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Review Article

Association between Mean Platelet Volume and Systemic Lupus Erythematosus: A Meta-Analysis

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Abstract

Background: This meta-analysis aimed to investigate the association between mean platelet volume (MPV) and systemic lupus erythematosus (SLE) disease activity, and laboratory parameters including the SLE Disease Activity Index (SLEDAI), C3 levels, anti-double-stranded DNA (anti-dsDNA) antibodies, and erythrocyte sedimentation rate (ESR).

Methods: The Medline, Embase, and Cochrane databases were searched comprehensively to identify relevant articles. Meta-Analyses were performed to assess differences in MPV between patients with SLE and control groups and between active and inactive SLE. A separate meta-analysis explored correlation coefficients between MPV and SLEDAI, C3, anti-dsDNA, and ESR.

Results: Fourteen studies comprising 659 patients with SLE and 682 controls were included. No significant difference in MPV was found between patients with SLE and control groups (standardized mean difference [SMD]: 0.406; 95% confidence interval [CI]: –0.087 to 0.899; $P = 0.107$). When stratified by ethnicity, the Arab population displayed markedly elevated MPV levels within the SLE group (SMD: 1.032; 95% CI: 0.475–1.588; $P < 0.001$), unlike their European and Asian counterparts. MPV levels were higher in the active disease group than in the inactive group, particularly among the Arab population (SMD: 2.100; 95% CI: 0.406–3.794; $P = 0.015$), while no significant difference was observed within the Asian population (SMD: –1.493; 95% CI = –4.465 to 1.479; $P = 0.325$). MPV did not correlate with SLEDAI (correlation coefficient: 0.252; 95% CI: –0.016 to 0.486; $P = 0.065$), ESR, C3, or anti-dsDNA.

Conclusion: MPV levels were generally higher in patients with SLE among the Arab population. Moreover, MPV and disease activity were positively correlated within the Arab population, underscoring the potential of MPV as a disease activity indicator in specific ethnic groups.

Keywords: Mean platelet volume; Systemic lupus erythematosus; Meta-analysis

Introduction

Systemic Lupus Erythematosus (SLE) is a multifaceted autoimmune disorder characterized by its complex clinical presentation, variable disease course, and multiple organ system involvement (1, 2). Consequently, the identification of reliable and accessible biomarkers is essential for accurate diagnosis, prognosis, and monitoring of disease activity in SLE (3, 4).

One such potential biomarker is the mean platelet volume (MPV), an indicator of platelet size

and function that has shown promise in reflecting inflammatory processes in various pathological conditions (5). Platelets are critical in both hemostasis and inflammation, playing a pivotal role in immune responses and contributing to the pathogenesis of various inflammatory disorders, including autoimmune diseases like SLE. MPV, obtained from routine complete blood count (CBC) analysis, is an indirect marker of platelet activation (5). Understanding the potential correlation between MPV and SLE activity could provide insights into the inflammatory aspects of this complex autoimmune disease.

The prevalence, severity, and clinical presentation of SLE exhibit notable ethnic disparities. Genetic, environmental, and sociodemographic factors contribute to these differences. Since MPV might be influenced by genetic and environmental factors, its association with SLE and related parameters may differ among various ethnic groups. Therefore, analyzing the MPV–SLE relationship across different ethnic populations could unravel novel insights into its potential as a biomarker, tailored to the specific characteristics of diverse patient cohorts. Measuring SLE disease activity is a clinical challenge due to the variability in disease presentation and the lack of a definitive diagnostic test. The SLE Disease Activity Index (SLEDAI) is a widely accepted scoring system that incorporates various clinical and laboratory parameters to assess disease activity. Additionally, complement component 3 (C3) levels, anti-double-stranded DNA (anti-dsDNA) antibodies, and erythrocyte sedimentation rate (ESR) are established biomarkers for monitoring disease activity and systemic inflammation in SLE. Investigating the correlation between MPV and these markers holds potential for identifying a simple, accessible, and noninvasive indicator of SLE disease activity.

This meta-analysis aimed to comprehensively assess the relationship between MPV and SLE by synthesizing evidence from a range of studies. Specifically, this study aimed to elucidate whether MPV levels differ between patients with SLE and control groups, determine the correlation between MPV and SLE disease activity as measured by SLEDAI, and explore the potential associations between MPV and critical laboratory markers such as C3, anti-dsDNA antibodies, and ESR.

