

Studies on Platelets/Lymphocyte Ratio in PubMed Database; 13-Year Analysis

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Abstract

Background: Platelets/Lymphocyte Ratio (PLR) has been investigated not only in hematological diseases but also in clinical conditions involving almost all organs and systems including inflammatory, neoplastic, and cardiovascular diseases.

Objectives: This study was planned to perform an analysis of the studies on PLR through the PubMed database, to measure the impact of the relevant studies on the diagnosis of diseases.

Methods: This analysis was performed on 16.01.2021 by searching with the word group "platelet lymphocyte ratio", "platelet lymphocyte ratio" in the PubMed database.

Results: The study included 723 articles, of which 580 (80.2%) were retrospective. It was determined that 420 (58.1%) of the studies were conducted by a single clinical department, 55.6% (n = 402) were indexed in SCI/SCI-E index, 56.7% (n = 410) were Open Access, and 58.8% (n = 425) had significant results related to the clinical condition studied. Most publications were from Turkey (n = 239, 33.1%), China (n = 211, 29.2%), and Japan (n = 55, 7.6%).

Conclusion: The majority of the analyzed studies were retrospective, and were SCI/SCI-E indexed. Their role in malignancy diagnoses was evaluated the most. A total of 59 different clinical conditions were evaluated and "platelet lymphocyte ratio" was found useful in the diagnosis of relevant clinical conditions in 58.8% of the studies. PLR is a value that is significantly associated with the diagnosis and prognosis of many diseases and can be obtained by a simple calculation from a complete blood count.

Keywords: Platelet Count, Lymphocytes, PubMed

1. Background

It is known that blood parameters and the ratios of these parameters with each other show changes during the course of diseases.^{1,2} Platelets/Lymphocyte Ratio (PLR), which can be easily calculated by Complete Blood Count (CBC), draws attention as a ratio used especially in the evaluation of inflammatory processes and immunological responses. PLR has been investigated not only in hematological diseases but also in clinical conditions involving almost all organs and systems including inflammatory, neoplastic and cardiovascular diseases.^{1,3,4}

Platelets are discoid-shaped small anuclear cell fragments originating from megakaryocyte stasis, with a diameter of 2-5 µm, a thickness of 0.5 µm and an average cell volume of 6-10 fL. Their number varies between 150 and 400 10⁹/L in healthy adults. In the past, platelets were named as cellular dust and it is known that they play important roles in hemostasis, wound healing, angiogenesis, inflammation and innate immune processes.^{5,6} Lymphocyte is a type of leukocyte (white blood cell). They constitute approximately half of the leukocytes circulating in the

blood. They are produced from pluripotential stem cells (hemocytoblast). An ordinary human body contains an average of 1012 lymphoid cells and lymphoid tissue constitutes 2% of the total body weight. Furthermore, 20-40% of leucocytes are lymphocytes. The normal value for lymphocytes is (1-5)×10⁹ per liter of blood. Lymphocytosis occurs especially in response to viral infections (chronic infections such as EBV, CMV, HIV, TB, and toxoplasmosis). It is also seen in Chronic Lymphocytic Leukemia (CLL) and some lymphoma diseases.^{7,8}

It has been shown that PLR can play a potential role in the diagnosis and treatment of various diseases such as preeclampsia, Glioblastoma, coronary artery calcification, erectile dysfunction, Peyronie's disease, pneumonia, deep venous thrombosis, determining activity in inflammatory bowel disease.⁹⁻¹⁶ However, there is a need for a clear understanding of the implications and limitations of previous studies on this topic.

2. Objectives

The present study aims to provide a comprehensive

analysis of research on PLR. We also aim to highlight Turkey's contribution to scientific research at the national level by examining its contributions in this field. In this context, the scientific publications obtained through literature searches on the PubMed database were evaluated and the descriptive characteristics and results of the studies containing the key concepts of this study were discussed.

3. Methods

All data collected for this study were obtained from the PubMed database. The information retrieved is publicly available and accessible to everyone. Ethics approval was not required for this study. The authors declare that human rights were respected in accordance with the Declaration of Helsinki.

