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Research Article

Analysis of Complete Blood Count-Derived Inflammatory Biomarkers in Patients Underwent Total Knee Arthroplasty: A Retrospective Study

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Abstract

Background: Pain, bleeding, and anemia are frequent complications of total knee arthroplasty (TKA). ***Objective***: To analyze CBC-derived biomarkers in patients who underwent TKA to predict postoperative complications. ***Methods***: This retrospective study evaluated neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR), monocyte-to-lymphocyte ratio (MLR), platelet-monocyte ratio (PMR), hemoglobin-platelet ratio (HPR), hemoglobin-lymphocyte ratio (HLR). ***Results***: A total of 99 patients' records were investigated; their average age was 64.57±8.4. Significant differences in NLR and HLR were noted between the patients who needed <5 days and ≥ 5 days of opioid analgesic (OPA). Hence, the patients with higher NLR and HLR needed longer OPA (≥ 5 days) than the patients with lower NLR and HLR. Likewise, NLR, MLR, PLR, and HLR were significantly higher in the patients who needed longer non-OPA (>20 days). Additionally, the duration of non-OPA usage had a significantly high positive correlation (r= 0.967, p<0.0001) with NLR, and a moderate positive correlation with PLR (r=0.535, p<0.0001) and HLR (r= 0.6216, p<0.0001). On the other hand, the pre-operative NLR, MLR, PLR, and HLR of the patients who needed blood transfusion ≥ 1.0 pint (0.47 L) was significantly higher than those who did not need blood transfusion. Blood transfusion showed a significantly positive correlation (r=0.8419, p<0.0001) with NLR; also, there was a moderate positive correlation with PLR (r=0.5257, p<0.0001) and HLR (r=0.5841, p<0.0001). ***Conclusions***: CBC-derived biomarkers can be utilized for predicting the duration and need for postoperative analgesics and blood transfusion.

Keywords: Biomarkers, Blood transfusion, Complete blood count, Correlation, Post-operative analgesic, Total knee arthroplasty.

تحليل المؤشرات الحيوية الالتهابية المشتقة من تعداد الدم الكامل لدى المرضى الذين خضعوا لتقويم مفاصل الركبة بالكامل: دراسة استعادية

الخلاصة

الخلفية: الالم و النزف الدموي و فقر الدم هي من المضاعفات الشائعة لجراحة تبديل مفصل الركبة. **الاهداف**: تناول البحث تحليل نتائج فحص المؤشرات الحيوية المشتقة من تعداد الدم الكامل قبل العملية في المرضى اللذين قاموا بجراحة تبديل مفصل الركبة, وذلك بهدف التنبؤ بالمضاعفات بعد هذه العملية الجراحية.**الطرائق**: هذه الدراسة من النوع الاستيعادي حيث تم حساب نسبة خلايا العدلات الى الخلايا الليمفاوية(NLR),نسبة الصفيحات الدموية الى الخلايا الليمفاوية(PLR), نسبة الكريات البيضاء احادية النواة الى الخلايا اللمفاوية(MLR), نسبة الصفيحات الدموية الى الكريات البيض الاحادية النواة(PMR),نسبة الهيموكلوبين الى الصفيحات الدموية(HPR), ونسبة هيموكلوبين الى الخلايا الليمفاوية(HLR).**النتائج**: لقد تم تسجيل نتائج 99 مريض, كان معدل العمر 64.57.كان هناك اختلافات كثيرة و واضحة في (NLR) و (HLR) لدى المرضى اللذين كانوا يحتاجون استخدام دواء المسكن الالام الافيوني اقل من 5 واطول من5 أيام p =0.0469 (and 0.0476). لذلك المرضى اللذين كان لديهم نسبة اعلى ل (NLR) و (HLR) كانوا يحتاجون استخدام المسكن الالام الافيوني لمدة أطول من 5 ايام مقارنة بالمرضى لديهم نسبة اقل من كل من (NLR)و (HLR).كذلك نسبة كل من (PLR),(NLR),(MLR) و (HLR) (p=0.0001, 0.0163, 0.0001, 0.0001) على التوالي كان اكثر بشكل ملحوظ في المرضى اللذين كانوا يحتاجون الادوية المسكنة الغير الافيونية لمدة اطول من 20 يوم.اضافة لهذا هناك علاقة خطية موجبة قوية وملحوظة بين المدة المحتاجة لاستخدام الادوية المسكنة الغير الافيونية و (NLR),(PLR) و (HLR). من ناحية اخرى المرضى اللذين كانوا يحتاجون عملية نقل الدم (بطل 1≥)كان لديهم نسبة اعلى من كل من (PLR),(MLR),(NLR) و (HLR) (p=1, 0.0179, < 0.001) على التوالي مقارنة مع المرضى اللذين لم يكونوا بحاجة الى عملية نقل الدم. ونسبة نقل الدم في هذا البحث اظهرت علاقة خطية موجبة قوية مع NLR (p- r=0.8419 value<0.0001) وعلاقة خطية موجبة معتدلة مع (PLR). **الأستنتاجات:** يمكن الاستفادة من تحليل نتائج فحص المؤشرات الحيوية المشتقة من تعداد الدم الكامل, للتنبؤ باستخدام الادوية المسكنة بعد العملية و مدة استخدام هذه الادوية, و كذلك الاحتياج الى عملية نقل الدم.

