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Assessment of variation in ESR and CRP levels after Hip and Knee Arthroplasties and their correlation with associated post operative infection

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ABSTRACT

Introduction: Routinely used inflammatory markers such as ESR and CRP are suggested to suspect post-operative infection at an early stage. Therefore their normal trend after arthroplasty surgeries need to be known and their variation from that trend need to be understood.
Methods: A prospective observational study was conducted. 75 patients undergoing THR or HRA surgeries of hip or TKR surgeries fulfilling the inclusion and exclusion criteria were considered for the study. Blood samples were collected preoperatively and postoperatively on day 1, 3, 5, 7 and 15 after surgery and sent to measure ESR and CRP values. Surgical site was assessed for presence of any discharge, which was sent for culture. Presence of any growth after 48 hours of incubation was diagnosed as infection.
Result: Values of both ESR and CRP raised after surgery. ESR reached its peak value on POD 5 while CRP reached its peak value on POD 3. Both ESR and CRP declined thereafter. On correlating these trends with infected cases, we reported a statistically significant correlation of CRP with infection on POD 15. However, ESR values did not show any significant correlation with infection in starting 15 days post-operatively.
Conclusion: There is a significant variation in levels of ESR and CRP after arthroplasty surgeries of lower limb. In infected cases, there is a deviation from this normal trend, that can be used to suspect post-operative infection. However, none of these parameters can be used to suspect it in starting 7 days after surgery.

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Introduction

There has been a huge growth in joint replacement surgeries in the past few years. Total Hip Replacement (THR), Total Knee Replacement (TKR) and Hemi Replacement Arthoplasty (HRA) of hip have gained widespread interest since these are generally accepted as a treatment of choice to relieve pain, correction of deformity, restore function near normal, thus improve the quality of life (1).

As the life expectancy of the population is increasing, joint replacement surgery is likely to increase significantly during the next few years. As a result, it can be appreciated that development of post-operative complications following joint replacement surgery is likely to increase (2). Although such operations have resulted in a great relief for patients, they may be accompanied with infections affecting the

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result of operation and patient's condition (3). Periprosthetic joint infection after total hip arthroplasty or total knee arthroplasty is one of the most dreadful complications and it has extremely negative effects on the physical, emotional, social, and economic aspects of patient's life (4).

Establishing an early diagnosis of deep infection after arthroplasty is difficult and diagnosing infection in later stages makes the management difficult. A correct and early diagnosis is essential in order to provide the most appropriate management. Early infection after surgery particularly requires fast and accurate diagnosis because a delay in treatment appears to be the most detrimental factor for a successful outcome (5).

If a correct and timely microbiological diagnosis of infections is done within 4 weeks, it could be possible to follow a conservative approach on the prosthesis, since microorganisms are not yet organized in biofilms. A delayed diagnosis (>4weeks) of early and late infections involves the necessity of prosthesis removal (6) due to the production of a structured and mature microbial biofilm. There is no universally accepted absolute reliable diagnostic test for detection of Periprosthetic joint infections (7). Diagnosis in prosthetic joint infections is challenging as symptoms are variable, and currently most of the diagnostic tests are non-specific. Normal inflammatory reactions after orthopedic prosthetic surgery may generate false positives, as these tests have high sensitivity but low specificity (8).

Despite considerable progress in orthopaedic surgery, comparing a range of biological markers with the ultimate aim of monitoring or predicting post-operative complications has not yet been extensively researched (3). Since post-operative recovery in patients undergoing hip or knee replacement is always characterized by a shift in basal laboratory parameters, the value of the routine use of these parameters in the detection of this major complication is controversial. Use of non specific inflammatory markers such as ESR and CRPis suggested to evaluate/diagnose infection following Total and hemi arthroplastry of hip and total knee arthroplasty. Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) levels are the most frequently used inflammatory markers and are suggested as part of the diagnostic algorithm in IDSA and American Academy of Orthopedic Surgeons (AAOS).