Materials and Methods

Selecting the most relevant studies and data

We sought studies that examined MPV in patients with SLE and healthy controls. To identify all available articles, the Medline, Embase, and Cochrane databases (up to August 2023) were searched. The keywords and subject terms used were "mean platelet volume" and "systemic lupus erythematosus." All references provided in the discovered articles were also searched to identify additional studies. Studies were considered admissible if at least one of the following conditions was satisfied: (1) they were case–control, cross-sectional, or cohort studies; (2) they included information on MPV in SLE and controls; or (3) they included data on the correlation between MPV and SLE activity as assessed by the SLEDAI, C3, anti-dsDNA, or ESR. There were no restrictions based on race or language.

Exclusion criteria were as follows: reviews, case reports, and studies with redundant or insufficient data. Data on methods and results were collected by two independent reviewers, with disagreements among the reviewers resolved by consensus. The primary author, publication year, nation, participant count, MPV mean and SD, and correlation coefficients between MPV and disease activity were obtained from each study. When the presented data were medians, interquartile ranges, or ranges, the mean and SD values were determined using aforementioned techniques (6, 7). Each component of the meta-analysis was graded according to its quality using the Newcastle–Ottawa Scale (8).

Meta-analysis relies on existing data from various studies. Ethical concerns may arise if the original studies have issues with data integrity, reliability, or if there are suspicions of data fabrication. Ensuring the reliability of the source data is crucial to maintaining the integrity of the meta-analysis. The meta-analysis was conducted in accordance

with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (9).

Analysis of statistical correlations

A meta-analysis was performed to assess MPV in patients with SLE, healthy controls, and both active and inactive SLE and the relationships between MPV and SLEDAI, C3, anti-dsDNA, and ESR in patients with SLE. To guarantee data integrity, results were presented as standardized mean differences (SMDs) and 95% confidence intervals (CIs). Using Cochran's Q test (10), we evaluated heterogeneity and variability both within and across trials. The hypothesis that all studies examined the same impact was investigated using a heterogeneity test. The equation "$I^2 = 100\% \times (Q - df)/Q$" (11) was used to calculate the effect of heterogeneity. I^2 assessed trial-to-trial consistency and whether the majority of the overall difference across trials was mostly due to heterogeneity rather than chance. I^2 varied between 0% and 100% (11), and I^2 values of 25%, 50%, and 75% were categorized as low, moderate, and high, respectively. Values of I^2 values were >50% or a significant Q value ($p < 0.10$) indicated study heterogeneity, the random-effects model was used (12). The fixed-effects model was used when the Q statistic ($p < 0.10$) failed to identify study heterogeneity. The model only included study heterogeneity and assumed that all studies evaluated the same underlying impact. The Comprehensive Meta-Analysis software (Biostat Inc., Englewood, NJ, USA) was used to make the statistical corrections for the current meta-analysis.

Sensitivity test, heterogeneity, and publication bias

To investigate the likely causes of the heterogeneity seen in the meta-analysis, meta-regression analyses were performed using the variables ethnicity, research quality, sample size, publication year, and data type. A sensitivity test was performed to determine the influence of each study's exclusion on the pooled SMD. Although funnel plots are often used to detect publication bias, interpreting them requires judgment and a range of studies with various sample sizes. Therefore, we evaluated publication bias using Egger's linear regression test (13), which identified funnel plot asymmetry using a natural logarithm scale of SMDs.

Results

Studies included in the meta-analysis

Computational and manual search methods initially located 147 studies. Twenty publications were selected for full-text examination based on their titles and abstracts (Fig. 1).

