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# Serum Calprotectin – a NET Product – as a Biomarker of Disease Activity in Patients with Systemic Lupus Erythematosus: A Single-Center Case-Control Study from Poland

Authors' Contribution:  
Study Design A  
Data Collection B  
Statistical Analysis C  
Data Interpretation D  
Manuscript Preparation E  
Literature Search F  
Funds Collection G

ACDEF 1 **Iwona Homa-Mlak**  
BCEF 1 **Marcin Mazurek**  
DEF 1 **Aleksandra Majdan**   
ACDE 1 **Radosław Mlak**  
ADEF 2 **Maria Majdan**   
ADEF 1 **Teresa Mełecka-Massalska**

1 Department of Human Physiology, Medical University of Lublin, Lublin, Poland  
2 Chair and Department of Rheumatology and Connective Tissue Diseases, Medical University of Lublin, Lublin, Poland

**Corresponding Author:** Iwona Homa-Mlak, e-mail: iwona.homa.mlak@gmail.com  
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**Background:** Calprotectin (S100A8/A9 or myeloid-related protein 8/14) is a heterodimeric S100 complex expressed in leukocytes. Calprotectin participates in development of the inflammatory response by binding to receptors for advanced glycation end-products (RAGE) and Toll-like receptors (TLR). The clinical activity of systemic lupus erythematosus (SLE) is evaluated using the Systemic Lupus International Collaborating Clinics (SLICC) criteria and the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI). This Polish single-center case-control study aimed to evaluate serum levels of calprotectin as a rapid diagnostic biomarker of SLE (59 patients with SLE were compared with 52 healthy controls).

**Material/Methods:** Calprotectin concentration was measured with the use of enzyme-linked immunosorbent assay (ELISA). The SLE activity of the patients was assessed by the SLEDAI scale. Statistical analysis of the results was carried out using MedCalc 15.8 software.  $P < 0.05$  was considered statistically significant.

**Results:** A significantly higher concentration of calprotectin was found in the study group compared to the control group (medians: 3.11 vs 2.45 ng/ml;  $P = 0.0013$ ). We found that calprotectin has high sensitivity (89.83%) and specificity (53.85%) in differentiating between SLE patients and healthy volunteers. We found that calprotectin has very high sensitivity (100%) and specificity (82.46%) in detection of patients with moderate and severe SLE assessed using SLEDAI.

**Conclusions:** Consistent with previous studies, serum calprotectin level was revealed to have potential as a rapid diagnostic biomarker of disease activity in patients with SLE.

**Keywords:** **Autoimmune Diseases • Lupus Erythematosus, Systemic • S-100 Calcium-Binding Protein Alpha Subunit**

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## Background

Neutrophils are among the essential cells of the immune system. They play a key role in defending the body against pathogens by means of various mechanisms, including phagocytosis and degranulation of cytoplasmic granular proteins with bactericidal activity. The impaired neutrophil function makes the host susceptible to various types of pathogens, which can be life-threatening [1,2]. In addition to the above-mentioned mechanisms, neutrophils demonstrate their function by creating extracellular neutrophil traps (NETs) [1,3]. NETs are induced by reactive oxygen species (ROS) produced by the nicotinamide adenine dinucleotide phosphate (NADPH) oxidase complex. This causes decondensation of chromatin induced by citrullinating peptidylarginine deiminase 4 (PAD-4) histones and the breakdown of intracellular membranes, which makes the mixing of nuclear and cytoplasmic components possible. Then the cytoplasmic membrane breaks and the NET structure is released [3-5]. The total NET composition is not yet thoroughly understood. It contains granular substances (eg, cathepsin G, myeloperoxidase, and lysozyme) derived from peroxisomes (catalase), glycolytic enzymes (alpha-enolase, transketolase), components of the cell nucleus (eg, histones H2A, H3, and H4), cytoplasm (S100A8, A9, and A12), and the cytoskeleton (eg, actin and plastin-2) [5].