Both have the advantage of being widely available and inexpensive. However, they are limited by their relative lack of specificity, a concern for patients with underlying inflammatory joint disease such as rheumatoid arthritis.The reported sensitivity of ESR and CRP in the diagnosis of periprosthetic joint infections varies between studies. While some authors report sensitivities as high as 91% for ESR and 95% for CRP. As such, the role of ESR and CRP in the definitive diagnosis of periprosthetic joint infections remains controversial, with some advocating the use of ESR and CRP to definitively rule-out periprosthetic joint infections, while others argue that this would result in an unacceptably high number of false negatives, resulting in a delay in the diagnosis of periprosthetic joint infections (9).

Other investigations to detect post-operative infections are very costly and invasive. Hence, we intend to use these (ESR, CRP, TLC and body temperature) low cost parameters in detecting post-operative infections following Total Joint Arthroplasty and Hemi-Replacement Arthroplasty of lower limb. It is anticipated that any changes in these measured parameters may provide future direction with respect to therapeutic intervention impacting treatment strategies and promoting patient recovery. This study is of clinical significance, since it helps in diagnosis of infection, i.e., a dreaded complication in any joint replacement surgery at an early stage. This also has an economical advantage as many unnecessary costly investigations can be avoided.

Materials and methods

A prospective observational study was conducted on 75 patients at a tertiary care teaching hospital , Delhi, India, on patients undergoing total or hemi arthroplasty of hip or total knee arthroplasty fulfilling the inclusion/exclusion criteria .The inclusion criteria was age more than 25 years, patients undergoing hemi replacement arthroplasty for fracture neck of femur, patients undergoing total hip replacement and total knee replacement .The exclusion criteria was patients with systemic inflammatory disorder, cerebrovascular disease, cardiovascular disease, patients with raised preoperative inflammatory markers as CRP, ESR, TLC, patients with diabetes mellitus. Patients with infection of other systems as urinary or respiratory system were excluded from the study. Participants were explained the procedure, benefit and risk associated with this and informed written consent was taken to participate in the study.

Venous blood sample was collected pre-operatively and post-operatively on day 1, 3, 5, 7 and 15 in sterilized vials which were sent to measure ESR and CRP levels and noted. We assessed the surgical site on post operative days 3,7 and 15 for any discharge from the surgical site. Post-operative infection was suspected if discharge is present at the surgical site. Wound swab was collected from the surgical site and sent for culture and

sensitivity. After 48 hours of infection, if results came positive, that was considered as presence of infection otherwise, absence of infection was considered.

Results

The work done was observed under different subsections to highlight the significance and correlation amongst them based on the statistical interpretation.These are as follows:

ESR variations

In this study, we observed the impact of THR, TKR and HRA surgeries on ESR levels. We observed the variation of ESR in our surgeries as shown in the figure 1. On day 0, it was (17.71 +8.13 mm/hr).On day 1, it was (39.12 +11.29 mm/hr). On day 3, it reached (72.83 +15.54 mm/hr).

It peaked on day 5(84.28+15.67), then started to decline with mean ESR value (81.88 +16.43 mm/hr) on day 7 and (67.59 +13.34 mm/hr) on day 15.The results were significant with p-value (<0.0001) as determined by paired t test.

Figure1: Comparison of erythrocyte sedimentation rate(mm/hr) between day 0 and follow up.

With respect to comparison amongst the three groups, that are THR, TKR and HRA we observed the following variation in ESR as shown in the figure 2.By analyzing the levels of ESR before and after THR sugery, we observed that ESR increased from the baseline level of (16.58+7.83 mm/hr) at day 0 to (37.81 +12.84 mm/hr) at day 1 and (70.72 +16.4 mm/hr) at day 3.

It reached its peak on day 5 with value of (86.16 +15.64 mm/hr) and then started to decline with (84.28 +15.21 mm/hr) on day 7 and (69.49+13.15 mm/hr) on day 15 post operatively with p-value of <0.0001 as determined by paired t test.

Figure2: Comparison of erythrocyte sedimentation rate(mm/hour) between day 0 and follow up.

By analysing the levels of ESR before and after TKR surgeries, we observed that ESR increased from the baseline level of (18.64 +6.27 mm/hr) on day 0 to (37.64 + 8.22 mm/hr) on day 1 and (87.36 ± 8.54 mm/hr) on day 3. It reached its peak on day 5 with value of (92.86 +7.59 mm/hr) and then the values started to decline with ESR level (89.57+8.61 mm/hr) on day 7 and (70.21+7.16 mm/hr) on day 15. The changes were significant with p-value of <0.0001 as determined by paired t-test.

