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Original Article

Mean platelet volume and neutrophil to lymphocyte ratio in lupus nephritis patients

Medicine

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ABSTRACT

Background: Systemic lupus erythematosus (SLE) is an autoimmune illness with uncertain cause that manifests itself clinically and laboratory as organ involvement with remission and return. Lupus nephritis (LN) is an immune complex glomerulonephritis that arises because of SLE in around 50% of patients. The neutrophil lymphocyte ratio (NLR) has been identified as an inflammatory marker. Also Mean platelet volume (MPV) has also been studied in chronic inflammatory disorders, implying that MPV and NLR might be employed as inflammatory indicators in LN.

Objective: to investigate the role of mean platelet volume (MPV) and neutrophil to lymphocyte ratio (NLR) as inflammatory markers for occurrence of lupus nephritis.

Methodology: This was a case control study conducted in Al-Zahraa University hospital on 60 patients diagnosed as SLE, 30 with lupus nephritis and 30 were controls. All patients were subjected to detailed history taking, physical examination, laboratory investigations for CBC, MPV, NLR, ESR, CRP, Serum creatinine, Serum urea, Serum uric acid, Serum albumin and the GFR was calculated.

Results: The mean age of the LN group was 27.4 ± 4.9 and 27.6 ± 4.7 for patients without lupus nephritis. The mean MPV was 10.3 ± 1.2 in cases with LN and 8.1 ± 0.5 in cases without LN. The NLR was 5.9 and ranged between 3.04 and 18.9 in cases with LN while in cases without NL, the mean NLR was 1.6 and ranged between 1.05 and 2.9 indicating that there was high significant difference between the 2 groups regarding MPV and NLR. NLR is positively correlated to platelet lymphocyte ratio (PLR). Both MPV and NLR values fail to correlate with any inflammatory markers in LN patients.

Conclusion: MPV and NLR could be used to predict LN but not as inflammatory markers in those patients.

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Keywords: Case control study, neutrophil-to-lymphocyte percentage, platelet-to-lymphocyte percentage, systemic lupus erythematosus, inflammatory markers.

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INTRODUCTION

Systemic lupus erythematosus (SLE) is an autoimmune illness with a variety of medical and laboratory findings [1]. SLE is marked by organ involvement and a remission and recurrence pattern [2].

Lupus nephritis (LN) is an immune complexity glomerulonephritis that occurs as a consequence of SLE in around half of the patients at some point throughout their disease. Kidney failure, cardiovascular illness, and mortality are all more likely in LN patients [3]. LN is identified by chronic proteinuria of >0.5 gm daily or larger than 3+ on a dipstick, as well as cellular casts of red blood cells, hemoglobin, granular, tubular, or mixed types [4]. In LN, glomeruli are where nephrotoxic autoantibodies are produced and harmful immune complexes are formed intravascularly. Autoantibodies may also attach to antigens already present in the basement membrane of the glomerulus, producing immunological complexes in situ [5].

The neutrophil lymphocyte ratio (NLR) has been reported as an inflammatory biomarker in cancer, ischemic damage, cardiovascular disease, and infection [6-9]. In persistent inflammatory disorders such as rheumatoid arthritis, ankylosing spondylitis, and Behcet's disorder, mean platelet volume (MPV) has also been

studied [10]. MPV and NLR might be employed as inflammatory indicators in LN because of their inflammatory functions [11, 12]. This research looked at the function of MPV and NLR as LN inflammatory indicators.

PATIENT AND METHODS

Study participants: This Hospital based case control study was done at Al-Zahraa University Hospital in Cairo, Egypt. As per the American College of Rheumatology (ACR), the research included 60 female individuals who had been diagnosed with SLE, [13, 14]. Thirty patients were diagnosed with LN based on 24-hour urine protein levels below 500 mg/dl and/or renal biopsy, whereas the control group of 30 patients was diagnosed as SLE without LN. Those who agreed to take part in the research willingly completed a written informed consent. The Research Ethics Committee of Al-Azhar University's Faculty of Medicine for Girls authorized all surgeries, which were conducted in conformity with the principles of the Helsinki Declaration.