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INTRODUCTION

Pain is the primary symptom of osteoarthritis (OA) and profoundly affects the quality of life of the patients [1]. Total knee arthroplasty (TKA) is the final stage of treatment for severe OA [2]. It is one of the most effective orthopedic procedures that provide significant pain relief, functional improvement, and enhanced patient quality of life [3]. Although TKA demonstrates effective clinical outcomes, post-operative complications such as pain, bleeding, and infection remain significant issues of this approach as pain and inflammation are severely implicated in the recovery process and long-term functional performance [4]. Emerging human studies have highlighted differences in proinflammatory mediators between OA patients and healthy individuals. Preclinical evidence indicates that proinflammatory mediators can sensitize both peripheral

and central nerves, potentially exacerbating clinical pain [5]. A recent study has also linked preoperative inflammatory profiles to the onset of chronic post-operative pain following TKA [6,7]. Currently, there is an advanced interest in exploiting the complete blood count (CBC) laboratory test, which is a non-expensive, reliable, easily obtained investigation into the diagnosis and prognosis of various diseases and the risk of mortality [8–10]. This could be monitored via deviation of several biomarkers such as the neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR), monocyte-to-lymphocyte ratio (MLR), platelet-monocyte ratio (PMR), hemoglobin-platelet ratio (HPR), hemoglobin-lymphocyte ratio (HLR), and lymphocyte-monocyte ratio (LMR) [11,12]. The CBC-derived inflammatory biomarkers have been documented as possessing potential prognostic and predictive value in the emergence of complications such as infection, delayed wound healing, and extended duration of hospitalization [13]. In many chronic inflammatory diseases, the use of NLR, PLR, and MLR is widely accepted. For instance, the use of these biomarkers was associated with some inflammatory cases, including irritable bowel syndrome [14,15], liver fibrosis [16], and thyroiditis [17]. The use of routine inflammatory biomarkers in the evaluation of the periprosthetic joint infection after TKA in patients with osteoarthritis has also been investigated [18,19]. Additionally, in several studies, elevated NLR and PLR were demonstrated as valuable biomarkers for predicting periprosthetic joint infection following TKA [8,20] and post-operative wound infection [21]. Moreover, a preoperative increase in NLR, PLR, MLR, and systemic immune inflammation index increases the adverse events and prolongs hospital stay in both total hip and knee arthroplasty [22]. Despite all these investigations, the application of the CBC-derived inflammatory biomarkers for predicting blood transfusion and post-operative medication interventions in patients who underwent TKA remains inadequately explored. Therefore, this study aimed to analyze the role of pre-operative CBC-derived biomarkers in predicting post-operative pain and blood loss in patients who underwent TKA. This was performed by exploring the correlation between pre-operative CBC-derived inflammatory biomarkers and the duration of postoperative opioids (OPA), non-opioid analgesics (non-OPA), and blood transfusion. The goal is to provide insight for developing an algorithm to predict and optimize medication regimens as well as blood management strategies.

METHODS

Study design and setting

This was a retrospective study conducted at the orthopedic department of Zhyan Private Hospital and included patients who underwent TKA between 2022 and 2024. For data collection, electronic medical records, or files of eligible TKA patients, were reviewed to extract pre-operative CBC-derived inflammatory biomarkers, including neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR), monocyte-to-lymphocyte ratio (MLR), platelet-monocyte ratio (PMR), hemoglobin-platelet ratio (HPR), and hemoglobin-lymphocyte ratio (HLR). Other inflammatory markers such as C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) have also been reported. On the other hand, the duration of postoperative opioid and non-opioid analgesics (OPA and non-OPA) and frequency of blood transfusion were recorded.