By analysing the levels of ESR before and after HRA surgery, the levels were (19.67+9.9 mm/hr) on day 0 of surgery and started to increase with ESR value (43.39 + 8.41 mm/hr) on day 1 of surgery and (66.56 +10.22 mm/hr) on day 3 of surgery. It reached peak value of (73.11 +14.78 mm/hr) on day 5 and then started to decline with ESR values (70.17 + 18.37 mm/hr) on day 7 and (61 +15.74 mm/hr) on day 15 post operatively with p-value <0.0001 as determined by paired t-test.

CRP variation

In our study, we observed the impact of THR,TKR and HRA surgeries on CRP levels.

Overall, we observed the variation in CRP levels before and after surgery as shown in the figure 3.On day 0, mean baseline levels were observed as (3.69 + 1.4 ng/ml), which raised to (45.12 + 17.58 ng/ml) on day 1 post operatively, which reached its peak on day 3 with mean value of (99.4 +40.7 mg/dl) and then started to decline with mean values of (56.97 + 22.27 ng/ml) on day 5, (44.77 + 18.62 ng/ml) on day 7 and (25.56 + 13.89 ng/ml) on day 15. These variations were significant with p-value of <0.0001 as determined by paired t-test.

Figure3: Comparison of C-Reactive protein(ng/mL) between day 0 and follow up.

By analyzing the variation in CRP levels before and after individual group of surgeries, which are THR, TKR and HRA surgeries, we observed the following results as shown in the figure 4.With regards to the variations of CRP with respect to THR surgery, we observed that CRP concentration increased from the baseline level of (3.53 + 1.38 ng/ml) on day 0 to (47.97 + 13.68 ng/ml) on day 1 and reached its peak to mean CRP value of (99.29 + 22.85 ng/ml) on day 3, the CRP levels then started to decline with mean concentration (57.37 + 15.59 ng/ml) on day 5, (45.86 + 12.73 ng/ml) on day 7 and (24.24+ 7.68) on day 15, but remained at a higher level than the baseline value as determined by paired t-test.

By analyzing the levels of CRP with regards to TKR surgery, we revealed that CRP concentration increased from the baseline value of (3.98 + 1.05 ng/ml) on day 0 before surgery to (61.06+ 10.55 ng/ml) on day 1 of surgery and reached its peak value of (150.23 + 18.25 ng/ml) on day 3 after surgery. The mean CRP concentration then started to decline with value (85.32 + 13.39 ng/ml) on day 5 ,(66.39 + 11.57 ng/ml) on day 7 and (37.22 + 10.37 ng/ml) on day 15 after surgery. The CRP concentration decline sharply but remained at a higher level than the basal value as determined by paired t-test.

With regards to CRP and HRA surgery, we observed that the CRP concentration increased from baseline mean value of (3.87 +1.66 ng/ml) to(25.9 +13.28 ng/ml) on day 1 and reached peak value of (60.15 + 43.66 ng/ml) on day 3 post operatively (approximately 20 folds). The CRP concentration then started to decline gradually with mean value of (33.96 + 14.06 ng/ml)on day 5; (25.34 + 14.78 ng/ml)on day 7 and (19.62 + 21.39 ng/ml)on day 15 but remained at values higher then the baseline as determined by paired t-test.

ASSOCIATION OF ESR WITH INFECTION

In our study, we observed the ESR values before and after arthroplasty surgeries and these variations were compared amongst the noninfected and infected groups as shown in the figure 5.In the non infected group, we observed that the mean ESR values raised from the baseline values of (17.77 + 8.22) mm/hr on day 0 pre operatively to (39.21+11.41) mm/hron day 1, (73.01 +15.71)mm/hr on day 3 and reached its peak value of (84.1+15.83)mm/hr on day 5. It then started to decline thereafter with mean ESR value of (82.07 +16.58)mm/hr on day 7 and (66.99 +13)mm/hr on day 15 .

Figure4: Comparison of C-Reactive protein(ng/mL) between day 0 and follow up.