3.1. Procedure and Study Protocol

This bibliometric analysis was performed on 16.01.2021 by searching with the word group "platelet lymphocyte ratio", "platelet lymphocyte ratio" in the PubMed database created within the National Library of Medicine by accessing from Düzce University. A total of 840 original articles (829 of which belong to the last decade) were identified through a 13-year search period from 2008 to 2020. Repeated results were excluded. Non-English articles whose full text could not be accessed were excluded from the study. The type (retrospective-prospective), WOS indexes (SCI/E, AHCI, ESCI, SSCI, Other), subject areas, Open Access information, number of authors and number of citations were analyzed. The abstracts and/or full texts of all articles were analyzed and

the number of cases included in the studies, whether significant results were obtained and "new study proposal" information in the suggestions section were evaluated.

3.2. Statistical Analysis

The conformity of the data to normal distribution was analyzed by using the Shapiro-Wilk test. Kruskal-Wallis test and Mann Whitney U test with Bonferroni correction were used as post hoc tests for the comparison of non-normally distributed characteristics in more than two independent groups. The relationships of categorical variables were analyzed by Pearson and Exact Chi-square test. As descriptive statistics, median for numerical variables, IQR (interquartile range Q3-Q1) including Q3 (quartile 3) and Q1 (quartile 1), and number and % values for categorical variables were given. SPSS Windows version 24.0 package program was used for statistical analyses and $P < 0.05$ was considered statistically significant.

4. Results

The study included 723 articles, of which 580 (80.2%) were retrospective and 143 (19.8%) prospective. It was determined that 420 (58.1%) of the studies were conducted by a single clinical department, 55.6% ($n = 402$) were indexed in SCI/SCI-E index, 56.7% ($n = 410$) were Open Access, and 58.8% ($n = 425$) had significant results related to the clinical condition studied. The median number of authors was 6 (4-8), the number of citations was 9 (2-25), and the number of cases was 199 (104-354) (Table 1).

Table 1. Descriptive Data

Parameter	N	%
Method		
Retrospective	580	80,2
Prospective	143	19,8
Journal Index		
AHCI	87	12
SCI-E	402	55,6
E-SCI	187	25,9
SSCI	22	3
DIĞER	25	3,5
Counts of Departments		
1	420	58,1
2	152	21
3	94	13
4	37	5,1
5	13	1,8
6	3	0,4
7	3	0,4
8	1	0,1
Open Access		
Yes	410	56,7
No	313	43,3
Significant Result		
Yes	425	58,8
No	298	41,2
New Study Proposal		
Yes	474	65,6
No	249	34,4
Counts of authors M (IQR)	6 (4-8)	-
Counts of citations M (IQR)	9 (2-25)	-
Counts of Case M (IQR)	199 (104-354)	-

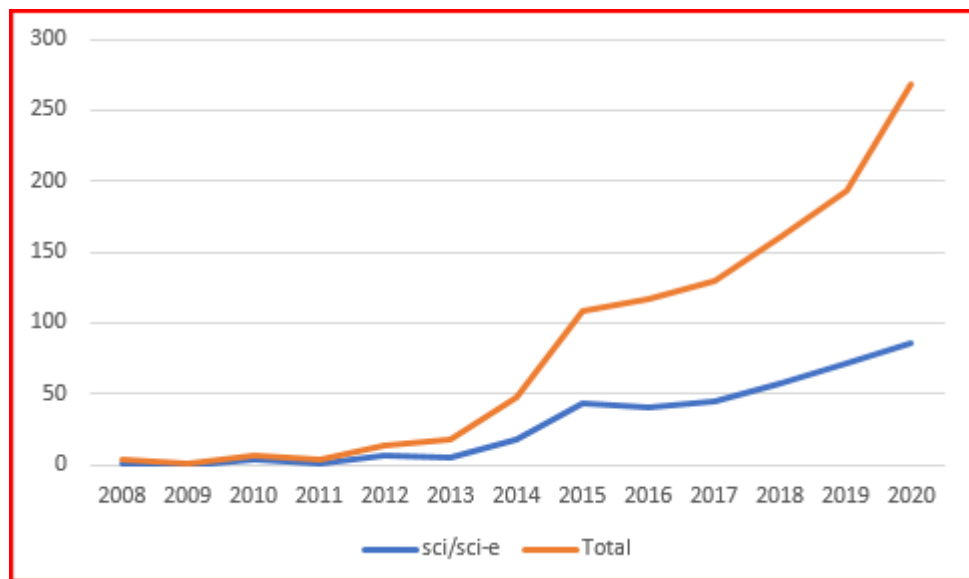


Figure 1. The Number of Publications by Year.

