Original Article

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Variations of inflammatory markers levels (ESR and CRP) in the perioperative period of total knee arthroplasty

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ABSTRACT

Background: The preferred method of treatment for severe osteoarthritis of the knee is total knee arthroplasty (TKA). TKA has been linked to a significant increase in inflammatory markers such as erythrocyte sedimentation rate (ESR)—a test that measures how quickly red blood cells settle to the bottom of a test tube—and C-reactive protein (CRP)—a protein made by the liver that increases when there's inflammation in the body. **Aim:** Assessment of the typical time trend and physiological kinetics of CRP and ESR during the early postoperative period over 4 weeks **Methods**: The study was conducted in the Basrah arthroplasty center, from June 2022 to October 2023. The study sample consisted of patients undergoing TKA operations with no history of inflammation, infection, uncontrolled chronic disease, or any autoimmune disease. We enrolled 34 uncomplicated cases. ESR and CRP were measured over time. **Results**: The highest mean CRP values (123.2 ± 101.0) mg/L were in the first week and then started to decrease; the ESR highest reading was in the second week (66.4 ± 31.2) mm/h and then declined. The difference was significant from the baseline reading for both markers. **Conclusion**: In the initial postoperative period, CRP remains a better acute phase reactant than ESR and has a more expected pattern.

Keywords: Total knee arthroplasty, CRP, ESR

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INTRODUCTION

Advanced joint osteoarthritis (OA) is at present treated with total knee arthroplasty (TKA) or total hip replacement (THA), modern and successful procedures. Patients experienced moderate to severe pain in the early stages of their recovery following surgery,[1–4] as well as apparent inflammation, which was seen as a rise in inflammatory cytokines such as interleukin (IL), C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR).[5,6] Subsequently, patients were unable to achieve the appropriate knee joint function following TKA surgery due to ongoing postoperative discomfort and inflammation.[7,8]

In the field of orthopedics, CRP and ESR are acute-phase reactants that are produced in response to inflammation, injury, and cancer and can be used to

identify probable infections.[9,10] However, their levels can remain elevated for up to 3 months following TKA even in the absence of infection.[11] While CRP follows a predictable pattern with an instantaneous peak at the third postoperative day followed by a gradual reduction over time, ESR continues to rise for a longer period of time after surgery.[12,13] The time frame for the postoperative phase of CRP and ESR value normalization varies across studies and people.[14,15]

There are additional acute phase proteins than CRP and ESR. Other acute-phase proteins include coagulation proteins (fibrinogen, prothrombin, etc.), transport proteins (haptoglobin, ceruloplasmin, 1-trypsin inhibitor, etc.), and complement elements (C3, C4, C5, etc.). The fact that CRP and ESR increase in levels significantly higher than basal levels, have a relatively short lag time from the moment of disability, and have reasonable costs makes them the preferred markers for monitoring the acute phase after surgery.[16]

Appreciating that a single CRP or ESR reading has very little importance and that trends over a period of time must be seen to maximize its value is crucial. The goal of this study was to assess the typical time trend and physiological kinetics of CRP and ESR during the early postoperative period over a 4-week period in an Iraqi population following uncomplicated knee replacement surgeries and to align the trend with the body of existing literature as well as identify the time at which CRP and ESR start to normalize.

MATERIALS AND METHODS

This prospective study was carried out in an arthroplasty center in Al Basra with the agreement of Al Basra Health Directorate. It spanned from June 2022 to October 2023, providing a substantial timeframe to accrue, evaluate, and interpret the necessary data. All of the patients included in the study provided verbal consent.

The cohort comprised 34 adults who underwent unilateral TKR due to different indications, including OA, rheumatoid arthritis/inflammatory arthritis, posttraumatic degenerative joint disease, or osteonecrosis with cartilage destruction. Exclusion criteria encompassed comorbidities affecting the values of acute-phase reactants during the perioperative phase, such as infection, cancer, or inflammatory condition. Additionally, patients with abnormal preoperative serum CRP (normally less than 10 mg/L) or ESR (normally, 0–15 mm/hr in males, 0–30 mm/hr in females) readings or both were excluded from the study.

A sophisticated history, examination, and appropriate investigations were done on the patients to exclude the liability of post-TKA that might affect CRP and ESR readings.

TKA was performed using a medial parapatellar approach through a straight midline incision. Samples of blood were drawn a day before surgery and after 1, 2, 3, and 4 weeks; 2 mL of blood samples were taken for the CRP and ESR tests. With a normal reference range of 0–10 mg/dL, an analytical kit relying on the ELIZA principle was used for quantitative CRP measurement, and by employing the Wintrobes method with a reference range of 0–30 mm/hr, ESR was calculated.

The representation of discrete categorical data was usually a number or a percentage (%). The mean and standard deviation of continuous data were provided. Kolmogorov–Smirnov tests of normality were used to gauge the normality of quantitative data. A one-way ANOVA was used to compare the groups for data that were normally distributed, and then the post hoc multiple comparison test was performed. The significance level was set at a p-value of <0.05 with a confidence interval (CI) of 95%. Statistical Package for the Social Sciences (SPSS version 26) was used for all analyses.

RESULTS

This study involved 34 patients who were subjected to knee joint replacement. There were 21 female and 13 male patients. Age ranged from 41 to 72 years (Figure 1).

ESR: The values show a notable increase during the first and second weeks postoperatively, followed by a decline in the third week. The observed fluctuation was statistically significant (p-value < 0.05).

CRP: There is a remarkable spike in CRP levels during the first week, which then decreases considerably by the second and third weeks. The differences were statistically significant ($p < 0.05$) (Table 1).