Figure5: Association of trend of erythrocyte sedimentation rate(mm/hr) at different time intervals with infection.

While in the infected group , ESR increased from the baseline value of (15.5 +3.54)mm/hr on day 0 preoperatively to (36+7.07) mm/hr on day 1, (66 +4.24)mm/hr on day 3 and reached a peak value of(91 ± 5.66)mm/hr on day 5. It declined on day 7 with values of (75+8.49) mm/hr and and again increased after that to reach a value of (89.5+2.12) on day 15 which is approx 5.6 times the baseline values. The difference had the p-value of 0.017 as determined by t-test. The correlation of ESR at different time interval with infection is given in table 1.

Table 1: Correlation of ESR at different time intervals with infection (Point Biserial correlation coefficient).

Infection	Correlation coefficient	P value
Erythrocyte sedimentation rate(mm/hr) day 0	-0.045	0.700
Erythrocyte sedimentation rate(mm/hr) day 1	-0.046	0.695
Erythrocyte sedimentation rate(mm/hr) day 3	-0.073	0.533
Erythrocyte sedimentation rate(mm/hr) day 5	0.071	0.542
Erythrocyte sedimentation rate(mm/hr) day 7	-0.07	0.552
Erythrocyte sedimentation rate(mm/hr) day 15	0.274	0.018

ASSOCIATION OF CRP WITH INFECTION

In our study, we observed the values of CRP before and after arthroplasty surgeries on day 0,1,3,5,7 and 15. These variations were compared amongst non-infected and infected groups as shown in figure 6. In the non-infected group we observe that the mean CRP values raised from the baseline value of (3.71+1.4)ng/ml on day 0 preoperatively to (45.94 + 17.08)ng/ml on day 1 post operatively. It reached to its peak value of (101.36 +39.46) ng/ml on day 3 and then started to decline thereafter with values of (57.63 + 22.19)ng/ml on day 5, (44.93 + 18.82)ng/ml on day 7 and (24.29 + 11.65)ng/ml on day 15 which was still 6.5 times the baseline value.While in the infected group, the baseline CRP values were observed as (3.01 + 1.53) ng/ml on day 0 preoperatively.

Figure 6: Association of trend of CRP at different time intervals with infection.

It then started to rise thereafter with values of (15.12 + 1.94)ng/ml on day 1, (28.1 + 4.76)ng/ml on day 3, (33.09 + 8.97) on day 5, (38.64 +8.32)ng/mlon day 7 and (71.9 + 9.08)ng/mlon day 15 which was approx. 23.9 times the baseline value. The difference was significant with p-value of <0.0001 as determined by t-test. Correlation of CRP at different time intervals with infection shown in table 2.

Table 2: Correlation of CRP at different time intervals with infection.(Point Biserial correlation coefficient)

Infection	Correlation coefficient	P value
C-Reactive protein(ng/mL) day 0	-0.082	0.486
C-Reactive protein(ng/mL) day 1	-0.284	0.013
C-Reactive protein(ng/mL) day 3	-0.292	0.011
C-Reactive protein(ng/mL) day 5	-0.179	0.125
C-Reactive protein(ng/mL) day 7	-0.055	0.641
C-Reactive protein(ng/mL) day 15	0.556	<.0001

DISCUSSION

By analyzing the variations in these non-specific markers, we get a normal trend in their variations over time as a response to surgery, and also we can see the variations in this trend because of early post-operative infection. Thus, it may help us to make an early diagnosis of post-operative infection using these non-specific parameters and contribute to various preventive and protective strategies.

This study is a modest contribution to the ongoing discussion about the assessment of variation in non-specific inflammatory after hip and knee arthroplasties and there correlation with associated post operative infection; which would provide a better understanding of the topic.

CRP VARIATION

While comparing the 3 groups, THR, TKR and HRA, we assessed that the mean CRP values raised from the baseline in all the 3 groups and peaked on day 3. The peak mean CRP values were highest in TKR, followed by THR and least in HRA. The CRP started to decline after day 3 post operatively in all 3 groups but did not reach to its baseline value by day 15. Thus, we demonstrated from this study that CRP is an effective and sensitive method of measuring acute inflammatory response post surgery.