Inclusion criteria

We evaluated the medical records of the following patients: those aged 18 and above, with preoperative CBC profiles and documented postoperative analgesics and frequency of blood transfusion. Patients indicated for TKA including severe OA and other inflammatory diseases such as rheumatoid arthritis.

Exclusion criteria

We excluded the medical records of the following patients: those with incomplete CBC-component profiles, non-inflammatory joint diseases such as post-traumatic arthritis or avascular necrosis as the primary indication for TKA, patients with conditions such as gout, which are metabolic rather than inflammatory, patients with knee deformities due to congenital conditions or trauma, and patients with severe comorbid conditions (e.g., severe cardiovascular disease, uncontrolled diabetes, advanced renal disease) that significantly increase the risk of surgery or affect postoperative complications.

Outcome measurements

Basic demographic data, including age, sex, degree of OA, duration of post-operative analgesics (OPA and non-OPA), and number and quantity of blood transfused postoperatively, were obtained from the patient record system of the hospital. The CBC-derived inflammatory biomarkers such as NLR, PLR, MLR, PMR, HPR, and HLR were evaluated based on the previous studies [8,23,24]. The predictive value of CBC-derived inflammatory biomarkers (NLR, PLR, PMR, MLR, HPR, and HLR) in patients who underwent TKA was assessed and analyzed in the enrolled patients. The patients were subdivided into two subgroups in terms of duration and types of postoperative analgesic administration and frequency or number of blood transfusions. The CBC-derived parameters were compared among the two subgroups. Additionally, the correlations of these parameters were calculated with these postoperative variables.

Ethical considerations

This project was approved by the Ethics and Research Registration Committee of the College of Pharmacy, University of Sulaimani, with a registration number (PH138-24 on 28.11.2024). Formal consent was not required for this retrospective study, and all data was kept confidential.

Statistical analysis

All statistical analyses were performed using GraphPad Prism Version 10.4.1 (2024) LLC. US. For continuous variables, the data were expressed as mean ± standard deviation (SD), and categorical variables were statistically described as numbers (n) and percentages (%). An unpaired t-test was applied to determine the differences between the CBC parameters among the subgroups receiving OPA and non-OPA. *p*-value <0.05 was considered statistically significant. The correlations between pre-operative CBC-derived biomarkers and the duration of postoperative analgesics administration were evaluated using Pearson's correlation test.

RESULTS

A total of 99 patients' records met the inclusion criteria of this retrospective study. The demographic characteristics, including age, sex, degrees of OA, medication history, duration of post-operative opioid analgesic (OPA) and non-opioid analgesic (non-OPA) regimens, frequency of blood transfusion, and postoperative antibiotic protocol, are summarized in Table 1.

Table 1: Demographic characteristics of the patients underwent total knee arthroplasty in the study (n=99)

Variables	Results
Age (year)	64.57±8.4
Sex	
Female	81(81.8)
Male	18(18.2)
Degree of OA	
3	49(49.5)
4	50(50.5)
Duration of OPA and non-OPA	
Patients used postoperative OPA for <5 days	52(52.5)
Patients used postoperative OPA for ≥5 days	47(47.5)
Patients used postoperative non-OPA for ≤ 20 days	58(58.6)
Patients used postoperative non-OPA for > 20 days	41(41.4)
Frequency of postoperative blood transfusion (pint)	
0	50(50.5)
1-2	39(39.4)
3-4	10(10.1)
Duration of antibiotic (day)	
5	73(73.7)
7	26(26.3)

Data presented as mean±SD, number, and percentage. OA: Osteoarthritis, OPA: Opioid analgesic.

The mean age was 64.57±8.4, with a higher number of females [81 (81.8%)] than males [18 (18.2%)]. The number of patients who used postoperative OPA for <5 days and ≥5 days was 52 (52.5%) and 47 (47.5%), respectively. Patients used postoperative non-OPA for ≤ 20 days and > 20 days were 58 (58.6) and 41 (41.4), respectively. The number of patients who received post-operative blood ≥1 pint was 49 (49.5%). The components of the complete blood count (CBC) of all included data, which are expressed as mean±SD, are shown in Table 2.