NETs are a defense mechanism, but they can also exert toxic effects. In an inflammatory environment, they can stimulate an autoimmune reaction in the body by releasing autoantigens such as nucleic acids and proteins [3]. The proteins contained in NETs can constitute a target for the formation of immune complexes and autoantibodies, and they induce further NET formation, which results in positive feedback [3].

Calprotectin (S100A8/A9 or myeloid-related protein 8/14 – MRP8/14) is a heterodimeric S100 complex expressed in leukocytes [6]. It is released by phagocytes at the site of inflammation [7]. After being released from neutrophils and monocytes, it modulates the inflammatory response [8]. The extracellular calprotectin induces inflammation by binding to receptors for advanced glycation end-products (RAGE) and pattern recognition Toll-like receptors 4 (TLR4) located on the surface of leukocytes and endothelial cells [9]. This causes the release of pro-inflammatory cytokines such as interleukin-1 $\beta$  (IL-1 $\beta$ ), interleukin-6 (IL-6), and tumor necrosis factor (TNF- $\alpha$ ) [9]. Recent studies indicate that calprotectin may be a useful biomarker in monitoring the activity of autoimmune diseases, including inflammatory bowel disease and rheumatoid arthritis (RA) [8].

Systemic lupus erythematosus (SLE) is an autoimmune multi-system disease. It is most common in women of childbearing age, but it is also increasingly prevalent in patients over the age of 40 years [10]. The concurrent inflammation can develop

in various organs and the elevated level of autoantibodies against nuclear antigens (eg, anti-nuclear antibodies, ANA), double-stranded DNA (dsDNA), histones and proteins (eg, anti-thyroid peroxidase antibodies, and TPOAb) is also observed. In addition, in SLE patients excessive neutrophil activity is commonly observed, even at an early stage of the disease [11]. The EULAR/ACR 2019 criteria have a novel structure with use of anti-nuclear antibodies (ANA) as an (obligatory) entry criterion [12]. (Noninfectious) fever is the one new criterion. All criteria items now have individual weights (from 2 to 10) and are structured in domains, within which only the highest item is counted. There is one common attribution rule, counting criteria only if there is no more likely alternative explanation. Ten points are sufficient for maintaining the classification. The new criteria have reached a sensitivity of 96.1% and a specificity of 93.4%. Classification is not the same as diagnosis [13-15]. Diagnosis is not dependent on fulfilling classification criteria. All attempts to withhold therapies from SLE patients not fulfilling SLE classification criteria must be countered, since this would clearly be inappropriate and dangerous. Second, classification criteria are not meant for screening. They should only be employed if there is reason to believe a patient could have SLE. SLE is characterized by periods of remission and exacerbation. During exacerbations, the risk of premature death increases significantly, mainly due to infection or cardiovascular disorders. To measure disease activity in patients with SLE, certain clinical methods for evaluating disease activity can be used. One of them is SLEDAI-2K; the original version was introduced in 1985 [16,17]. In 2002, it was modified to reflect persistent active disease in those descriptors that had previously been considered new or recurrent occurrences (SLEDAI-2K) [17,18]. SLEDAI-2K is an index allowing for disease activity assessment and considers specific manifestations in 9 organs or systems that were noted in the last 10 days. In total 24 items are assessed: 8 items with 8 points each, 6 items with 4 points each, 7 items with 2 points each, and 3 items each with 1 point each. Therefore, patients can score from 0 to 105 points [18]. To capture those items of permanent change that has occurred in patients after a diagnosis of SLE, regardless of attribution, the Systemic Lupus International Collaborating Clinics (SLICC)/ American College of Rheumatology Damage Index (SDI) can be used [19,20]. It consists of 41 items covering 12 organ systems. Within each scale or system, there is a variable number of components (up to 6). Thirty-one items score 1 point each if present. Six items can score a maximum of 2 points each; 1 item can score a maximum of 3 points [20,21].

Therefore, this Polish single-center case-control study aimed to evaluate serum levels of calprotectin as a rapid diagnostic biomarker of SLE (52 healthy controls were compared with 59 patients with SLE treated in the Clinic of Rheumatology and Systemic Connective Tissue Diseases of the Medical University of Lublin).

