International Journal of Orthopaedics Sciences

E-ISSN: 2395-1958
P-ISSN: 2706-6630
IJOS 2023; 9(3): 95-98

https://www.orthopaper.com
Received: 20-05-2023
Accepted: 28-06-2023

Dr. Arjun Krishnan
M.S. Department of Orthopedics, Saveetha Medical College, Thandalam, Chennai, Tamil Nadu, India

Dr. Raja Sujith Kumar
M.S. Department of Orthopedics, Saveetha Medical College, Thandalam, Chennai, Tamil Nadu, India

Dr. Meenakshi Rakesh
M.S. Department of Orthopedics, Saveetha Medical College, Thandalam, Chennai, Tamil Nadu, India

Dr. Nitheesh
M.S. Department of Orthopedics, Saveetha Medical College, Thandalam, Chennai, Tamil Nadu, India

Dr. Yeshwanth Subash
Professor, Department of Orthopedics, Saveetha Medical College and Hospital Thandalam, Chennai, Tamil Nadu, India

Corresponding Author:
Dr. Yeshwanth Subash
Professor, Department of Orthopedics, Saveetha Medical College and Hospital Thandalam, Chennai, Tamil Nadu, India

The significance of C-reactive protein (CRP)/albumin to globulin ratio (AGR) test as a valuable diagnostic tool for periprosthetic joint infection, a single centre retrospective study

Dr. Arjun Krishnan, Dr. Raja Sujith Kumar, Dr. Meenakshi Rakesh, Dr. Nitheesh and Dr. Yeshwanth Subash

DOI: https://doi.org/10.22271/ortho.2023.v9.i3b.3414

Abstract
Introduction: Periprosthetic joint infection (PJI) is a very serious complication that can occur after total knee arthroplasty (TKA) and total hip arthroplasty (THA). Timely and accurate diagnosis of PJI is crucial for preserving the implanted prosthesis, restoring joint function, and reducing morbidity rates. However, diagnosing PJI remains challenging due to the absence of a definitive "gold standard "test with absolute accuracy. To assess the effectiveness of various clinical indicators in diagnosing periprosthetic joint infection (PJI), we will evaluate the comparative performance of serum C-reactive protein levels, erythrocyte sedimentation rate, albumin to globulin ratio (A/G).
Methods: This is a retrospective study, we collected clinical data of 30 patients diagnosed in our department between January 2021 to July 2023 with periprosthetic joint infection following total knee arthroplasty or total hip arthroplasty (less than 90 days considered acute or more than 90 days considered chronic). Patient demographic data were compared and we evaluated the relative sensitivity and specificity of pre-operative ESR and CRP/AGR values as predictors for diagnosing Periprosthetic joint infection.
Results: Among 30 patients 21 had positive culture results, 9 patients had negative culture results. Based on the culture reports the most common organism involved is Staphylococcus aureus 85.71% followed by Staph. epidermidis 14.28%. For culture sensitive patients the diagnosing accuracy for in culture patients CRP is 91.75%, ESR is 69.46%, CRP/AGR 93.75%, whereas in culture negative the threshold for diagnosing accuracy for CRP is 60%, CRP/AGR is 61%, ESR is 51%.

Keywords: Periprosthertic joint infection, ESR, CRP, CRP/AGR, total hip arthroplasty, total knee arthroplasty

Introduction
Periprosthetic joint infection (PJI) is a highly severe complication that can occur following total knee arthroplasty (TKA) and total hip arthroplasty (THA) [1]. The incidence of periprosthetic joint infection (PJI) after primary total knee arthroplasty (TKA) or total hip arthroplasty (THA) is estimated to be around 0.5 to 2.5%. Additionally, there are approximately 1.5 infections per 1000 person-years related to PJI. This highlights the importance of vigilance and preventive measures to mitigate the risk of this serious complication [2–5]. Periprosthetic joint infection (PJI) exerts a detrimental effect on joint mobility and significantly diminishes patient quality of life. It leads to considerable morbidity and results in substantial healthcare expenses. In the United States, the annual cost of revision operations after PJI was approximately $566 million in 2009, and it is projected to rise significantly to $1.62 billion by the year 2020. This highlights the economic burden and emphasizes the need for effective prevention and management strategies for PJI [5]. The incidence of PJI in THA and TKA is estimated to be around 2.0%-2.4% [5]. Timely and accurate diagnosis of PJI is crucial for preserving the implanted prosthesis, restoring joint function, and reducing morbidity rates. However, diagnosing PJI remains challenging due to the absence of a definitive "gold standard "test with absolute accuracy.