Table 2: The component of complete blood count and derived inflammatory biomarkers of the patients underwent total knee arthroplasty (n=99)

Parameters	Result
White blood cells (10^9/L)	7.88±2.12
Monocytes, Basophils, Eosinophils (mixed cells)	6.48±3.47
Lymphocytes %	32.72±8.65
Neutrophils (10^9/L)	4.91±1.91
Neutrophils %	61.21±9.00
Red blood cells (10^{12}/L)	4.63±0.48
Hb g/dl	12.99±1.30
Platelets (10^9/L)	254.28±69.81
Monocytes %	4.36±3.26
Monocytes absolute 10^9	340.2±255.1
NLR	2.203±1.57
PLR	109.44±45.18
PMR	1.19±0.82
MLR	0.15±0.13
HPR	0.05±0.01
HLR	5.65±2.16

Data presented as mean±SD. CBC: complete blood count, Hb: Hemoglobin, NLR: Neutrophil to lymphocyte ratio, PLR: Platelet to lymphocyte ratio, PMR: Platelet to monocyte ratio, MLR: Monocyte-to-lymphocyte ratio, HPR: Hemoglobin to platelet ratio, HLR: Hemoglobin to lymphocyte ratio.

In the current study, the CBC components of all the patients were analyzed based on the duration of postoperative analgesics and frequency of blood transfusion. Comparative statistical analysis was performed to explore the association between the CBC-derived inflammatory biomarkers and the length of postoperative OPA and non-OPA administration. Significant differences in terms of NLR and HLR were noted between the patients who needed <5 days and ≥ 5 days OPA (p = 0.0469 and 0.0476, respectively). Hence, the patients with higher NLR and HLR needed longer OPA (≥ 5 days) than the patients with lower NLR and HLR who needed OPA < 5 days. For all the other CBC-derived biomarkers, HPR, MLR, PMR, and PLR, there were no significant differences (p = 0.0595, 0.2199, 0.4859, and 0.1329, respectively) between the two subgroups, i.e., receiving < 5 days and ≥ 5 days OPA (Figure 1). The pre-operative blood levels of ESR and CRP in patients who needed post-operative OPA for < 5 days and ≥ 5 days were also analyzed statistically. It has been found that there were no significant differences in blood levels of ESR among both subgroups (p >0.05). However, CRP blood level was significantly higher in patients who were receiving post-operative OPA for <5 days. Hence, the patients with higher CRP needed more than 5 days OPA (Figure 2).

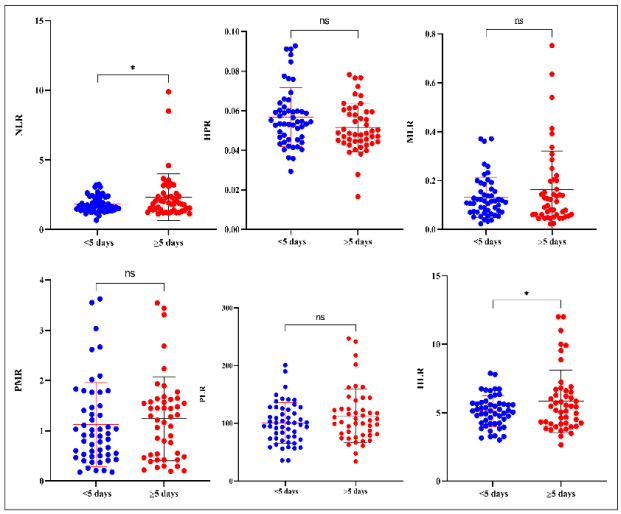

Figure 1: Preoperative CBC-derived biomarkers and duration of postoperative OPA. An unpaired t-test was applied to determine the differences between the CBC-parameters among the subgroups receiving <5 days OPA and ≥ 5 days OPA. $p<0.05$ was considered statistically significant. NLR: Neutrophil to lymphocyte ratio, HPR: Hemoglobin to platelet ratio, MLR: Monocyte-to-lymphocyte ratio, PMR: Platelet to monocyte ratio, PLR: Platelet to lymphocyte ratio, HLR: Hemoglobin to lymphocyte ratio, ns: non-significant.