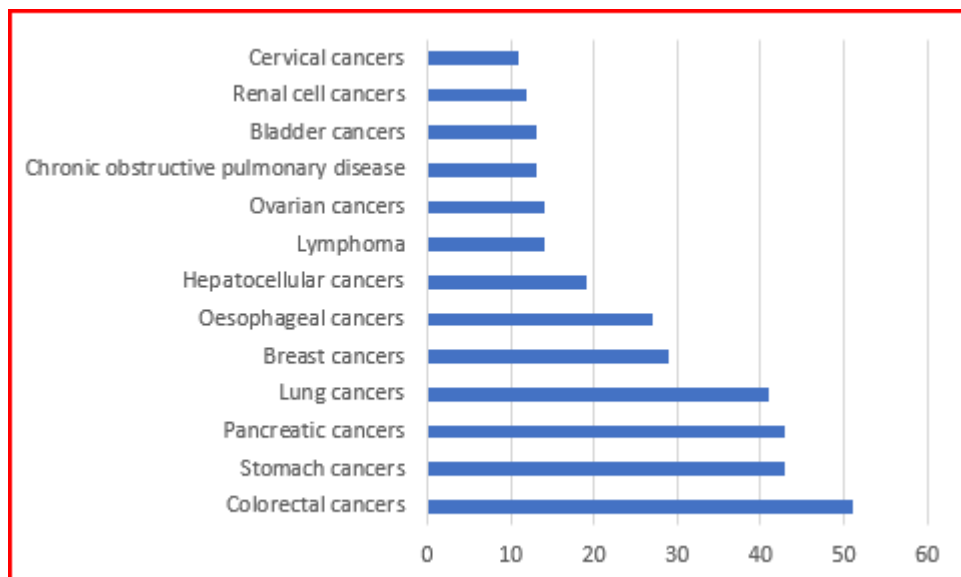


Figure 2. Most Studied Clinical Conditions.

It was observed that the number of publications followed an increasing trend starting from 2011 (0.3%) until 2020 (25.3%) (Figure 1). Colorectal cancers ($n = 51$, 7.1%), gastric cancers ($n = 43$, 5.9%), pancreatic cancers ($n = 43$, 5.9%) and lung cancers ($n = 41$, 5.7%) were the most studied clinical conditions (59 different clinical conditions were studied in total) (Figure 2). Most publications were from Turkey ($n = 239$, 33.1%), China ($n = 211$, 29.2%), and Japan ($n = 55$, 7.6%) (Figure 3).

Strong statistically significant positive correlations were found between the number of years since publication and the number of citations ($r = 0.659$; $P = 0.001$). No correlation was observed between the number of cases and the number of citations ($P > 0.05$) (Table 2).

There was no correlation between the number of cases

in the studies and significant or insignificant results ($P = 0.347$). Although 58.8% of the publications included the recommendation "to continue studies on the relevant topic", this was not different between the studies with significant results and those without significant results ($P = 0.676$).

There was no statistical difference between the number of citations of retrospective type publications and prospective type publications ($P = 0.399$). The number of citations of articles published in AHCI, SCI-E, and ESCI indexed journals was significantly higher than the number of citations of articles published in SSCI indexed journals ($P < 0.05$). There was no difference between the number of citations and the country and clinical status of the study ($P > 0.05$). The number of authors of the articles

did not differ between countries ($P = 0,645$). The distribution of the open access status of the articles according to the countries was statistically significantly different ($P = 0,009$). It was seen that Romania, Cyprus, Iran, Belgium, Mexico, Poland, China, South Korea had significantly higher rates of open access publications. The

distribution of the study type status of the articles published in the journals according to the countries was statistically significantly different ($P = 0,001$). Jordan, Austria, Costa Rica, Bulgaria, Belgium, Indonesia, Bosnia and Herzegovina, USA, China and Japan had statistically significantly higher rates of retrospective type of publications.