Albumin, a major serum protein component, is inversely related to the inflammatory process. Hypoalbuminemia, historically considered a marker of malnutrition, has been recognised as a biomarker of inflammation. Serum globulin (GLB), which includes complement components and ceruloplasmin, increases during inflammation. Therefore, albumin to globulin ratio (AGR), which considers ALB and GLB, shows promise as an inflammation biomarker, although its application in detecting PJI has not been studied. D-dimer, fibrinogen, fibrin degradation (FDP), and platelet count are new biomarkers that have shown good performance in PJI studies. The neutrophil to lymphocyte ratio (PLR) is simple inflammation biomarkers used in various diseases, including hepatitis virus infection, rheumatic disease and infective endocarditi. According to research conducted by Shang *et al*., alpha-defensin-gamma-interferon ratio (AGR) demonstrated promising diagnostic value for periprosthetic joint infection (PJI). Furthermore, the study indicated that AGR could serve as a predictive marker for negative culture results and aid in determining the optimal timing for second-stage reimplantation in PJI cases. These findings highlight the potential clinical utility of AGR in managing and improving outcomes for patients with PJI [6]. This study aims to evaluate the diagnostic accuracy of CRP, ALB, GLB, AGR and fibrinogen as biomarker for PJI. We hypothesised that these biomarkers would show promise in diagnosing PJI.

Materials and Methods

The study design involved a retrospective analysis of clinical data obtained from patients who were diagnosed with peri prosthetic joint infections. The data collection period spanned from January 2021 to July 2023 from our institution. The collected data consists of various parameters such as age, gender and pre-operatic serum markers including erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), globulin (GLB), Albumin to globulin ratio (A/G), CRP/AGR ratio. This study was conducted after getting approval by the Institutional Review Board and informed consent was obtained.

The study included individuals who met specific criteria for patient inclusion, which were as follows: patients diagnosed with Periprosthetic Joint Infection (PJI) after undergoing total knee arthroplasty or total hip arthroplasty within 90 days, considered Acute, and more than 90 days, considered Chronic prosthetic joint infection. Additionally, patients who had been diagnosed with loosening and received appropriate treatments in our department, such as revision arthroplasty or spacer insertion surgery, during the mentioned study period were also included. Patient should have the following lab values in pre-operative measurements of CRP, ESR, GLB, A/G and CRP/AGR. Patients excluded in the study, who has been previously diagnosed with systemic inflammatory disease such as Inflammatory bowel disease, gout, sarcoidosis, multiple myeloma, lymphocytic leukemia, rheumatoid arthritis. Presence of any tumours, History of trauma or dislocation within the past two weeks, missing key data required for analysis, Patients not willing for re-surgery and post-operative period follow up.

A total of 46 patients were admitted in our hospital and diagnosed either with periprosthetic joint infection (PJI) or aseptic loosening during the specified study period. Among them, 30 patients met the inclusion as well the exclusion criteria. PJI was diagnosed under MSIS (Musculo skeletal infection Society Criteria. Blood samples were collected from all the patients in morning after they get admitted in our hospital. These samples were utilized to measure the values of C-reactive protein (CRP), globulin (GLB), erythrocyte sedimentation rate (ESR), albumin-to-globulin ratio (A/G), CRP and Albumin globulin ratio (CRP/AGR).

Quantitave data are analysed using IBM SPSS version 22, given in mean +/- standard deviation and compared through non-parametric tests as appropriate, with P value <0.05.