Our results are in general accordance with White J,et al10, who demonstrated that the CRP levels

peaked on day 2 post operatively after TKR , which concluded it as a reliable indicator of infection after TKR and THR. Similar to the results of our study, it showed a higher peak level of CRP in TKR than in THR and demonstrated that peak count of CRP may vary but its level decrease at a similar rate thereafter .Okafor B, et al11 performed a study,which demonstrated CRP to reach its peak value on day 2 and decline sharply by day 4 after THR and TKR surgeries .Previous study by Geihl JP, et al12 demonstrated the CRP levels to peak on day 2 and 3.

Previous study by BilgenO,et al13 demonstrated that CRP concentration peaked on day2 after THR and TKR surgeries .Values were higher in TKR than THR and returned to basal level early in THR than in TKR. This suggested that bone and bone marrow trauma was higher in TKR than in THR , thus degree of inflammation was higher and for longer duration in TKR than THR .In previous study performed by MargheritiniF,et al14, it was reported that the CRP concentration reached its peak value at day 3 after THR and TKR surgeries and returned to its baseline value by day 15.In another study by Park K,et al15, it was reported that CRP concentration reached its peak value on day 2, and then declined gradually to reach its baseline value within 40 days in bilateral TKR and within 14 days in unilateral TKR .

In a study done by HonsawekS,et16 al, he demonstrated CRP to be elevated on 1stpost operative day and fell to preoperative values at 2nd day post operatively. Thus, concluding CRP as the inflammatory biomarker of choice and major acute phase reactant in orthopaedic surgeries .Similar to our result, Huges FS, et al2, in its study reported CRP concentration to reach its peak on day3 post operatively after THR and TKR surgeries .In agreement withKatoh N, et al5, who demonstrated the CRP concentration to rise at day1, reach its peak value at day 3 and decrease thereafter, but remained significantly higher than baseline at day 14 , our study showed similar results .Previous study by Neumaier M, etal17, reported that CRP peaked on day 2 and 3 post operatively indicating CRP to be the basic inflammatory marker which is more significant and common than WBC or ESR .Previous study by Wasko K, et al18, also reported the CRP values to rise after THR and TKR surgeries and reach their peak values on day 3. It then decrease thereafter on day 5 but were still higher than basal value. Falzarano G,et al19, in their study, reported CRP values to be higher in TKR than in THR similar to our study.

ESR VARIATION

While comparing the 3 groups in our study, that are THR , TKR and HRA surgeries, we observed that the mean ESR values started to increase after surgeries in all three groups and reached to its peak on day 5. The peak ESR value was highest in TKR group. The mean ESR values then started to decline thereafter in all the three groups but remained elevated even after 15 days of surgery.

The result are in agreement with previous study done by Geihl JP, et al12,who demonstrated the ESR levels to rise after THR and TKR surgeries and reached its peak after 5-6 days post operative.In previous study done by Moreschini O, et al20, ESR levels were reported to rise after THR and TKR surgeries and peak on day 5 and reduced 3 folds by day 60 post operative.Margheritini F14, et al, in their study demonstrated that ESR raised gradually postoperatively, peaked on day 5 and remained elevated even on 30th day post operative after THR and TKR surgeries in control to CRP which returned to itsnormal values by day 5 post operatively which interprets that CRP is more sensitive marker of post surgery inflammatory response than ESR.

Results of our study were in accordance with the previous studies done by Park K15, et al , which reported that ESR raised after TKR and reached its peak on day 5 in unilateral TKR and return to its baseline values after day 90 post operatively.Previous study done by Huges FS, et al2 reported ESR to reach its peak value on day 5 after THR surgery and on day 3 after TKR surgery.Nazem K, et al3 performed a study, in which they measured ESR levels after THR and TKR surgeries and demonstrated that ESR raised for firstfive days post operatively and then gradually declined for 3 months.

In another study by Lee YS21,et al, it was reported that during artrhoplasty, ESR started an upward trend from day 1 , peaked at day 5 and remained high till 6 weeks postoperatively.

ASSOCIATION OF ESR WITH INFECTION

With regards to the variation in mean ESR values following arthroplasty surgeries amongst non-infected and infected groups, we observed that the ESR values in non-infected group started to increase from the baseline value to reach its peak on day day 5 and then started to decline thereafter till day 15 but couldn't reach near to its baseline value.