## Material and Methods

The patients were diagnosed in the Clinic of Rheumatology and Systemic Connective Tissue Diseases of the Medical University of Lublin. Three inclusion criteria were used: diagnosis of SLE, specified degree of disease progression according to SLEDAI, and absence of any infectious or neoplastic disease. Each patient was told the purpose of the research and signed the informed consent form to participate in the study. The approval of the Bioethics Committee (KE-0254/21/2016) was obtained. The material used to assess the level of calprotectin was serum derived from venous blood from all subjects enrolled in the study. Before the test, the material (serum) was stored at  $-70^{\circ}\text{C}$ . The serum concentration of this protein was measured according to the manufacturer's instructions using the Human S100A8 (protein S100-A8) ELISA Kit (FineTest, China). For ELISA, flat-bottomed 96-well plates were filled with 0.1 ml of standard solutions or diluted (1: 10) serum samples with dilution buffer and incubated at  $37^{\circ}\text{C}$  for 90 min. After washing twice (Wellwash Versa Microplate Washer, Thermo Scientific), 0.1 ml of diluted biotin-labeled antibody (1: 100) was added and the plate was incubated for 60 min at  $37^{\circ}\text{C}$ . After washing 3 times, the plate was incubated at  $37^{\circ}\text{C}$  for 30 min with 0.1 ml diluted HRP-streptavidin conjugate (1: 100). Finally, after washing 5 times, the ELISA plate was incubated for 15 min with TMB substrate (90  $\mu\text{l}$ ) and next the reaction was stopped with a stop solution (50  $\mu\text{l}$ ). For quantification of the optical density (OD) at 450 nm, estimation of the model curve linear regression equation and S100A8 concentration was performed with the use of Multiskan FC Multiplate Photometer (Thermo Scientific) [22]. The study subjects were divided according to the stage of SLE progression determined by SLEDAI. In addition, routine laboratory tests were performed on all patients participating in the study. We assessed morphological (RBC, HGB, WBC, NEUT, LYM, PLT, OB), biochemical (CRP, total protein, creatinine, GFR), and immunological (dsDNA, C3, C4, IgG, IgM, and IgA) parameters.

### Statistical Analysis

MedCalc 15.8 (MedCalc Software, Belgium) was used to perform statistical analysis.  $P < 0.05$  was considered statistically significant. Most scientific studies in medicine consider a  $P$  value of  $< 0.05$  as rejection of the null hypothesis, thus 0.05 was the value used for type I error (alpha). In the case of type II error (beta), we started with a cut-off of 0.2 to achieve 80% statistical power. The sample size calculation was based on previously published data. The calculations were based on a serum calprotectin concentration (expressed as means and corresponding standard deviations) comparison in SLE patients and healthy controls. Considering the difference in means and corresponding standard deviations, as well as the ratio of sample sizes in compared groups reported in the study quoted [13], the minimal number of subjects in our study was estimated to be 7 (4 in the study group and 3 in

the control). Subsequently, considering that these are relatively small numbers, we decided to increase the power of the test to 99.999%. This change increased the sample size of the study group to 14 patients. Moreover, to achieve maximum reliability of obtained results, we decided to enlarge the study group by about 400%. Thus, we estimated that at least 56 subjects should be included in the study group. Quantitative variables and some demographic and clinical factors used to describe the study and control groups are presented by means of descriptive statistics: measures of central tendency and dispersion (median, range). Due to the non-normal distribution of the data in the case of analyzed continuous variables (tested with the use of the D'Agostino-Pearson test), in further analyses we used non-parametric tests. The Spearman rank correlation test was used to assess the correlation of calprotectin concentration and selected demographic, clinical and laboratory factors (continuous variables). Using the Mann-Whitney U test, analysis of the difference in the concentration of calprotectin in the control and the study group was performed, as well as within some subgroups of patients, in relation to the selected demographic and clinical factors: duration of disease or SLE degree of progression according to SLEDAI. The analysis based on ROC curves was used to assess the diagnostic utility of determining the level of calprotectin in SLE detection and in differentiation between specific clinical conditions.