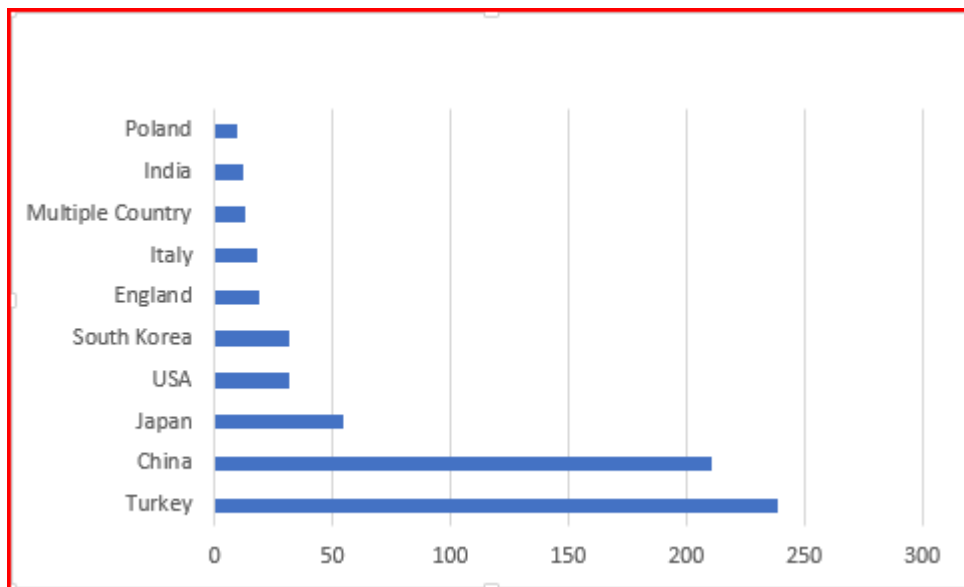


Figure 3. Country Distribution of Publications with One or More Values.

Table 2. Correlation of the Number of Authors, Citations and Cases

		Counts of authors	Counts of citations	Counts of Case
The year since publication	r	0,072	0,659	-0,011
	p	0,054	0,001	0,778
Counts of authors	r		0,055	0,066
	p		0,138	0,077
Counts of citations	r			-0,012
	p			0,739
	r			723

5. Discussion

The majority of the analyzed studies were retrospective, and the majority were SCI/SCI-E indexed. Over the past years, the number of studies on the subject and the number of citations to the articles have been increasing. Their role in malignancy diagnoses was evaluated the most. A total of 59 different clinical conditions were evaluated and "platelet lymphocyte ratio" was found useful in the diagnosis of the relevant clinical conditions in 58.8% of the studies.

A large number of biomarkers have been associated with diseases. In addition to observational data such as anthropometric measurements, many body tissues and fluids such as blood, urine, cerebrospinal fluid, tissue, cell lines, faeces, saliva, sweating, tears, neurofilaments, pleural fluid are used to obtain information and diagnose diseases.⁹ This biomarker may play a role in any of the processes of prediction, cause, diagnosis, progression-regression or treatment outcome of diseases.¹⁰ Predicting a clinical condition before it occurs, understanding the severity, and predicting possible bad outcomes are the

most common situations in which biomarkers are used. However, they have important disadvantages. Personal factors (genetics, environmental influences, age, gender, ethnicity, etc.) are among these disadvantages.

PLR has been the subject of many studies in recent years as one of these biomarkers. The number of publications on the subject is gradually increasing over the past years. This may be related to the increase in the number of academic journals and scientific articles worldwide over the years (the total number of articles grew by 22.78% between 2018 and 2022).¹¹

Meta-analyses have been performed for many clinical conditions related to PLR. Actually, PLR may be useful in showing inflammatory bowel disease activity,¹² it is not useful in the diagnosis of pre-eclampsia,¹³ it has a role in the diagnosis of Glioblastoma and can be used as a cheap marker,¹⁴ it is associated with Erectile Dysfunction and Peyronie's disease,¹⁵ it is effective in predicting stroke-related pneumonia,¹⁶ is not reliable in showing the severity of coronary artery calcification,¹⁷ and may be effective in predicting the need for preoperative adjuvant