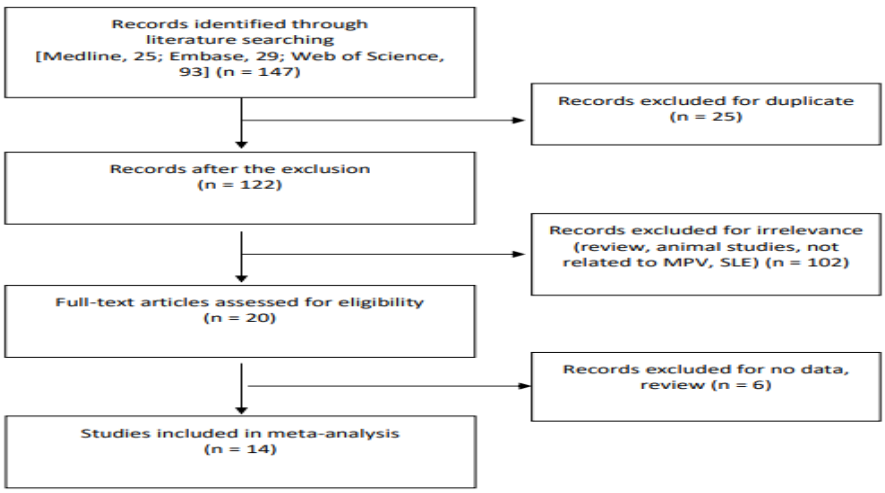

Fig. 1: The study selection process

Six studies which lacked MPV data or were reviews were eliminated. Accordingly, 14 studies with 659 patients with SLE, 682 controls, 284 active SLE, and 227 inactive SLE (14-27) met the inclusion criteria (Table 1, Fig. 1). Each study received a quality rating score between 6 and 7. An overview of the features of the studies that made up the meta-analysis are shown in Table 1 and 2.

Table 1: Characteristics of the individual studies included in the meta-analysis: SLE vs. Control

Authors	*Ethnicity*	*Groups*	*Number*		*Correlation Coefficient*[a]	*Results*			*Study quality*
			SLE	Control		SMD*	Magnitude*	*P*-value	
Taha, 2022(17)	Arab	MPV	100	100	0.514	1.012	Large	<0.001	6
Uzkeser, 2021(19)	European	MPV	39	45	0.329	1.308	Large	<0.001	6
Talat, 2021(16)	Arab	MPV	50	50	0.530	0.508	Medium	0.012	7
Hartmann, 2018(23)	Latin American	MPV	81	58	-0.290	-0.636	Medium	<0.001	7
Chen, 2018(15)	Asian	MPV	91	113	NA	-0.369	Small	0.009	7
Yolbas, 2016(20)	European	MPV	51	55	NA	-0.188	Small	0.336	6
El-Garf, 2016(18)	Arab	MPV	29	36	-0.190	1.675	Large	<0.001	6
Qin, 2015(21)	Asian	MPV	154	151	0.218	0.460	Small	<0.001	7
Safak,2014(22)	European	MPV	44	44	NA	-0.954	Large	<0.001	6
Yavuz, 2014(14)	European	MPV	20	30	0.550	1.449	Large	<0.001	6

SLE: Systemic lupus erythematosus, SMD: Standardized mean difference, MPV: Mean platelet volume, [a]: SLEDAI; Systemic lupus erythematosus disease activity index, *Magnitude of Cohen's *d* effect size: 0.2–0.5, small effect; 0.5–0.8, medium effect; ≥0.8, large effect; NA: Not available.

Table 2: Characteristics of the individual studies included in the meta-analysis: Active vs. Inactive SLE

Authors	*Ethnicity*	*Groups*	*Number*		*Results*			*Study quality*
			Active	Inactive	SMD*	Magnitude*	*P*-value	
Taha, 2022(17)	Arab	MPV	29	18	6.329	Large	<0.001	6
Talat, 2021(16)	Arab	MPV	25	25	0.984	Large	0.001	7
Chen, 2018(15)	Asian	MPV	57	34	0.003	Small	0.988	7
Ayna, 2017(26)	European	MPV	78	30	0.607	Medium	0.006	7
Khan, 2017(24)	Asian	MPV	25	25	-3.030	Large	<0.001	6
Galil, 2016(27)	Arab	MPV	16	48	1.504	Large	<0.001	6
Delgado-Garcia, 2016(25)	Latin American	MPV	36	36	0.692	Medium	0.004	6
El-Garf, 2016(18)	Arab	MPV	18	11	0.089	Small	0.817	6

SLE: Systemic lupus erythematosus, SMD: Standardized mean difference, MPV: Mean platelet volume, *Magnitude of Cohen's *d* effect size: 0.2–0.5, small effect; 0.5–0.8, medium effect; ≥0.8, large effect.