## Results

### Study and Control Group Characteristics

The study group consisted of 59 patients, including 51 women (86.44%) and 8 men (13.56%). The median age in the study group was 36 years (range 19-72 years). SLE activity was assessed using SLEDAI; 86.4% of patients were classified as having mild SLE. In turn, 10.2% of patients had moderate SLE, while 3.4% had active SLE (Table 1). A panel of laboratory tests was performed on all patients and differences in calprotectin values in relation to morphological and biochemical factors were examined. The control group consisted of 52 healthy volunteers matched with respect to age (median 38 years, range 22-64 years) and sex (84.62% women and 15.38% men) (Table 1).

### Differences in Calprotectin Concentration in Patients with Systemic Lupus Erythematosus in Relation to Demographic and Clinical Factors

We examined the serum concentration of calprotectin in patients depending on sex, age, and duration and severity of disease. The level of calprotectin was not significantly associated with sex, age, duration of the disease, or its activity. A statistically significant higher serum calprotectin concentration was found in the study group as compared to the control (medians: 3.11 vs 2.45 ng/ml;  $P = 0.0013$ ) (Table 2).

**Table 1.** General characteristic of the study group.

Variable	n (%) or median (range)	
	Study group (n=59)	Control group (n=52)
Male	8 (13.56%)	8 (15.38%)
Female	51 (86.44%)	44 (84.62%)
Age (years)	36.5 (19-72)	38.0 (22-64)
Duration of the disease (years)	6 (0-37)	–
SLEDAI		
Mild	51 (86.4%)	–
Moderate	6 (10.17%)	–
Severe	2 (3.39%)	–

n – number, SLEDAI – Systemic Lupus Erythematosus Disease Activity Index.

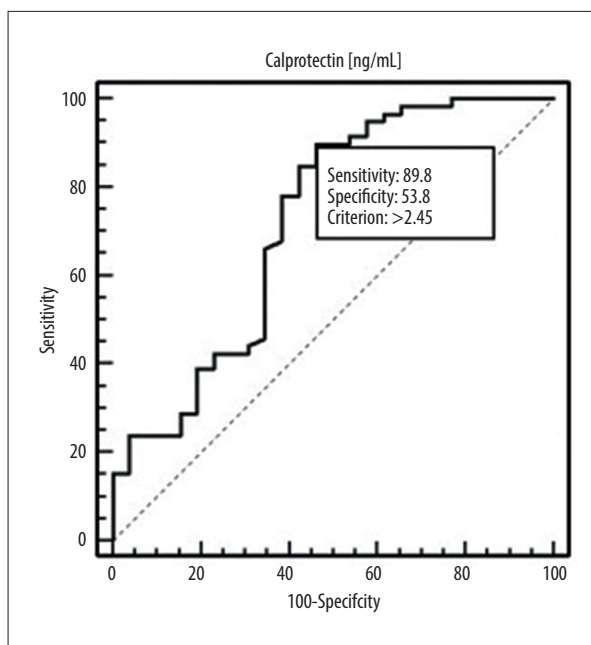
**Table 2.** Differences in calprotectin value depending on demographic and clinical factors in the study group.

Variable	Median	p
Male	3.10	0.7735
Female	3.11	
Age (years)		0.0562
<36.5	3.14	
>36.5	3.06	
Duration of the disease (years)		0.8611
<6	3.11	
>6	3.10	
SLEDAI		0.6907
Mild and moderate	3.11	
Severe	3.41	
SLEDAI		0.2030
Mild	3.11	
Moderate and severe	3.39	
Calprotectin [ng/ml]		0.0013*
Study group	3.11	
Control group	2.45	

\* Statistically significant results. SLEDAI – Systemic Lupus Erythematosus Disease Activity Index.