Inclusion criteria were adult SLE patients according to ACR 2012 and those with LN by 24-hour protein in urine more than 500 mg/dl, and/or renal biopsy. **Exclusion criteria** include those who were < 18 years, with other autoimmune diseases, other causes of renal insufficiency, sever acute infections, or malignancy.

Methods: All patients were subjected to a standardized questionnaire, which specially emphasized duration of the disease, the system involved, and the treatment received. Physical examination was done on all patients and body mass index (BMI) was computed as weight in kg/ length in square meters. Resting blood pressure (BP) was taken as a mean of 3 occasions. Laboratory investigations include complete blood picture with differential WBCs count, ESR, anti-double-stranded DNA (dsDNA), quantitative CRP, C3 and C4 complement level, serum creatinine, serum urea, serum uric acid, serum albumin, and 24 hours albumin in urine. To calculate the estimated glomerular filtration rates (eGFR), the modifying diet in renal dysfunction (MDRD) equation was utilized (eGFR [ml/(min (1.73m2)] =186× (Scr, mg/dl)-1.154 ×(age, year)-0.203 ×0.742(female)×1.233} [15]. NLR and MPV were estimated. Renal biopsy was done on selected patients.

Statistical analysis

SPSS Version 25 was employed to analyze the data. Numbers and percentages were utilized to convey categorical data. Normally dispersed ongoing variables were assigned the mean ± standard deviation. Ongoing variables that were not normally dispersed were represented as medians (minimum- maximum). The Chi-square test was used to analyze categorical data across two groups and the student t test was utilized to compare normally dispersed ongoing variables across two groups. To assess parametric correlation between continuous variables, Pearson correlation was done. P-value of $\leq$0.05 has been considered significant

RESULTS

In the present study, the mean age of female patients with lupus nephritis was 27.4 ± 4.9 30 years, ranging between 20 to 34 years and it was 27.6 ± 4.7 years, ranging between19 to 35 years for the SLE female patients without lupus nephritis as a control group.

The sociodemographic and clinical findings of SLE with and without LN were shown in (table 1). Systemic manifestations, SBP and DBP were substantially higher significantly in SLE patients with LN compared with those without LN (P<0.05).

Table (1): Sociodemographic and clinical findings of SLE with and without nephritis

Variables	SLE with LN (n = 30)	SLE without LN (n = 30)	Stat. test	P-value
Age /years	27.4 ± 4.9	27.6 ± 4.7	0.1613#	0.8
Disease duration/ months	23 (1-50)	12 (1-27)	1.2#	0.2
System affected: n (%) CVS Vascular Skin Neuro Joints	 8 (26.7%) 3 (10%) 13 (43.3%) 3 (10%) 3 (10%)	 1 (3.3%) 3 (10%) 8 (26.7%) - -	13.4^	0.001*
BMI	25.9 ± 1.8	26 ± 1.8	0.22#	0.9
SBP	136.7 ± 10.6	129 ± 9.2	3.00#	0.004*
DBP	83.3 ± 9.6	76 ± 8.1	3.18#	0.002*

BM: Body mass index; SBP: Systolic blood pressure; DBP: Diastolic blood pressure, #: Student t.-Test, ^: Chi Square, *: Significant p value (p < 0.05).

Comparison between blood indices of SLE patients regarding to LN was shown in (table 2). There was highly statistically substantial enhance in TLC in LN patients compared with those without LN (P<0.05). The

differential WBCs count revealed highly statistically substantial rise in neutrophils and decrease in lymphocyte counts in LN patients compared to those without LN. NLR is substantially enhanced in LN patients compared to SLE patients without LN. The HB concentration and platelet numbers were not substantially variant in both groups. However, the MPV and PLR were substantially raised in patients with LN compared to those without LN ($p \leq 0.001$).Correlation between NLR as well as MPV and inflammatory markers in LN patients was represented in (table 3). There was substantial positive correlation between NLR and PLR ($P \leq 0.05$) (figure 1). However, no other substantial correlations were reported in other studied parameters.

