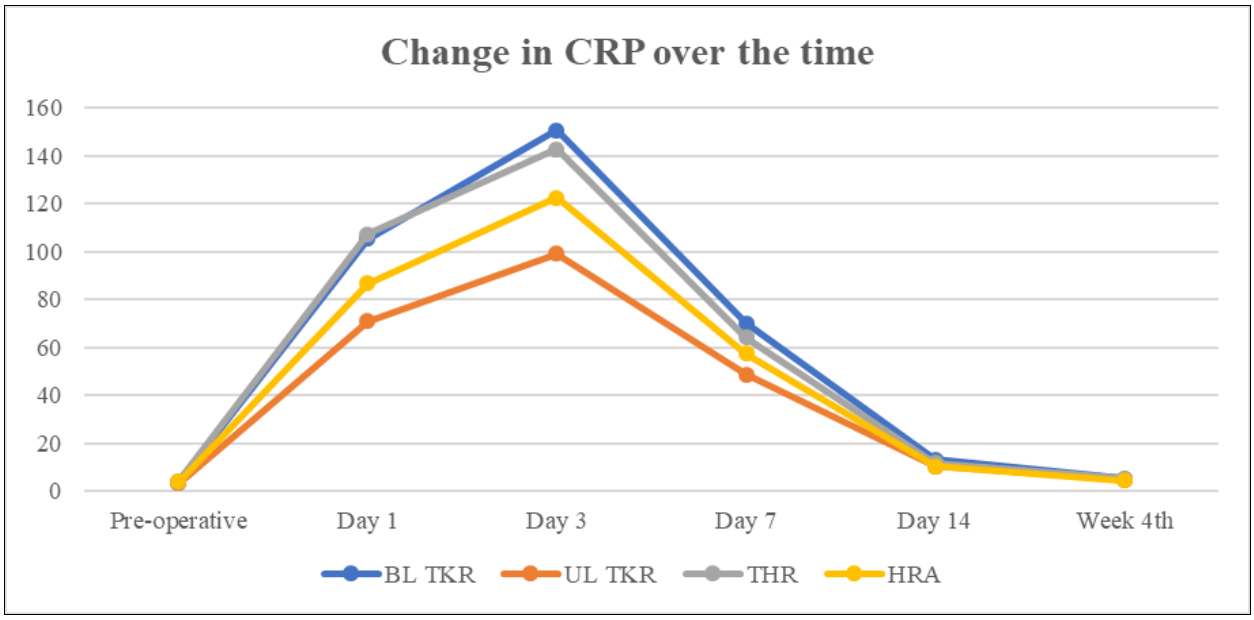

Fig 2: Change in CRP value over time in patients undergoing different surgeries

Discussion

Infection is a nightmare for the orthopaedic surgeon performing total joint replacements [16-17]. Thus, besides clinical, and radiological findings we also need objective tests to exclude the possibility of infection. ESR and C-reactive protein have been broadly used to determine the presence of infection after arthroplasty but in the early preoperative phase interpretation of the value and trend of ESR and C-reactive protein is quite difficult. Because acute phase reactants like ESR and CRP show normal physiological trends after the immediate postoperative period due to surgery-induced soft tissue damage. In the current study, CRP and ESR differ in normal temporal patterns of post-operative levels after uncomplicated THR and TKR, and HRA procedures.

Compare to ESR, CRP levels react more sensitively and rapidly compare to ESR. In the current study, CRP levels quickly touched a peaked-on day 3rd, and after that levels decreased in a biphasic pattern. The first peak occurred after day 3rd, after that CRP levels declined rapidly, and the second phase came after day 7th with a steady decline until normalization at the end of the 3rd week. In comparison to CRP level, ESR levels peaked on 3rd day and gradually decreased but continued higher above the normal reference level (0-30mm/ hr) at the end of 3rd week.

These findings are in concordance with previous studies in the literature evaluating the postoperative levels of CRP and ESR after TKR or THR. However, in the present study, the CRP trend in THR and TKR in the Indian population differed from those published in the literature in some aspects. According to a study done by White *et al.* [10] and Bilgen *et al.* [12], the CRP trend of total knee and total hip replacement shows. The mean value of TKR is higher than THR patients.