Comparing MPV in a meta-analysis between SLE patients and controls

In the present meta-analysis, MPV was not different between the SLE and control groups (SMD: 0.40; 95% CI: –0.087 to 0.899; p = 0.107) (Table 3, Fig. 2).

Table 3: Meta-analysis of MPV levels in SLE: SLE vs. Control

Groups	*Population*	*No. of studies*	*Test of association*			*Test of heterogeneity*		
			SMD*	95% CI	*P*-value	Model	*P*-value	I^2
All	Overall	10	0.406	-0.087-0.899	0.107	R	< 0.001	94.5
Ethnicity	European	4	0.390	-0.712-1.492	0.488	R	< 0.001	95.4
	Arab	3	1.032	0.475-1.588	< 0.001	R	< 0.001	82.0
	Asian	2	0.490	-0.763-0.862	0.905	R	< 0.001	95.1
	Latin American	1	-0.636	-0.982- -0.291	< 0.001	NA	NA	NA
Sample size	Small (< 100)	0.645	-0.379	-0.379-1.669	0.217	R	< 0.001	95.5
	Large (≥ 100)	5	0.196	-0.382-0.774	0.507	R	< 0.001	94.6

MPV: Mean platelet volume, SLE: Systemic 0.390lupus erythematosus, LN: Lupus nephritis, CI: Confidence interval, R: Random effects 1.032model, NA: Not applicable. *: Magnitude of Cohen's d effect size (SMD): 0.2–0.5, small effect; 0.5–0.8, medium0.490 effect; ≥ 0.8, large effect. MPV was not different between the SLE and control groups. The Arab population, but not the European or Asian populations, had significantly higher MPV levels in the SLE group