Post hoc testing revealed the between-group differences as below:

ESR: Significant statistical differences were reported in weeks 2 and 3 compared with the preoperative values. Other differences were not statistically significant.

CRP: CRP levels exhibit a statistically significant increase between the preoperative and first week ($p = 0.015$) and between the preoperative and second week ($p = 0.036$).

Other differences were not statistically significant (Table 2).

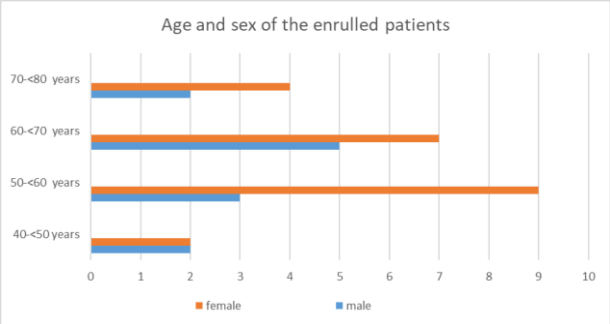

Figure 1: Age and sex distribution of the studied patients

Table 1: Follow-up parameters preoperatively and weekly thereafter for three weeks

	Preoperative	First week	Second week	Third week	p-value*
ESR (mean ± SD)	22.3 ± 10.1	53.1 ± 36.3	66.4 ± 31.2	54.9 ± 22.0	0.007
CRP (mean ± SD)	5.8 ± 2.7	123.2 ± 101.0	36.4 ± 31.1	27.6 ± 22.6	0.008

*Repeated measure ANOVA

Table 2: Post hoc testing of parameters

	Post hoc p-values for Bonferroni test					
	Preop. vs week 1	Preop. vs week 2	Preop. vs week 3	Week 2 vs week 3	Week 2 vs week 4	Week 3 vs week 4
ESR	0.127	0.003	0.008	0.439	0.999	0.630
CRP	0.015	0.036	0.999	0.078	0.092	0.999

DISCUSSION

We evaluated the ESR and CRP levels both before and after surgery to track the progression of the inflammatory response in the early postoperative phase. The mean preoperative ESR level reached its peak in the third week, then it started to decline in the fourth week. While the quantitative CRP measurement in this study showed the highest mean level at one week and then started to decline subsequently over the second and third weeks.

Various studies have attempted to explain the perioperative variability in ESR after TKA in the past. The mean preoperative ESR was 22.2 ± 12.14 mm/hr in a Korean research on 108 patients with TKA surgeries, according to Park et al., and it increased to 42.13 ± 37.37 mm/hr on the second postoperative day; additionally, before surgery, the CRP levels were 1.64 ± 2.23 mg/dL; these levels rose to 59.08 ± 35.42 mg/dL on the first postoperative day and 151.26 ± 54.34 mg/dL on the second postoperative day.[13] In a different study conducted in Iran by Nazem et al., 35 TKA patients were included. It was discovered that the preoperative and second postoperative day ESR values (in mm/hr) with mean ± SD were 19.1 ± 12.9 and 75.33 ± 28.1, correspondingly, and the preoperative in comparison postoperative days 1 and 2 CRP values were 4.07 ± 2.9, 58.5 ± 24.5, and 68.2 ± 15.3 in sequence.[15] The maximal values of ESR and CRP were detected on the fifth and second postoperative days, respectively, in both of the studies mentioned above, which monitored ESR and CRP levels for 6 weeks at multiple times. A quantitative judgment on the percent change of pre- and postoperative increases in ESR and CRP cannot be determined with confidence because the standard deviation in the data sets of the Korean study, the Iranian study, and our study is significantly different.

Regarding normalization of CRP to their preoperative levels, although the CRP in this study started to decline from the second week, they didn't reach their preoperative level even at the end of the third week. In the research by Bilgen et al.,[17] the restored normal CRP level in TKA patients did not reach preoperative value until the end of the eighth week. CRP readings following TKA reached the average baseline at the end of the sixth week in a study conducted by Park et al.[13] In a different trial conducted by Londhe et al., unilateral TKA resulted in CRP normalization after 12 weeks as opposed to bilateral TKA at the 16th week. After 1 year following the procedure, TKA CRP values continued to be higher than the baseline values, according to the research by Nazem et al.[15]

The trend of ESR and CRP levels following a joint arthroplasty has been the subject of numerous studies in the past, but the majority of them point to study limitations that make it challenging to analyze and draw conclusions. Some of them are considering total hip and knee arthroplasty.[18,19] Because their levels rise quickly, they have a relatively short latency period, and they are inexpensive; ESR and CRP levels in post-TKA recipients

reflect an indicator of the acute inflammatory response following a surgical traumatic stimulation and can be used to monitor the course of postoperative recovery after TKA.[20] The rise in ESR and CRP can be seen as an indirect indication of tissue injury during the arthroplasty surgery because cases of infection discovered during the follow-up period were excluded from the study.[21,22] The present research also supports and emphasizes findings previously reported in the literature showing that CRP correlates with a higher degree of inflammatory activity and increases more quickly, and returns to normal earlier than ESR.[23,24]

This study has notable limitations, such as a small sample size that makes it challenging to extrapolate the findings to a wider population. Additionally, the impact of the demographical factors on the marker level was not assessed because of the relatively small sample size. A larger comparative study may therefore be conducted for this purpose.

CONCLUSIONS

In the initial postoperative period, CRP remains a better acute phase reactant than ESR and has a more expected pattern. CRP readings reach their peak during the first postoperative week and then gradually decrease. The normalization process to preoperative levels, though, may differ for various population groups and needs much more than three weeks for most of them.

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