**The Assessment of the Diagnostic Usefulness of the Calprotectin in the Detection of Systemic Lupus Erythematosus and Specific Clinical Conditions Using ROC Curve Analysis**

We examined the assessment of the diagnostic usefulness of the calprotectin in the detection of systemic lupus erythematosus and specific clinical conditions. The calprotectin was characterized with 89.83% sensitivity and 53.85% specificity in the



**Figure 1.** Receiver operating characteristic (ROC) curve – diagnostic utility of calprotectin concentration in detection of systemic lupus erythematosus (SLE).

differentiation of patients with SLE and healthy people (cut-off >2.45, AUC=0.720, 95% CI=0.612-0.812 p=0.0001) (Figure 1, Table 3). The calprotectin was characterized with 100% sensitivity and 82.46% specificity in the detection of patients with moderate and severe SLE assessed using SLEDAI (cut-off ≤2.37, AUC=0.842, 95% CI=0.724-0.924; p<0.0001) (Figure 2, Table 3). The calprotectin was characterized with 100% sensitivity and 59.09% specificity in the detection of patients with elevated level of IgA antibodies (cut-off >3090, AUC=0.716, 95% CI=0.507-0.874; p=0.0296) (Figure 3, Table 3).

**Assessment of Correlation Between Level of Calprotectin and Demographic and Clinical Factors in Patients with Systemic Lupus Erythematosus**

We examined the correlation between the level of calprotectin and demographic and clinical factors in patients with SLE. A statistically significant but weak negative correlation was found between the level of calprotectin and the concentration of complement component 3 (C3) protein (rho=-0.429, P=0.0012; Figure 4, Table 4). A statistically significant but weak positive correlation was noted between the level of calprotectin and dsDNA (rho=0.325, P=0.0277; Figure 5, Table 4).

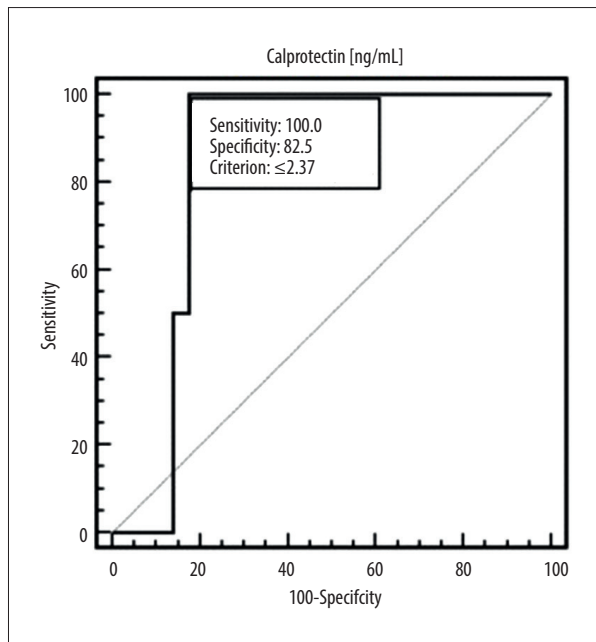
**Differences in Calprotectin Concentration in Relation to Clinical Manifestation of Systemic Lupus Erythematosus**

We examined the serum concentration of calprotectin depending on clinical manifestation of the disease. Only 1 result was

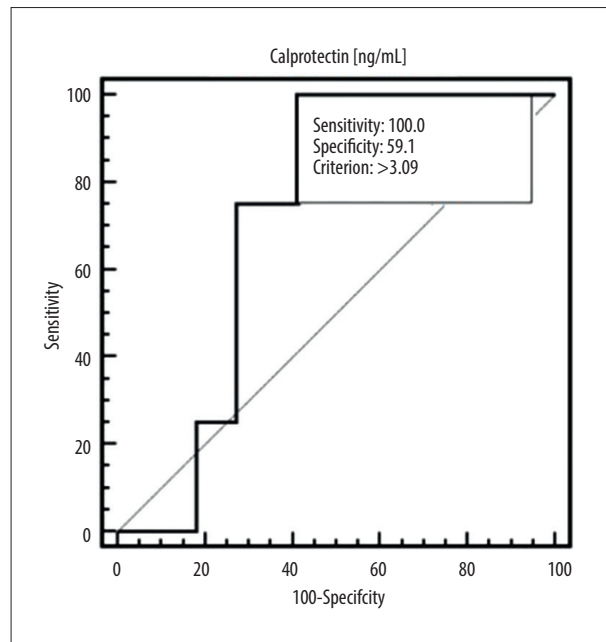
**Table 3.** Evaluation of diagnostic usefulness of calprotectin in detection of systemic lupus erythematosus (SLE) and specific clinical conditions by means of receiver operating characteristic (ROC) curve analysis.