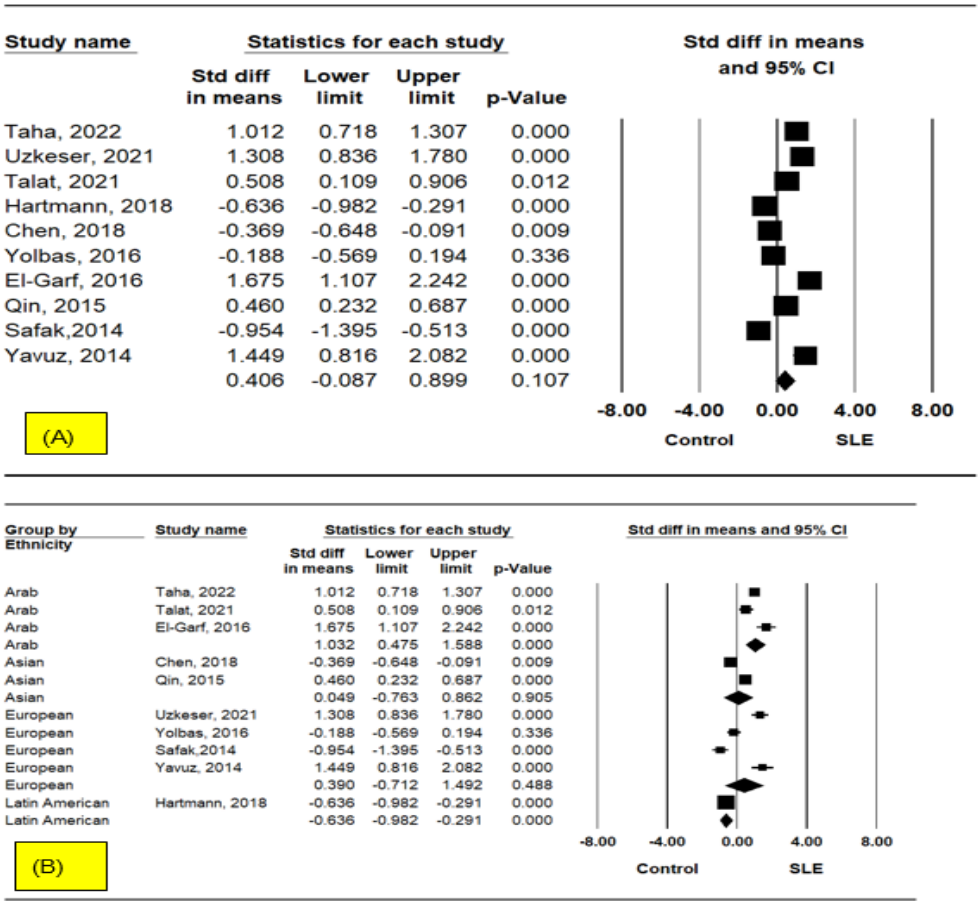

Fig. 2: The results of a meta-analysis of mean platelet volume in patients with systemic lupus erythematosus and controls across ethnic groups (A) and overall (B). MPV was not different between the SLE and control groups. The Arab population, but not the European or Asian populations, had significantly higher MPV levels in the SLE group

When stratified by ethnicity, the Arab population, but not the European or Asian populations, had significantly higher MPV levels in the SLE group (SMD: 1.032; 95% CI: 0.475–1.588; *P* = 0.001) (Table 2, Fig. 2). When analyzed by sample size, MPV was similar between the SLE group and control groups in both small (<200) and large (≥200) sample sizes (SMD: 2.100; 95% CI: 0.406–3.794; *P* = 0.015 and SMD: –1.493; 95% CI: –4.465 to 1.479; *P* = 0.325, respectively) (Table 2). When stratified by disease activity, MPV levels were higher in the active disease group than the inactive disease group in Arab cohorts, but not in Asian cohorts (Table 4, Fig. 3).

Table 4: Meta-analysis of MPV levels in SLE: Active vs. Inactive SLE

Groups	***Population***	***No. of studies***	***Test of association***			***Test of heterogeneity***		
			SMD*	95% CI	*P*-value	Model	*P*-value	I^2
All	Overall	8	0.793	-0.198-1.785	0.117	R	< 0.001	
Ethnicity	European	1	0.617	0.178-1.036	0.006	NA	NA	NA
	Arab	4	2.100	0.406-3.794	0.015	R	< 0.001	95.0
	Asian	2	-1.493	-4.465-1.479	0.325	R	< 0.001	97.6
	Latin American	1	0.692	0.216-1.167	0.004	NA	NA	NA

MPV: Mean platelet volume, SLE: Systemic lupus erythematosus, LN: Lupus nephritis, CI: Confidence interval, R: Random effects model, NA: Not applicable. *: Magnitude of Cohen's d effect size (SMD): 0.2–0.5, small effect; 0.5–0.8, medium effect; ≥ 0.8, large effect. MPV levels were higher in the active disease group than the inactive disease group in Arab cohorts, but not in Asian cohorts

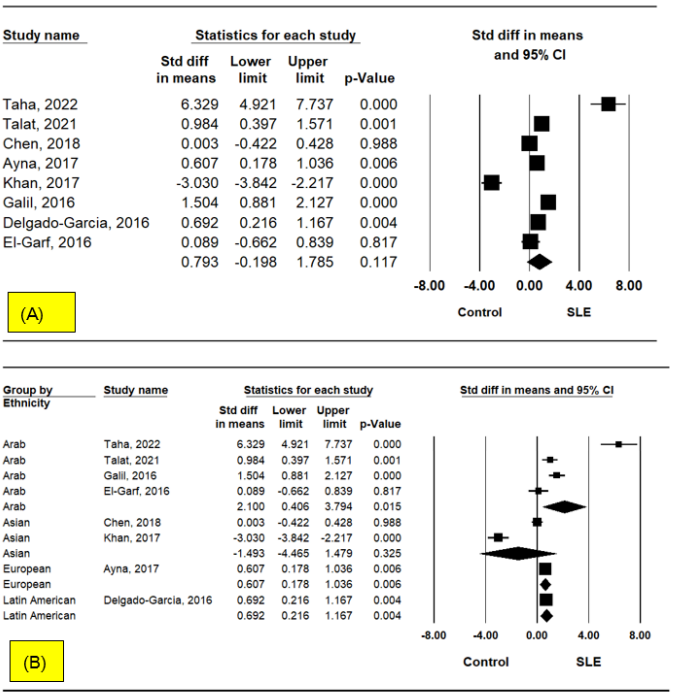

Fig. 3: A meta-analysis of the link between mean platelet volume levels and systemic lupus erythematosus (A), between mean platelet volume levels and active or inactive systemic lupus erythematosus in each ethnic group (B). MPV levels were higher in the active disease group than the inactive disease group in Arab cohorts, but not in Asian cohorts