While in infected group, ESR raised from its baseline value to reach its peak on day 5, its value declined on day 7 and then again raised by day 15 after surgery. The results of our study compared well with another study done byMoreschini O, et al20 who demonstrated that if ESR values remain unchanged/increase after few days of surgery, then it denotes infection.

Our finding complement well with the results of the study done byHonsawek S, et al16 which reported that a sustained elevation of ESR post operatively must raise concern of early post operative complications.

ASSOCIATION OF CRP WITH INFECTION

With regards to the variation in mean CRP values following arthroplasty surgeries amongst non-infected and infected groups, we observed that the CRP values in non-infected group started to increase from the baseline value to reach its peak on day 3 and started to decline thereafter while in infected group the CRP values started to rise from the baseline values following surgeries gradually till day 7. It then increased dramatically to reach a very high value (24 times the baseline value) on day 15.

Results of our study are in accordance with the previous study done by White J, et al10, which reported that a rise in CRP levels after day 3 may indicate infection. It also demonstrated that it is not the absolute level, but the trend after the peak concentration of CRP has been reached , that indicates infection .Our finding complement well with the results of the study done by Okafor B, et al 11, who demonstrated that if CRP doesn't decline after day 4 post operatively, then it suggests presenceof infection. Thus, it indicates that CRP helps in an early diagnosis of infection before it is evident clinically .The results of our study compared well with another study done by Margheritini F, et al 14, who demonstrated that if CRP does not decrease to nearly normal values after 2 weeks or if there is a new rise, then complication should be suspected and additional tests to rule out infection are required. It also reported that a combination of normalvalues of ESR and CRP is a reliable indicator for predicting the absence of infection.

Another study done by Honsawek S, et al16, demonstrated that the sustained elevation of ESR and CRP must raise a concern of early complication post operatively .Neumaier M, et al17, in their study reported that a second rise in CRP values trend by day 4 occurs in case of bacterial infection and thus, it can be used as on early marker of post of infection .Keiboom JV, et al22, in their study proved that CRP is the most valuable tool to diagnose infection post operatively followed by ESR. Although three-level approach is available for the diagnosis of postoperative infection in TKR, THR AND bipolar(23), but our study shows ESR and CRP is good, low cost and early indicator for infection after TKR, THR AND bipolar hemiarthroplasty.

CONCLUSION

Evidence from this study suggests that we have obtained significant variation in levels of ESR and CRP after total and hemi arthroplasty of hip and total knee arthroplaty.

Also while correlating these parameter with post operative infection, we have demonstrated that the correlation of ESR with infection was not significant in starting 15 days making it a non sensitive tool for early diagnosis of post operative infection while correlation of CRP with infection was significant at day 15 postoperaty.

Thus , we demonstrated that by tracing ESR and CRP after surgery, we can get a trend, which when deviated from its normal trend in its post operative course, can suggest post operative complication, but none of these parameters is sensitive enough to give a significant variation in first 7 days after surgery to diagnose early post operative infection.

Although, the number of infected cases in our study were very few because of certain limitations and further studies are required for better exploration of the correlation of these parameters with associated post operative infection. Our work could provide a sound platform for further research.

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Conflict of interest

Authors declare that have no competing interest.