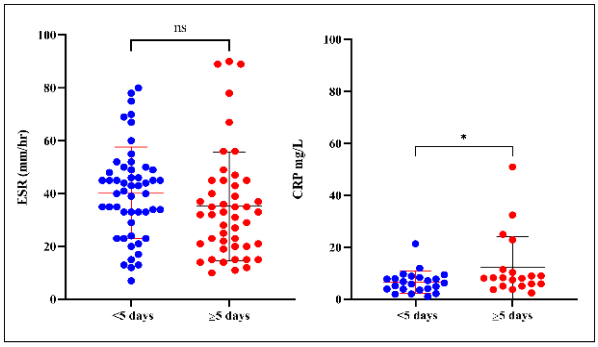

Figure 2: The preoperative blood level of ESR and CRP in patients needed postoperative OPA for <5 days and ≥ 5 days. An unpaired t-test was applied to determine the differences between ESR and CRP among the subgroups receiving <5 days OPA and ≥ 5 days opioid analgesic. $p<0.05$ was considered statistically significant. CRP: C-reactive protein. ESR: erythrocyte sedimentation rate, OPA: Opioid analgesic, ns: non-significant.

A comparative statistical analysis was performed to explore the relation of CBC-derived biomarkers as a predictor for post-operative administration of non-OPA. The patients' data were categorized into two subgroups: postoperative non-OPA administration for ≤ 20 days and > 20 days. It has been found that the patients with higher preoperative CBC-derived biomarkers needed longer postoperative non-OPA, as shown in Figure 3. In particular, NLR, MLR, PLR, and HLR were significantly higher (p= 0.0001, 0.0163, 0.0001, and 0.0001, respectively) in patients who needed longer non-OPA (> 20 days). For the other CBC biomarkers, HPR and PMR, there were no significant differences (p= 0.0594 and 0.4939, respectively) between the two subgroups: those who received non-OPA after surgery for less than 20 days and those who received it for more than 20 days (Figure 3).

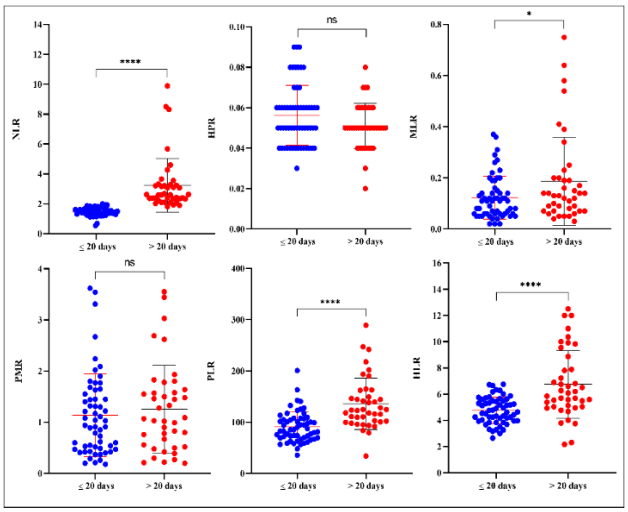

Figure 3: Preoperative CBC-derived biomarkers and duration of post-operative non-OPA. An unpaired t-test was applied to determine the differences between the CBC-parameters among the subgroups receiving postoperative non-OPA for ≤ 20 days and >20 days. $p<0.05$ was considered statistically significant. CBC-complete blood count, NLR: Neutrophil to lymphocyte ratio, HPR: Hemoglobin to platelet ratio, MLR: Monocyte-to-lymphocyte ratio, PMR: Platelet to monocyte ratio, PLR: Platelet to lymphocyte ratio, HLR: Hemoglobin to lymphocyte ratio, non-OPA: Non-opioid analgesic, ns: non-significant.

There were no significant differences in ESR among both subgroups. However, patients with a high significant level of CRP ($p<0.05$) needed > 20 days of non-OPA (Figure 4).

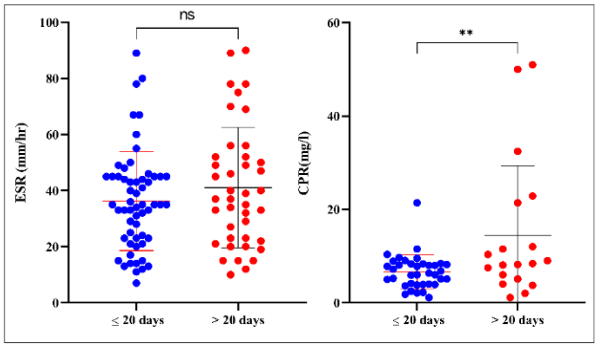

Figure 4: Preoperative blood level of ESR and CRP in patients needed postoperative non-OPA for ≤ 20 days and >20 days. An unpaired t-test was applied to determine the differences between ESR and CRP among the subgroups receiving non-OPA for ≤ 20 days and >20 days. $p<0.05$ was considered statistically significant. CRP: C-reactive protein, ESR: erythrocyte sedimentation rate, non-OPA: non-opioid analgesic, ns: non-significant.