Results

We conducted a retrospective analysis from January 2021 to July 2023 of patients with Periprosthetic joint infection following TKA or THA group consisted of 30 patients. CRP, ESR and CRP/AGR ratio were taken into comparison in the study. The average age was 58.4 years ranging from 47 to 72 years. Among 30 patients 21 had positive culture results, 9 patients had negative culture results (Figure 4). Based on the culture reports the most common organism involved is Staphylococcus aureus 85.71% followed by Staph. Epidermidis 14.28%. (Figure1) Average values for culture sensitive CRP/AGR values 69 (Ranging from 29 to 96) (Figure 3). Average CRP value is 66.85 mg/L (ranging from 46 mg/L to 94 mg/L) (Figure 2). ESR average value of 55 mm/hr(ranging from 27 mm/hr to 98 mm/hr) (Figure 1). Average values for culture negative CRP/AGR 15.22 (ranging from 8 to 44) (Figure 3). CRP average value 15.77 mg/L ranging from (11 mg/L to 23 mg/L) (Figure 2). ESR 32.77 mm/hr ranging from (27 mm/hr to 39 mm/hr) (Figure 1). For culture sensitive patients the diagnosing accuracy for in culture patients CRP is 91.75%, ESR is 69.46%, CRP/AGR 93.75%, (whereas in culture negative the threshold for diagnosing accuracy for CRP is 60%, CRP/AGR is 61%, ESR is 51% (Table 1)

Discussion

Periprosthetic joint infection (PJI) is a serious complication that can occur following total knee arthroplasty (TKA) or total hip arthroplasty (THA) and often leads to the need for joint revision surgery. The incidence of PJI in THA or TKA is estimated to be around 2.0%-2.4%. Accurate diagnosis of PJI is crucial for preserving the implanted prosthesis, resting joint function and reducing the morbidity rates. However, diagnosing PJI remains challenging due to the absence of a definitive gold standard test with absolute accuracy. In our study we aim to evaluate the diagnostic accuracy of CRP, Albumin, Globulin Albumin to globulin ratio, ESR as biomarker for PJI. Angkananard *et al.* [7] highlighted the usefulness of NLR as a predictor for infected patient outcomes. Meyer *et al.* on the other hand discovered a correlation between A/G ratio values and infection status. Additionally, Schmilovitz-Weiss *et al.* [8] reported that the A/G ratio can predict cancer patient outcomes. These findings have prompted numerous researchers to investigate the associations between GLB, NLR, A/G ratio and PJI. Yu *et al*., in their study demonstrated that NLR values were more accurate than CRO levels in the early diagnosis of PJI. Ina separate study Yu *et al* found both GLB and A/G ratio to hold promising biomarker in diagnosing PJI.

Gaertner *et al.* [9] provided evidence of anto-infeciton functions of platelets, specifically in the collection and bundling of bacterial functions. Similarly, Parvizi *et al* [10] demonstrated that PVR (platelet volume ratio) increased in patients with PJI, with diagnostic sensitivity, specificity. However, the diagnostic value of platelet count and PVR was found to bemired compared to Globulin, AGR and fibrinogen. In a multicenter cohort study conducted by Benito *et al.* [11],

they analysed 2288 cases of PJI with microbiological diagnosis. Their research revealed that staph aureus, Staph. Epidermidis, Pseudomonas aeruginosa, Enterococcus, faecalis and Propoini bacterium, acneus, in decreasing order accounted for more than 80% of PJI's. In our study, Staph epidermidis was most prevalent pathogen, followed by staphylococcus aureus. There were no significant changes in level of GLB, AGR, fibrinogen and CRP between culture positive and culture negative PJI patients. However, the diagnostic accuracies of these biomarkers were lower in culture negative PJI compare to culture positive PJI.

According to our literature review, our study demonstrates that CRP/AGR offers superior diagnostic performance for PJI when compared to traditional biomarkers such as CRP and ESR. The culture result of the pathogen is the most valuable indicator when diagnosing PJI and can assist in selecting appropriate antibiotics. However, in certain cases, the microbiological culture may yield negative results due to various factors such as microbiological, host and antibiotic interactions. Previous studies have reported that the occurrence of culture negative PJI range from 5% to 42&. We observed a significant difference in CRP, ESR, AGR between culture positive PJI subgroup and culture negative PJI group, suggesting that these biomarkers hold potential for predicting negative culture outcomes. Nonetheless, all tested biomarkers demonstrated lower diagnostic accuracies for culture negative PJI compared to culture positive PJI. Therefore, it's crucial to prioritise the diagnosis of culture negative PJI.