References

1. Singh J. Epidemiology of Knee and Hip Arthroplasty: A Systematic Review. Open Orthop J. 2011;5:80-85.
2. Hughes S, Hendricks B, Edwards D, et al. Lower limb orthopaedic surgery results in changes to coagulation and non-specific inflammatory biomarkers, including selective clinical outcome measures. Eur J Med Res. 2013;18:40.
3. Nazem K, Motififard M, Yousefian M. Variations in ESR and CRP in total knee arthroplasty and total hip arthroplasty in Iranian patients from 2009 to 2011. Adv Biomed Res. 2016;5:148.
4. Zajonz D, Wuthe L, Tiepolt S, Brandmeier P, et al. Diagnostic work-up strategy for periprosthetic joint infections after total hip and knee arthroplasty: a 12-year experience on 320 consecutive cases. Patient Saf Surg. 2015;9:20.
5. Katoh N, Nishino J, Nishimura K, et al. Normal sequential changes in neutrophil CD64 expression after total joint arthroplasty. J Orthop Sci. 2013;18:949-954.
6. Tande AJ, Patel R. Prosthetic joint infection. Clin Microbiol Rev.2014;27:302-345.
7. Abou El-Khier NT, El GanainyAel-R, et al. Assessment of interleukin-6 and other inflammatory markers in the diagnosis of Egyptian patients with periprosthetic joint infection. Egypt J Immunol. 2013;20:93-99.
8. Yildirim K, Misir A, Kizkapan TB, et al. Neopterin, Interleukin-6, Procalcitonin, C-Reactive Protein And PET-CT Staining As Markers In Infected Total Knee Prosthesis, A Retrospective Analysis. Acta Orthop Belg. 2017;83:624-630.
9. McArthur BA, Abdel MP, Taunton MJ, et al. Seronegative infections in hip and knee arthroplasty: periprosthetic infections with normal erythrocyte sedimentation rate and C-reactive protein level. Bone Joint J. 2015;97-B:939-940.
10. White J, Kelly M, Dunsmuir R. C-reactive protein level after total hip and total knee replacement. The Journal of Bone and Joint Surgery. 1998;80(5):909-911.
11. Okafor B, MacLellan G. Postoperative changes of erythrocyte sedimentation rate, plasma viscosity and C-reactive protein levels after hip surgery. J Bone Joint Surg Br. 1998;80:909-911.
12. Giehl JP, Kluba T, Lebherz C. The course of inflammatory mediators after elective orthopedic interventions. Z Orthop Ihre Grenzgeb. 2000;138:181-184.
13. Bilgen Ö, Atici T, Durak K, Karaeminoğullari O, Bilgen M. C-Reactive Protein Values and Erythrocyte Sedimentation Rates

after Total Hip and Total Knee Arthroplasty. J Int Med Res. 2001;29:7-12.
14. Margheritini F, Camillieri G, Mancini L, Mariani PP. C-reactive protein and erythrocyte sedimentation rate changes following arthroscopically assisted anterior cruciate ligament reconstruction. Knee Surg Sports Traumatol Arthrosc. 2001;9:343-345.
15. Park K, Kim T, Chang C, et al. Normative Temporal Values of CRP and ESR in Unilateral and Staged Bilateral TKA. Clin Orthop Relat Res. 2008;466:179-188.
16. Honsawek S, Deepaisarnsakul B, Tanavalee A, et al. Erratum to: Relationship of serum IL-6, C-reactive protein, erythrocyte sedimentation rate, and knee skin temperature after total knee arthroplasty: a prospective study. Int Orthop. 2011;35:31-35.
17. Neumaier M, Scherer M. C-reactive protein levels for early detection of postoperative infection after fracture surgery in 787 patients. Acta Orthop. 2008;79:428-432.
18. asko M, Struminski M, Bobecka-Wesolowska K, et al. Neutrophil-to-lymphocyte ratio shows faster changing kinetics than C-reactive protein after total hip and knee arthroplasty. J Orthop Translat. 2017;10:36-41.
19. Falzarano G, Piscopo A, Grubor P, et al. Use of Common Inflammatory Markers in the Long-Term Screening of Total Hip Arthroprosthesis Infections: Our Experience. Adv Orthop. 2017;2017:9679470.
20. Moreschini O, Greggi G, Giordano MC, et al. Postoperative physiopathological analysis of inflammatory parameters in patients undergoing hip or knee arthroplasty. Int J Tissue React. 2001;23:151–154.
21. Lee Y, Lee Y, Han S, et al. Natural progress of D-dimer following total joint arthroplasty: a baseline for the diagnosis of the early postoperative infection. J Orthop Surg Res. 2018;13:36.
22. Van den Kieboom J, Bosch P, J. Plate J, et al. Diagnostic accuracy of serum inflammatory markers in late fracture-related infection. Bone Joint J. 2018;100-B:1542-1550.
23. Martin McNally ,Ricardo Sousa, Marjan Wouthuyzen-Bakker, et al. The EBJIS definition of periprosthetic joint infection. Bone Joint J. 2021;103-B:18-25.