therapy in cases of non-small cell lung cancer.¹⁸ There are original articles, meta-analyses or systematic reviews showing that PLR values are associated with mortality in chronic renal failure patients (duration uncertain),¹⁹ are poor in the diagnosis of renal cell cancer,²⁰ are not effective in predicting functional outcomes after acute ischemic stroke,²¹ high PLR values negatively affect survival in malignant melanoma,²² and are effective in the detection of retinal vein occlusions.²³ On the other hand, there are tests or diagnostic methods that can be used in the diagnosis and follow-up of all these clinical conditions and that can provide more precise information. Despite all this evidence, it is difficult to say that the PLR value is not a scientific evidence, on the other hand, when the methods of accessing information are examined, it is seen that scientists have adopted methods that lead to precise information. Many modalities used as gold standard distinguish one disease from another with certainty. From this point of view, PLR can be used as a prognostic marker, but its adoption as a definitive diagnostic method does not seem very plausible.

There are numerous meta-analyses and reviews discussing the advantages and disadvantages of PLR according to each clinical situation. However, this study was designed to provide an overview of this marker. Martinez et al. emphasized that PLR may be useful for the diagnosis of sepsis but may be misleading in immunosuppressed patients such as cancer patients (most commonly compared with CRP).²⁴ Lui et al. stated that PLR reflects the severity of the clinic in psoriasis follow-up.²⁵ Lee et al. also reported that it was elevated in systemic lupus erythematosus attacks in correlation with other inflammatory markers (CRP, ESR, CRP, C3, and anti-dsDNA antibody levels).²⁶ Nourigheimasi et al. reported that it is useful as a marker of sepsis in burn patients compared with other markers (procalcitonin (PCT), and C-reactive protein).²⁷ All these meta-analyses and reviews emphasize that PLR is an inflammatory biomarker. Therefore, it is expected to be elevated like other markers in non-immunosuppressed patients. This expected situation has been the subject of many studies and yielded results as expected. PLR has no superiority over other inflammatory markers and the disadvantages are similar.

It is quite remarkable that most of the publications were from Turkey (n = 239, 33.1%) and China (n = 211, 29.2%). In addition, 2/3 of all publications (which are only publications searched in PubMed and Web of Science) are from these two countries. According to 2022 data, China is the country with the highest number of academic publications worldwide.¹¹ However, Turkey ranks 16th among the countries with the highest number of publications in the world according to 2020 data.²⁸ In a previous study we conducted on "mean platelet volume", Turkey was the country with the highest number of publications.² This may be related to the fact that whole

blood parameters are easily accessible, cheap and can be obtained with a simple calculation. The fact that the majority (80.2%) of the publications we analyzed were retrospective may also be explained in this way. Many reasons can explain why PLR has been the subject of studies in recent years. It can be said that it has been the subject of frequent studies due to reasons such as the increase in academic publication concerns and the number of academic journals,^{11,24} the fact that it is an easily accessible biomarker, that it can be rapidly planned retrospectively, that it shows an increase in inflammatory conditions and that this has never been reported.

5.1. Limitation

The most important limitation of this study was that it is difficult to summarize in a single article due to the large number of clinical conditions studied in almost all clinical branches. In more than half of the included studies, PLR was found to support the relevant clinical conditions. Therefore, it is difficult to make a clear statement about the usability of the marker. The fact that the included studies were only from the PubMed database seems to be a significant disadvantage.

6. Conclusion

To conclude, PLR is a value that is significantly associated with the diagnosis and prognosis of many diseases and can be obtained by a simple calculation from a CBC. There is no disease group in which it is included in the definitive diagnostic criteria alone. Since it can be easily obtained, it is preferred in retrospectively planned studies.

Research Highlights

What Is Already Known?

PLR, which can be easily calculated by CBC, draws attention as a ratio used especially in the evaluation of inflammatory processes and immunological responses.

What Does This Study Add?

- In this study, a total of 59 different clinical conditions that may be similar or overlapping were evaluated and PLR was found to be useful in the diagnosis of relevant clinical conditions in 58.8% of the studies.
- PLR is preferred in retrospectively planned studies.

Author Contributions

MB and HG contributed to conception; MB and HG contributed to design; MB contributed to supervision; HG, SA, and KS contributed to data collection and processing; KS contributed to analysis and interpretation; MB, SK and HG contributed to literature review; HG, MB contributed to writing; MB, SK contributed to critical review.

Conflict of Interest Disclosures

All authors declared that they have no conflict of interest.

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