Limitations in our study, being a retrospective study its subject to inherent limitations associated with this study design. The exclusion of patient with auto-immune diseases introduces some bias, there is no universally accepted gold standard for diagnosing PJI. MSIS (Musculoskeletal infection society) criteria however, is considered the best diagnostic method, although they have low sensitivity for patients with low-virulence bacterial infections.

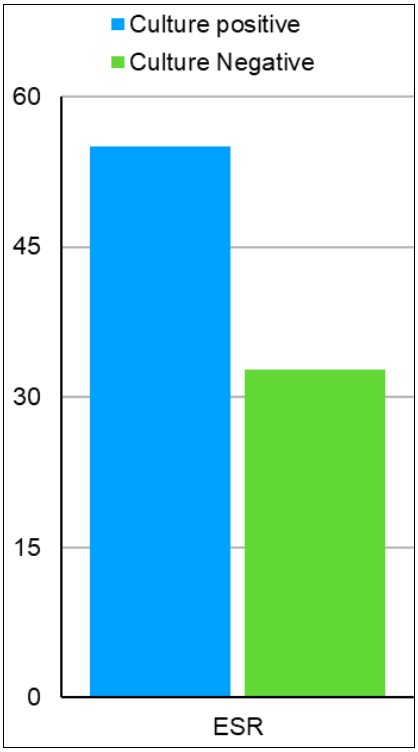

Fig 1: Mean ESR value to culture positive and negative PJI

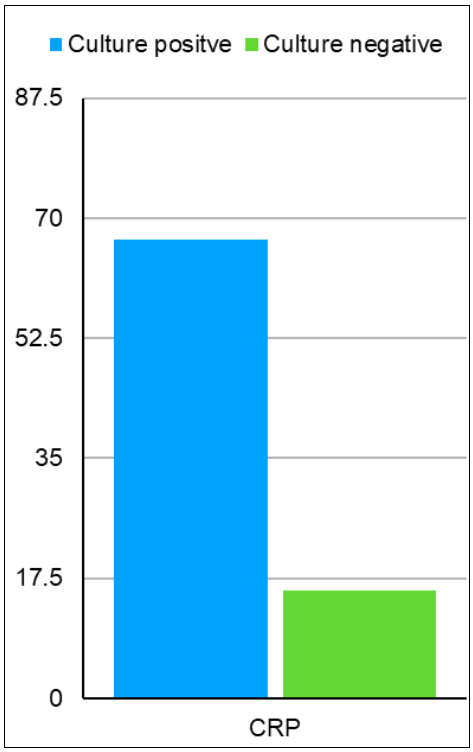

Fig 2: Mean CRP value to culture positive and negative PJI

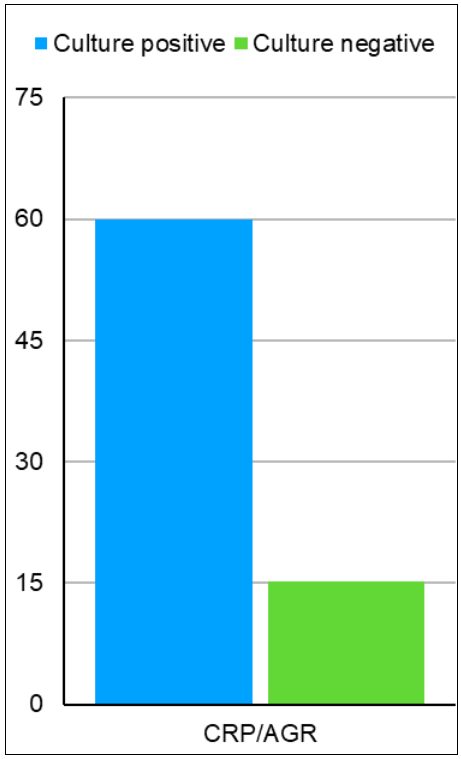

Fig 3: Mean CRP/AGR value to culture positive and negative PJI

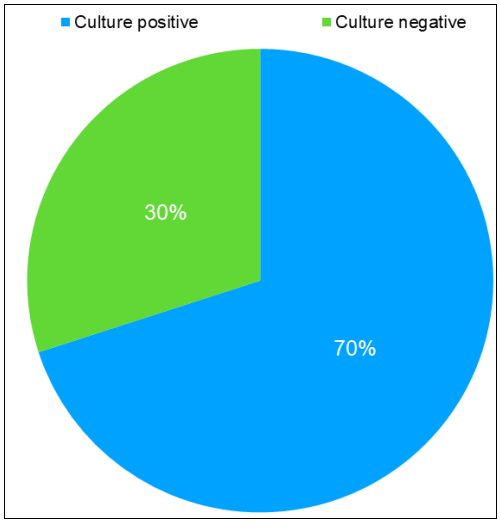

Fig 5: Culture sensitivity results

Conclusion

In conclusion, our findings indicate that the patients diagnosed with PJI (Periprosthetic joint infection) exhibited significantly elevated levels of ESR, CRP, CRP/AGR. These biomarkers show promising results for the diagnosis of PJI. However, when used alone, CRP/AGR demonstrated excellent diagnostic performance, followed by CRP and ESR with good diagnostic performance.

Declarations

Funding: None

Conflict of interest: None declared

Ethical approval: Not required

References

1. Tetreault MW, Wetters NG, Aggarwal V *et al*. The Chitranjan Ranawat Award: Should prophylactic antibiotics be withheld before revision surgery to obtain

appropriate cultures? Clin Orthop Relat Res. 2014;472:52–56. https://doi.org/10.1007/s11999-013-3016-5
2. Huotari K, Peltola M, Jamsen E. The incidence of late prosthetic joint infections: A registry-based study of 112,708 primary hip and knee replacements. Acta Orthop. 2015;86:321–325. https://doi.org/10.3109/17453674.2015.1035173
3. Gundtoft PH, Overgaard S, Schonheyder HC, *et al*. The "True" incidence of surgically treated deep prosthetic joint infection after 32,896 primary total hip arthroplasties: A prospective cohort study. Acta Orthop. 2015;86:326–334. https://doi.org/10.3109/17453674.2015.1011983