Table (2): Comparison between blood indicesin SLE patients with and without lupus nephritis

Variables	SLE with nephritis (n = 30)	SLE without nephritis (n = 30)	Stat. test#	P-value
Haemoglobin gm/dl	8.5 ± 1.8	9.2 ± 2.2	0.18	0.2
Platelets 10^3/uL	178 (49-500)	205 (39-344)	0.172	0.2
TLC10^3/uL	9.5 (1.6-14.8)	6.6 (2.8-16.1)	3.02	0.003*
Neutrophils, /ml	7180 (1299-13424)	3746 (1607-9354)	4.3	0.001*
Lymphocytes /ml	1087 (229-2667)	2197 (932-4315)	3.8	0.001*
NLR	5.9 (3.04-18.9)	1.6 (1.05-2.9)	5.2	0.001*
PLR	0.1(0.03-0.5)	0.08(0.02-0.1)	6.7	0.001*
MPV/fl	10.3 ± 1.2	8.1 ± 0.5	9.2	0.001*

NLR: neutrophil lymphocyte ratio; PLR: platelet lymphocyte ratio; MPV: mean platelet volume, #: Student t.-Test,*: Significant p value ($p < 0.05$).

Table (3): Correlation of neutrophil lymphocyte ratio and mean platelet volume with inflammatory markers of lupus nephritis patients

Variables	NLR (n = 30)		MPV (n = 30)	
	r	P value	r	P value
Urea	0.2	0.3	-0.008	0.9
Creatinine	0.2	0.2	0.04	0.8
Uric acid	0.08	0.7	0.1	0.5
Albumin	-0.03	0.9	-0.01	0.9
24 hours urinary albumin	0.003	0.9	-0.05	0.8
eGFR	-0.3	0.2	-0.06	0.7
ESR 1st hour	-0.05	0.8	0.2	0.2
CRP	0.07	0.7	-0.2	0.3
C3	-0.08	0.7	0.3	0.1
C4	-0.005	0.9	-0.1	0.5
Anti dsDNA	0.2	0.2	0.1	0.6
PLR	0.6	0.001*	0.3	0.5

LN: lupus nephritis; NLR: neutrophil lymphocyte ratio; MPV: mean platelet volume; eGFR: estimated glomerular filtration rate; ESR: erythrocyte, sedimentation rate; CRP: C reactive protein; C3: complement 3, Test: Pearson correlation,*: Significant p value ($p < 0.05$).