Variable	AUC [95% CI]	Sensitivity %	Specificity	Cut-off point	p
Study group vs control group	0.720 (0.612-0.812)	89.83	53.85	>2.45	0.0001*
SLEDAI Mild vs moderate and severe	0.842 (0.724-0.924)	100.00	82.46	≤2.37	<0.0001*
SLEDAI Mild and moderate vs severe	0.504 (0.370-0.637)	62.50	13.73	≤3.77	0.9789
GFR [ml/min/1.73 m <sup>2</sup> ]	0.508 (0.374-0.640)	86.11	34.78	≤3.57	0.9253
ESR [mm/h]	0.544 (0.409-0.674)	27.27	92.31	>3.76	0.5664
CRP [mg/l]	0.676 (0.542-0.792)	50.00	86.67	≤2.42	0.0668
dsDNA	0.565 (0.430-0.694)	40.74	81.25	>3.25	0.3994
IgG [mg/dl]	0.617 (0.393-0.809)	33.33	100.00	≤1.64	0.6035
IgA [mg/dl]	0.716 (0.507-0.874)	100.00	59.09	>3.09	0.0296*

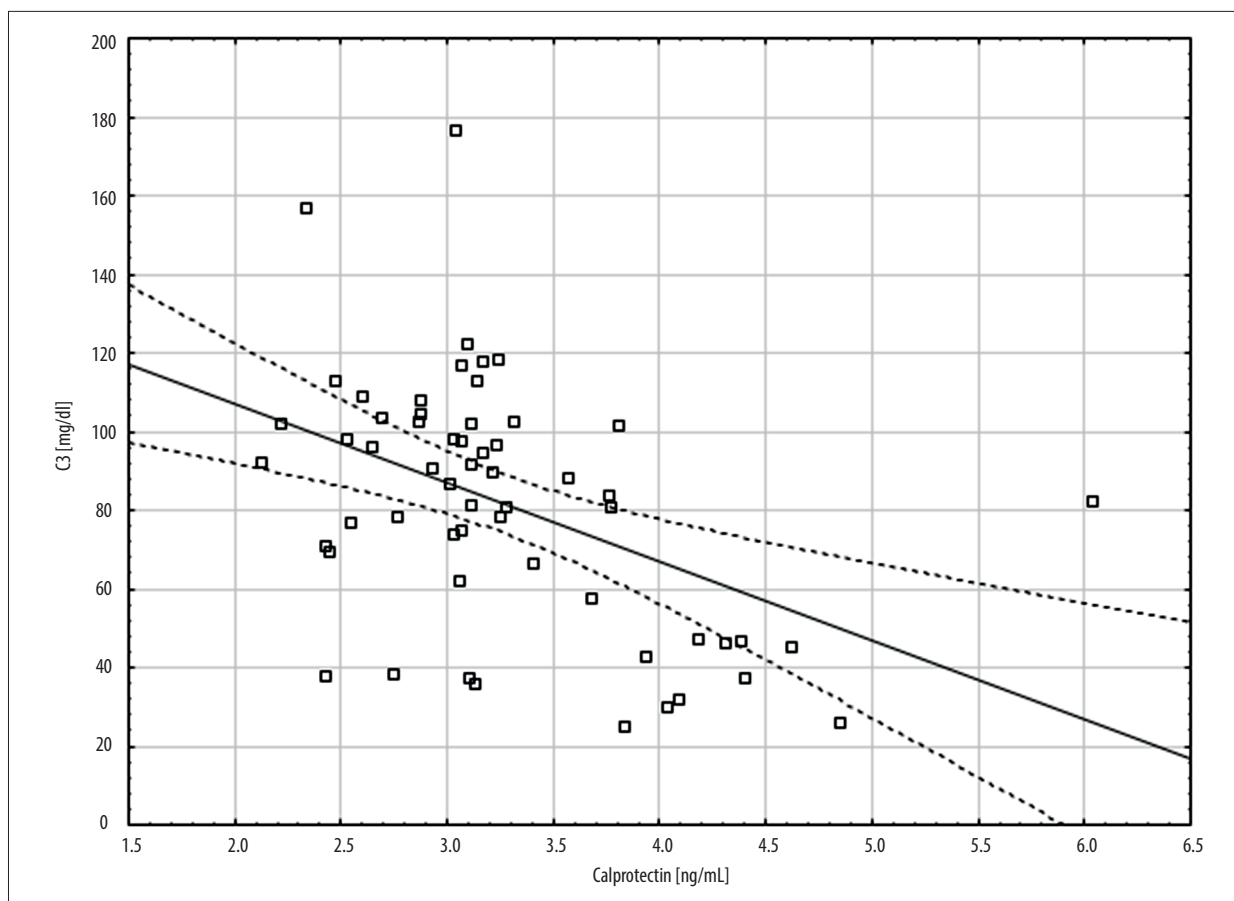
\* Statistically significant results. AUC – area under the curve; CRP – C reactive protein; CI – confidence interval; dsDNA – double-stranded DNA; GFR – glomerular filtration rate; IgA – Immunoglobulin A; IgG – immunoglobulin G; ESR – erythrocyte sedimentation rate; SLEDAI – Systemic Lupus Erythematosus Disease Activity Index.