MPV and clinical results: a relationship

There was no association between MPV and SLEDAI (correlation coefficient: 0.252; 95% CI: –0.016 to 0.486; P = 0.065) ESR, C3, and anti-dsDNA (Table 5, Fig. 4).

Table 5: Meta-analysis of the correlation coefficient between MPV level and SLIDAI, C3, ESR, and anti-dsDNA in SLE

Parameters	*No. of studies*	*Test of association*			*Test of heterogeneity*		
		Correlation coefficient	95% CI	*P*-value	Model	*p*-value	I^2
SLEDAI	7	0.252	-0.016-0.486	0.065	R	< 0.001	87.1
ESR	3	0.217	-0.198-0.566	0.305	R	0.011	77.6
C3	2	-0.024	-0.5965-0.563	0.943	R	0.030	78.6
Anti-dsDNA	2	0.226	-0.088-0.499	0.157	R	0.129	56.5

MPV: Mean platelet volume, SLEDAI: Systemic lupus erythematosus disease activity index, ESR: Erythrocyte sedimentation rate, CI: Confidence interval, R: Random effects model, NA: Not available. There was no association between MPV and SLEDAI, ESR, C3, and anti-dsDNA.

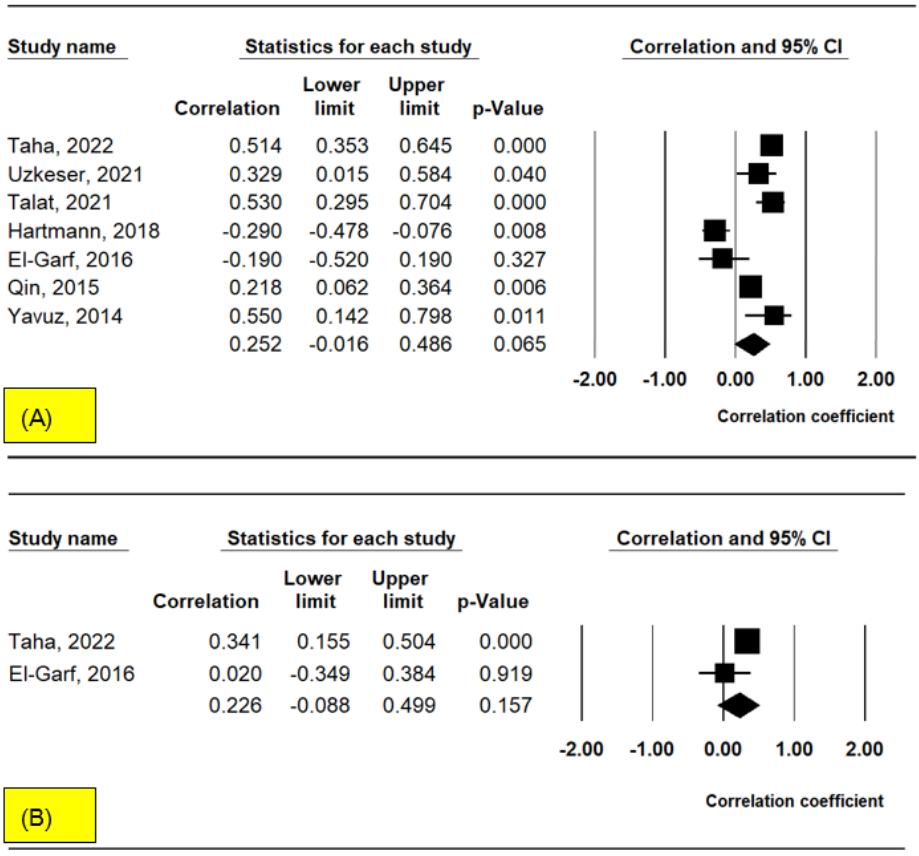

Fig. 4: A meta-analysis of the correlation between mean platelet volume and SLEDAI (A) and anti-dsDNA (B). There was no association between MPV and SLEDAI and anti-dsDNA