The current study showed different trends, the mean value of CRP was higher in THR compared to the TKR group. This difference could be connected that the relatively younger population in the THR group. The higher incidence of secondary hip osteoarthritis demanding total hip replacement is higher as compared to the Western population [18].

The mean peak value of CRP on day 3rd following THR and TKR was found to be in similarity to that in the previous literature [9-12]. However, the time varied across CRP to reach to baseline is different in different studies. After joint replacement surgery, it is equally important for the surgeon to know the rising trend after touching the baseline value to expect the possibility of infection. In the present study, CRP values were normalized to preoperative values by the end of 4th week following THR and TKR.

The declining trend of CRP after a total hip replacement was noted only after the 7th day in a study done by Aaltp *et al.* [9] compared to day 3rd in the current study. While in both studies, CRP values normalize at the end of 3rd week.

In the study by Bilgen *et al.* [12] in TKR patients the normalization value only reached preoperative value after the end of 8th week. In a study by Park *et al.* [13] values of CRP after TKR reached the normal reference at the end of 6th week. In another study done by Londhe *et al*, the normalization of CRP level after unilateral TKR reached 12th weeks compare to Bilateral TKR at the end of 16th weeks. In the study done by Nazem *et al.* [15] on the Iranian population, It was found that after 1 year of procedure (TKR and THR) CRP levels were still higher compared to the normal baseline levels.

This discrepancy in the normalization of CRP values could be connected to multiple factors like the surgical approach used in surgery, the degree of surgical dissection performed, the duration of surgery, and post-operative rehabilitation protocol (19), the demographical and geographical characteristics of the population may also seem to play an important contributing role in the CRP and ESR trends after an arthroplasty procedure. The operating surgeon should be aware of these factors, and CRP & ESR trends after an arthroplasty procedure should be interpreted in light of the above elements before making any decision.

Though there are numerous studies in the literature evaluating CRP and ESR trends post-total hip and knee replacement surgeries, very few have evaluated the effect of racial factors affecting CRP values [20]. Most of the studies have primarily been done on a subset of the European population [9-13] and to the best of the author's knowledge, very few have studied the early post-operative trend of CRP and ESR on a subset of the Asian population [14, 15].

The present study is an attempt to fill this gap in the literature by evaluating the CRP and ESR trend in an Indian population. Also, most of the published literature has evaluated CRP and ESR trends in THR and unilateral TKR, whereas the present study has gone a step further by evaluating the CRP and ESR

trends in THR, unilateral TKR, and simultaneous bilateral TKR.

This present study also confirms and highlights the facts previously recorded in the literature [21-27] that CRP correlates with a higher degree of inflammatory activity with a more rapid increase and a faster return to normal than ESR at the end of 3rd week.

CRP shows a more predictable response with less atypical patterns and appears to be a better indicator of acute-phase response than ESR. CRP and ESR levels in THR and Bilateral TKR follow a similar trend with comparable values suggesting that surgical trauma induced by these two surgeries appears to be the same.

However, CRP and ESR levels after unilateral TKR, though following a similar trend as THR and simultaneous bilateral TKR groups, had much lower mean values, suggesting that the surgical trauma induced in U/L TKR is much less than the other two groups.

Limitations

In the present study, ESR was not followed for longer than three weeks to see when it was normalized. Also, since ESR was not followed long enough it could not be compared with other studies in the literature which had a longer follow-up period of ESR. Also, the number of patients in the current study was less, so the result cannot be normalized to the whole Indian population so a study with a higher number of patients is recommended.

Conclusion

CRP continues to be the best acute phase reactant in the early postoperative phase with a relatively typical pattern as compared to ESR. CRP values peak at postoperative day 3rd and then show a gradual decline. However, its normalization to pre-operative values may vary among different groups of the population. In light of this fact, the authors suggest that large multicentric studies involving different population groups may validate the plausible effect of demographical and geographical factors on CRP and ESR trends after total hip and knee arthroplasty.

Conflict of Interest

Not available

Financial Support

Not available

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