4. Beam E, Osmon D. Prosthetic joint infection update. Infect Dis Clin North Am. 2018;32:843–859. https://doi.org/10.1016/j.idc.2018.06.005
5. Kurtz SM, Lau E, Watson H, *et al*. Economic burden of periprosthetic joint infection in the United States. J Arthroplasty. 2012;27:61–65. https://doi.org/10.1016/j.arth.2012.02.022
6. Shang G, Fei Z, Xu H, *et al*. Globulin and albumin to globulin ratio precisely diagnose periprosthetic joint infection and determine the timing of second-stage reimplantation. J Orthop Surg Res. 2022;17:12. https://doi.org/10.1186/s13018-021-02899-0
7. Angkananard T, *et al*. Neutrophil Lymphocyte Ratio and Cardiovascular Disease Risk: A Systematic Review and Meta-Analysis. Biomed Res Int. 2018;2018:2703518
8. Schmilovitz-Weiss H, *et al*. Serum globulin levels in predicting the extent of hepatic fbrosis in patients with recurrent post-transplant hepatitis C Infection. Clin Transplant. 2007;21(3):391-397.
9. Gaertner F, Ahmad Z, Rosenberger G, Fan S, Nicolai L, Busch B, *et al*. Migrating platelets are Mechano-scavengers that collect and bundle bacteria. Cell. 2017;171(6):1368–82. https://doi.org/10.1016/j.cell.2017.11.001
10. Parvizi J, Jacovides C, Adeli B, Jung KA, Hozack WJ, Mark B. Coventry Award: Synovial C-reactive protein: A prospective evaluation of a molecular marker for periprosthetic knee joint infection. Clin Orthop Relat Res 2012;470:54-60.
11. Benito N, Franco M, Ribera A, Soriano A, Rodriguez-Pardo D, Sorli L, *et al*. Time trends in the aetiology of prosthetic joint infections: A multi centrecohort study. Clin Microbiol Infect. 2016;22(8):731–732.

How to Cite This Article
A Krishnan, R Sujith Kumar, M Rakesh, Nitheesh, Y Subash. The significance of C-reactive protein (CRP)/albumin to globulin ratio (AGR) test as a valuable diagnostic tool for periprosthetic joint infection, a single centre retrospective study. International Journal of Orthopaedics Sciences. 2023;9(3):95-98.