Sensitivity test, publication bias, and heterogeneity

There was between-study heterogeneity in meta-analysis of MPV levels in SLE patients and controls, as well as correlations in SLE patients (Tables 2, 3). Although sample size, data type, or research quality did not substantially affect the heterogeneity in the meta-analysis of MPV levels in patients with SLE ($P = 0.001$), ethnicity and publication year did. The outcomes of this meta-analysis were unstable, as shown by sensitivity analysis, which found that two studies significantly influenced the pooled SMD (22, 23). The meta-analyses revealed no signs of publication bias, and the funnel plot demonstrated symmetry (Egger's regression test *P*-values >0.1).

Discussion

The association between MPV and SLE activity holds clinical significance, as inflammation plays a central role in the pathogenesis of SLE. Larger platelets, indicated by an increased MPV, are associated with heightened platelet activity and increased release of proinflammatory cytokines, potentially exacerbating the inflammatory milieu in SLE. This study's findings corroborate the potential of MPV as a biomarker, as increased MPV levels suggest heightened platelet activation and subsequent release of proinflammatory mediators. These findings are consistent with the observed higher MPV levels in patients with SLE, particularly in the Arab population, highlighting the potential utility of MPV in gauging disease activity in specific ethnic cohorts.

The ethnic disparities observed in SLE have long been acknowledged, with varying prevalence, clinical presentation, and disease severity across different populations. The notable elevation of MPV in the Arab population suggests potential genetic and environmental influences on MPV levels, affecting its association with SLE. This emphasizes the importance of tailoring biomarker assessments to specific ethnic groups to enhance their accuracy and clinical relevance. Further research into the genetic and environmental determinants of MPV in different populations could provide a deeper understanding of these disparities. The correlation analyses undertaken in this meta-analysis provide valuable insights into the relationship between MPV and key SLE disease activity markers, such SLEDAI, complement C3 levels, anti-dsDNA antibodies, and ESR. Notably, the lack of a significant correlation between MPV and SLEDAI suggests that although MPV may reflect certain aspects of disease activity, it may not be a comprehensive indicator of overall disease severity. This underscores the multifactorial nature of SLE and the need for a combination of biomarkers to accurately capture disease dynamics. While the correlations between MPV and established markers are not uniformly strong, they point to the potential of MPV as a supplementary tool in assessing SLE activity, especially in certain ethnic populations.

This meta-analysis differs from a previous meta-analysis (28), because in the present study five more studies included, and further meta-analysis was conducted on MPV levels between SLE and control. The result of this meta-analysis on no significant difference in MPV level between active SLE patients and inactive SLE patients in Asians was in agreement with this previous study. However, this meta-analysis showed that MPV levels were higher in the active disease group than in the inactive group among the Arab populations.

One limitation of this study was the inherent heterogeneity across the included studies. The variability in study designs and patient populations in assessing MPV and SLE could contribute to potential biases and inconsistencies in the meta-analysis. Although efforts were made to address this heterogeneity through subgroup analyses based on factors such as ethnicity and sample size, residual heterogeneity may still influence the overall findings. One of the notable strengths of this study was its comprehensive approach to synthesizing evidence from a wide range of studies. By conducting a meta-analysis involving a large number of patients with SLE from diverse populations and employing rigorous statistical methods, this study offers a robust overview of

the relationship between MPV and SLE (29). The large sample size enhances the generalizability of the findings and increases the statistical power to detect potential associations (2, 30, 31). Furthermore, the subgroup analyses based on ethnicity and sample size contribute to a nuanced understanding of how these factors influence the observed associations, providing valuable insights into the potential utility of MPV as a biomarker in specific patient populations.

Conclusion

This meta-analysis sheds light on the potential of MPV as a biomarker for SLE. The observed elevation of MPV levels, particularly in the Arab population unlike previous meta-analysis, and its associations with certain disease activity markers offer valuable insights into its role in reflecting inflammatory processes and disease dynamics.

Journalism Ethics considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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Conflict of interest

The authors declare that there is no conflict of interests.

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