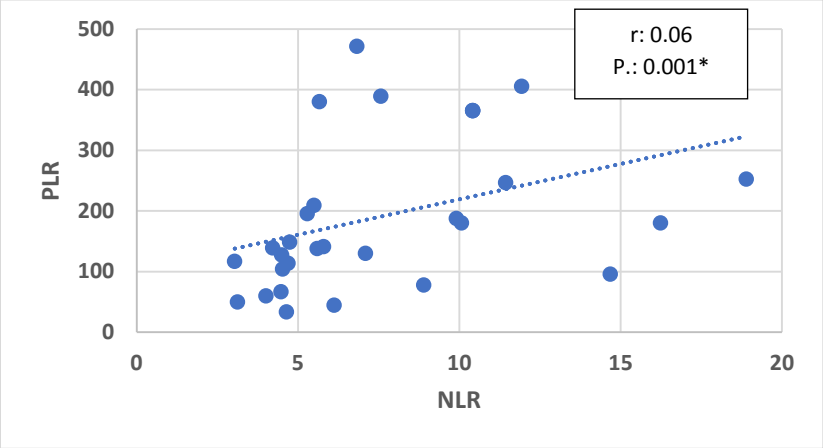

Figure (1): Correlation between NLRand PLR in LN patients

DISCUSSION

This case control study was carried out on 60 SLE females with and without LN to investigate if the mean platelet volume (MPV) and neutrophil to lymphocyte ratios (NLR) can be used as an inflammatory parameter in lupus nephritis. Increased NLR was reported in association with chronic kidney disease in both pre -dialysis and dialysis patients as that of Okyay et al. [16]. Huang et al. [17]was also demonstrated that great NLR levels may be a good predictor of early -stage diabetic nephropathy, and NLR readings may give valuable information on inflammation in diabetic nephropathy . Moreover, Yilmaz et al. [18]showed that in individuals with severe sepsis, NLR outperforms C -reactive protein and WBC in predicting the progression of acute renal damage. MPV and NLR were showed to be considerably greater in LN patients compared to SLE controls without LN in this investigation. The results of Li et al. [19], are similar to that of the current research, who investigated the link between NLR values and SLE patients with LN and found that LN patients had a substantially higher NLR than SLE patients without LN and controls. LN is considered a process of chronic inflammation in which inflammatory cells and complement mediate this effect. The research results were also in line with Ata Bora et al. [20]. Results that reported in active LN, MPV and NLR levels are much higher than in SLE without renal impairment. It can be concluded that MPV and NLR could be helpful to detect flares in LN patients. Another study by Talat et al. [21] was found that MPV in the SLE children was substantially greater than control group and MPV was higher in active patients. Yolbas et al. [22]also in comparing with a healthy control group, SLE patients had greater NLR and PLR. NLR was also considerably greater in hypocomplementemic SLE patients than in normocomplementemic SLE patients. For example, Wu et al. [23] reported that NLR and PLR levels in SLE patients were substantially greater than in healthy controls. Both ratios were linked to the SLE disease Activity Index in a substantial way (SLEDAI -2K). Only NLR had to be substantially larger in SLE patients who had LN. In SLE patients, NLR may be used as a prediction of renal impairment, and it corresponds to the histological renal biopsy classifications [24]. Correlations among NLR and other measures in SLE patients with LN demonstrated a statistically substantial positive association between NLR and PLR in the current investigation. In LN patients, however, NLR had no connection with any of the inflammatory markers (ESR, CRP, C3, C4, or Anti dsDNA).

In the current investigation, PLR was shown to be considerably larger in patients with LN compared with those without LN. This result was in line with Abdulrahman et al. [25]study who have found that both NLR and PLR were considerably greater in SLE patients compared to controls, and both ratios were substantially greater in patients with active LN and similar in naïve and relapsing LN patients . As regard to MPV, despite its substantially greater level in patients with LN compared to those without LN, no statistically substantial correlations have been found with any of the studied parameters. In line with our findings, research by Abd -Elhafeez et al. [26] NLR and PLR were investigated as activity indicators in SLE patients with LN. They found that the NLR had a high diagnostic value for illness activities, but the PLR had a reduced diagnostic value. Yolbas et al. [22]also in comparing to a healthy control group, SLE patients had greater NLR and PLR . Contradictory to our results, a meta-analysis by Lee and Song. et al. [27]has been carried out to combine the evidence for MPV, NLR, and PLR for LN patients. They discovered that NLR and PLR were linked to SLE activity as examined by the SLE Disease Activity Index (SLEDAI). They proposed that NLR and PLR might be valuable markers for assessing the severity of SLE inflammation. Moreover, Ayna et al. [20] found In the LN group, there was a positive connection among NLR and CRP. The discrepancy might be attributed to our study's limited sample size and the fact that we did not look into the effects of therapy on NLR and PLR.

CONCLUSION

In SLE patients with LN, NLR, MPV, and PLR were considerably greater than in those without LN. NLR is

positively correlated to PLR. Neither NLR nor MPV correlated with any inflammatory markers in LN patients. MPV and NLR may serve as indicators in prediction of LN but not as inflammatory markers in those patients.

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Conflicts of Interest: The authors declare no conflicts of interest regarding the publication of this paper.