The correlation between the duration of postoperative opioid analgesic administration versus pre-operative CBC-derived biomarkers, ESR, and CRP blood level was calculated using Pearson's test. There is a non-significant correlation between the duration of OPA usage and these biomarkers, as shown in Table 3. The correlations between preoperative CBC-derived biomarkers, ESR, and CRP blood level and the duration of post-operative non-opioid analgesic administration were calculated using Pearson's test as shown in Table 4.

Table 3: Correlation between duration of postoperative opioid analgesic administration versus preoperative CBC-derived biomarkers, ESR, and CRP blood level

Pearson correlation	Duration (day)							
	OPA *vs.* NLR	OPA *vs.* PLR	OPA *vs.* PMR	OPA *vs.* MLR	OPA *vs.* HPR	OPA *vs.* HLR	OPA *vs.* ESR (mm/hr)	OPA *vs.* CRP (mg/l)
r	0.146	0.142	0.117	0.06	-0.183	0.067	-0.101	0.077
95% CI	-0.053-0.334	-0.057-0.33	-0.082-0.308	-0.14-0.254	-0.367-0.015	-0.132-0.261	-0.293-0.098	-0.222-0.362
R^2	0.021	0.020	0.014	0.004	0.034	0.00449	0.010	0.006
p-value	0.149	0.161	0.248	0.558	0.07	0.51	0.32	0.617

The correlations between preoperative CBC-derived biomarkers, ESR, and CRP blood level and duration of postoperative opioid analgesic administration were calculated using Pearson's test. r: Pearson's rank correlation coefficient, CBC-complete blood count, NLR: Neutrophil to lymphocyte ratio, PLR: Platelet to lymphocyte ratio, PMR: Platelet to monocyte ratio, MLR: Monocyte-to-lymphocyte ratio, HPR: Hemoglobin to platelet ratio, HLR: Hemoglobin to lymphocyte ratio. OPA: Opioid analgesic. $p<0.05$ is considered statistically significant.

Table 4: Correlation between preoperative CBC-derived biomarkers, ESR and CRP blood level, and duration of postoperative non-opioid analgesic administration (n=99)

Pearson correlation	Duration (day)							
	non-OPA *vs.* NLR	non-OPA *vs.* PLR	non-OPA *vs.* PMR	non-OPA *vs.* MLR	non-OPA *vs.* HPR	non-OPA *vs.* HLR	non-OPA *vs.* ESR (mm/hr)	non-OPA *vs.* CRP (mg/l)
r	0.9671	0.5345	0.01672	0.3369	-0.02714	0.6216	0.2137	0.08273
95% CI	0.951-0.978	0.377-0.662	-0.181-0.213	0.15-0.501	-0.223-0.171	0.484-0.73	0.017-0.394	-0.216-0.367
p-value	<0.0001	<0.0001	0.8696	0.0006	0.7897	<0.0001	0.0337	0.589

The correlations between preoperative CBC-derived biomarkers, ESR, and CRP blood level and duration of postoperative non-opioid analgesic administration were calculated using Pearson's test. r: Pearson's rank correlation coefficient, CBC-complete blood count, NLR: Neutrophil to lymphocyte ratio, PLR: Platelet to lymphocyte ratio, PMR: Platelet to monocyte ratio, MLR: Monocyte-to-lymphocyte ratio, HPR: Hemoglobin to platelet ratio, HLR: Hemoglobin to lymphocyte ratio. non-OPA: Non-opioid analgesic. $p<0.05$ is considered statistically significant.

The duration of non-OPA usage had a strong positive linear correlation (r= 0.967, $p<0.0001$) with NLR; also, there was a moderate positive linear correlation with PLR (r= 0.535, $p<0.0001$) and HLR (r= 0.622, $p<0.0001$), a weak positive linear correlation with MLR (r= 0.337, p= 0.0006), and ESR (0.2137, p= 0.0337). While there was no significant correlation with PMR% (r= 0.017), HPR% (r= -0.027), and CRP (r= 0.083). Furthermore, the post-operative blood transfusion has been analyzed. It has been found that the pre-operative NLR, MLR, PLR, and HLR of the patients who needed blood transfusion ≥1 pint(s) were significantly higher than those who did not need blood transfusion (p-value was < 0.001, 0.0179, < 0.001, < 0.001, respectively) as shown in Figure 5.