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الملخص العربي

متوسط حجم الصفائح الدموية ونسبة العدلات إلى الخلايا الليمفاوية في مرضى التهاب الكلية الذئبي

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ملخص البحث

الخلفية: الذئبة الحمراء هي مرض مناعي ذاتي مع سبب غير مؤكد يتجلى سريريًا ومختبرًا كمشاركة العضو في مغفرة والعودة. التهاب الكلية الذئبي هو التهاب مناعي معقد للكبيبات ينشأ بسبب مرض الذئبة الحمراء في حوالي 50٪ من المرضى. تم تحديد نسبة الخلايا المتعادلة الى الخلايا الليمفاوية كعلامة التهابية. كما تمت دراسة متوسط حجم الصفائح الدموية في الاضطرابات الالتهابية المزمنة ، مما يعني أنه يمكن استخدام متوسط حجم الصفائح الدموية و نسبة الخلايا المتعادلة الى الخلايا الليمفاوية كمؤشرات التهابية في التهاب الكلية الذئبي.

الهدف: التحقيق في دور متوسط حجم الصفائح الدموية ونسبة العدلات إلى الخلايا الليمفاوية كعلامات التهابية لحدوث التهاب الكلية الذئبي.

الطرق: كانت هذه دراسة مقطعية أجريت في مستشفى جامعة الزهراء على 60 مريضاً تم تشخيص إصابتهم بمرض الذئبة الحمراء ، و 30 مصاباً بالتهاب الكلية الذئبي و 30 مريضاً تم تشخيصهم. خضع جميع المرضى لأخذ التاريخ التفصيلي والفحص البدني والفحوصات المخبرية: صورة دم كاملة و متوسط حجم الصفائح الدموية و نسبة الخلايا المتعادلة الى الخلايا الليمفاوية و معدل ترسيب خلايا الدم و بروتين C التفاعلي و مستوى كرياتينين الدم و مستوى اليوريا في الدم وحمض اليوريك في الدم وألبومين المصل و معدل الترشيح الكبيبي.

النتائج: كان متوسط عمر مجموعة التهاب الكلية الذئبي4.9 ± 27.4 و 27.6 ± 4.7 للمرضى غير المصابين بالتهاب الكلية الذئبي. كان متوسط متوسط حجم الصفائح الدموية1.2 ± 10.3 في حالات التهاب الكلية الذئبي و 8.1 ± 0.5 في الحالات التي لا تحتوي على التهاب الكلية الذئبي. كان نسبة الخلايا المتعادلة الى الخلايا الليمفاوية 5.9 وتراوحت بين 3.04 و 18.9 في حالات التهاب الكلية الذئبي بينما في الحالات الغير مصابة بالتهاب الكلية الذئبي ، كان متوسط نسبة الخلايا المتعادلة الى الخلايا الليمفاوية 1.6 وتراوح بين 1.05 و 2.9 مما يشير إلى وجود فرق كبير بين المجموعتين فيما يتعلق بمجموعات متوسط حجم الصفائح الدموية و نسبة الخلايا المتعادلة الى الخلايا الليمفاوية. يرتبط نسبة الخلايا المتعادلة الى الخلايا الليمفاوية ارتباطًا إيجابيًا بنسبة الخلايا الليمفاوية في الصفائح الدموية. فشل كل من قيم متوسط حجم الصفائح الدموية و نسبة الخلايا المتعادلة الى الخلايا الليمفاوية في الارتباط بأي علامات التهابية في مرضى التهاب الكلية الذئبي.

الاستنتاجات: يمكن استخدام متوسط حجم الصفائح الدموية و نسبة الخلايا المتعادلة الى الخلايا الليمفاوية للتنبؤ بالتهاب الكلية الذئبي ولكن ليس كواسمات التهابية في هؤلاء المرضى.

الكلمات المفتاحية: دراسة الحالة، نسبة العدلات إلى الخلايا الليمفاوية، نسبة الصفائح الدموية إلى الخلايا الليمفاوية، الذئبة الحمراء، علامات الالتهاب.

الباحث الرئيسي

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