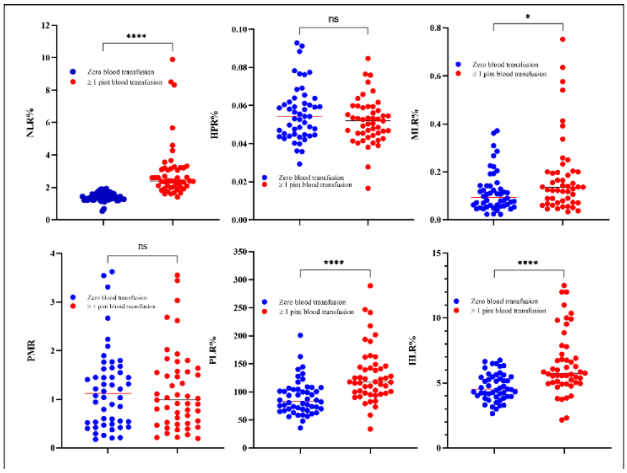

Figure 5. Preoperative CBC-derived biomarkers and frequency of blood transfusion. An unpaired t-test was applied to determine the differences between the CBC-parameters among the subgroups who needed blood transfusion ≥1 pint(s) and those who did not. $p<0.05$ was considered as statistically significant. CBC-complete blood count, NLR: Neutrophil to lymphocyte ratio, HPR: Hemoglobin to platelet ratio, MLR: Monocyte-to-lymphocyte ratio, PMR: Platelet to monocyte ratio, PLR: Platelet to lymphocyte ratio, HLR: Hemoglobin to lymphocyte ratio, ns: non-significant.

Meanwhile, the values of pre-operative HPR and PMR were similar with non-significant differences among the patients who post-operatively received blood and those who did not (p= 0.1318 and 0.8814, respectively). Furthermore, the correlations between post-operative blood transfusion versus pre-operative CBC-derived biomarkers were calculated using Pearson's test (Table 5). Blood transfusion showed a significant strong positive linear correlation (r= 0.8419, $p<0.0001$) with NLR; also, there was a moderate positive linear correlation with PLR (r= 0.5257, $p<0.0001$) and HLR (r= 0.5841, $p<0.0001$), and a weak positive linear correlation with MLR (r= 0.2571, p= 0.0102), while there was no significant correlation between blood transfusion with PMR% (r= 0.02801, p= 0.7832) and HPR% (r= -0.04105, p= 0.6866), as shown in Table 5.

DISCUSSION

The current analytical study was performed to explore the differences in the level of pre-operative CBC-derived inflammatory biomarkers and to correlate these data to the patient's need for post-operative analgesics and blood transfusion. The study found that the CBC-derived biomarkers, especially NLR, PLR, MLR, and HLR, have a predictive value in the assumption of TKA complications, including perioperative bleeding and postoperative intensity and duration of pain. The concept of utilizing CBC-derived biomarkers as diagnostic, prognostic, predictive, and screening tools has been studied for several decades; however, their broader applications in clinical fields and research have emerged recently [9,25]. In the hemato-oncology field, these biomarkers play a crucial role in the screening and diagnosis of malignancies [26].

Table 5: Correlations between preoperative CBC-derived inflammatory biomarkers and postoperative blood transfusion and (n=99)

Pearson correlation	Blood transfusion vs. pre-operative CBC-derived biomarkers					
	NLR	PLR	PMR	MLR	HPR	HLR
r	0.8419	0.5257	0.02801	0.2571	-0.04105	0.5841
95% CI	0.773-0.891	0.366-0.655	-0.17-0.224	0.063-0.433	-0.237-0.158	0.437-0.701
p-value	<0.0001	<0.0001	0.7832	0.0102	0.6866	<0.0001

The correlations between pre-operative CBC-derived biomarkers and blood transfusion were calculated using Pearson's test. r: Pearson's correlation coefficient, CBC-complete blood count, NLR: Neutrophil to lymphocyte ratio, PLR: Platelet to lymphocyte ratio, PMR: Platelet to monocyte ratio, MLR: Monocyte-to-lymphocyte ratio, HPR: Hemoglobin to platelet ratio, HLR: Hemoglobin to lymphocyte ratio. non-OPA: Non-opioid analgesic, ns: non-significant. $p<0.05$ is considered statistically significant.

In a clinical study, the laboratory findings of patients with hematological malignancies indicated that the absolute neutrophils, lymphocytes, monocytes, platelets counts, and total white blood cells were similar between the patients and control individuals who performed a routine laboratory test; however, the CBC-derived inflammatory biomarkers such as NLR, PLR, PMR, HLR, SII, and dNLR were markedly elevated in patients with blood malignancies compared to the controls with no cancer [26]. In the current study, the correlation between the duration of post-operative OPA and non-OPA administration versus ESR and CRP blood levels was also investigated. It has been found that there was a weak positive correlation with ESR and no significant correlation with CRP; this result aligns with the findings of a study conducted by Godoy et al. which clarifies that the preoperative monitoring of ESR and CRP was not recommended, and the study concluded that the routine preoperative CRP and ESR analysis is not necessary for elective TKA, as these biomarkers do not predict postoperative complications [27]. These biomarkers have played an important role in detecting and following up on various diseases for decades; they were frequently used pre-operatively in patients undergoing TKA. Despite their high sensitivity and moderate specificity for infection, studies in recent years have not identified a significant correlation between the preoperative elevation of these inflammatory biomarkers and the occurrence of perioperative infections. Consequently, the routine preoperative use of these biomarkers is not recommended [28,29]. However, a significant correlation was obtained between the duration of post-operative non-OPA usage and most CBC-derived biomarkers. This finding shows that these novel CBC biomarkers are superior to the routine inflammatory biomarkers in determining the postoperative medication regimen for pain. Consistent with the current findings, many studies demonstrated the predictive and prognostic value of NLR, PLR, MLR, and other CBC-derived biomarkers in various diseases. Anticipating the prognosis of rheumatological diseases such as rheumatoid arthritis, systemic lupus erythematosus, and ankylosing spondylitis, and the disease's course prediction was concluded by a clinical study conducted on 250 patients with rheumatological diseases by Taha et al. [12]. Additionally, predicting diabetic neuropathy and severity of proteinuria in patients with type 2 diabetes mellitus was exhibited by investigating these novel biomarkers in two other studies [30,31]. The mechanism by which these inflammatory biomarkers aid in the anticipation of severity of pain and duration of analgesic usage can be explained by the presence of a complex relationship between inflammation and pain in osteoarthritis [32]. Although pain in OA is multifactorial, numerous studies associated preoperative inflammatory profiles with the development of chronic postoperative pain following TKA [6,7]. Since current treatments are frequently inadequate to provide sufficient relief of pain, addressing inflammation via analyzing these CBC-inflammatory biomarkers continues to be a central strategy in optimizing analgesics in managing OA pain. In another part of the analysis, the prediction of blood transfusion by exploring pre-operative CBC-derived biomarkers has been observed. It has been found that the pre-operative NLR, MLR, PLR, and HLR of the patients who required ≥1 pint(s) of blood were significantly higher than those who did not need blood transfusion. Furthermore, blood transfusion exhibited a significant positive linear correlation with NLR and a moderate positive linear correlation with PLR and HLR. No comparative study has been found on the role of CBC-derived biomarkers in the prediction of blood transfusion rate in patients who underwent surgical procedures. However, in patients with acute heart disease requiring blood transfusion, hematological biomarkers can help in identifying an elevated mortality risk, as a lower platelet-to-neutrophil ratio (PNR) has been linked to higher mortality rates. Additionally, increased red cell distribution width (RDW) and NLR were associated with greater short-term and long-term mortality, respectively [33]. This study has several limitations that should be considered. First, the design of the study was retrospective, and certain biases, such as participant selection and incomplete data, could not be avoided. Second, the sample size is insufficient for finding the correlation between different variables. Third, the results were from a single hospital, which limits the generalization of the findings to broader populations, as patient demographics and treatment protocols may differ from those in other hospitals. Finally, the current study has not emphasized the role of CBC-derived biomarkers on antibiotic usage, as the hospital has had a standard protocol for the optimization of antibiotic administration. In this study, the analysis and assessment of the inflammatory biomarkers derived from CBC can offer a crucial understanding of a patient's systemic inflammation and immune response. This assists in the prediction of postoperative complications such as infection, delayed healing of the

wounds, bleeding, and coagulopathy. Additionally, in clinical practice, this approach helps the optimization of antibiotic usage.

Conclusion

CBC-derived biomarkers can be utilized for predicting the duration and need for postoperative analgesics and blood transfusion. Further study is recommended to investigate the analysis of these biomarkers in other surgical operations to optimize the pre-, peri-, and post-medications and anticipate the complications.

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Conflict of interests

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Data sharing statement

Supplementary data can be shared with the corresponding author upon reasonable request.

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