**Figure 2.** ROC curve – diagnostic utility of calprotectin concentration in detection of moderate or severe SLE (according to SLEDAI).



**Figure 3.** ROC curve – diagnostic utility of calprotectin concentration in detection of SLE with elevated level of immunoglobulin A (IgA) antibodies.



**Figure 4.** A scatter plot showing the correlation between complement component 3 (C3) (mg/dl) and calprotectin concentration (ng/ml).

statistically significant – higher serum calprotectin concentration was found in the SLE patients with myopathy as compared to the study group without myopathy (medians: 3.94 vs 3.09 ng/ml;  $P=0.0277$ ) (Table 5).

## Discussion

Neutrophils play an important role in the pathogenesis of autoimmune diseases (including SLE) and the associated organ damage. Cell death in the NET mechanism can be immunostimulatory, leading to activation of innate immune mechanisms. The elements of NETs have the ability to activate pDC (plasmacytoid dendritic cells), which can promote further activation of the immune system and increase INF type I synthesis, which is characteristic for SLE. The above mechanism may explain why infections are a common cause of SLE exacerbations [10,11,23,24]. One of the hypotheses is also based on the assertion that, in patients with SLE, the process of NET elements degradation is slower than in healthy people [25]. Hakkim et al indicated that the identification of patients in whom the degradation of NET elements is impaired can be

effective in identifying patients who may be at risk of developing nephritis [25]. Leffler et al showed that the inability to degrade NETs was correlated with increased SLE activity (assessed using SLEDAI), and lower levels of C3 and C4 proteins. In addition, pleurisy and kidney involvement were more common in these patients [26]. In another study, Leffler et al confirmed the former study results and demonstrated that the reduced ability to degrade NETs was associated with increased disease activity assessed using SLEDAI, with the development of nephritis, increased dsDNA, and low C3 [27]. Slow degradation of NET elements may be associated with SLE pathogenesis and clinical symptoms. Potentially, drugs that promote faster degradation of NET elements may be effective in some SLE patients [25-27].

According to the available scientific reports, calprotectin was identified as one of the main components of NETs [5]. We noted higher calprotectin concentration in the study group as compared to the control. Moreover, we found, that calprotectin has high sensitivity (89.83%) and specificity (53.85%) in differentiating between SLE patients and healthy volunteers. We found that calprotectin has very high sensitivity (100%) and

**Table 4.** Correlation between selected clinical and laboratory factors and calprotectin.

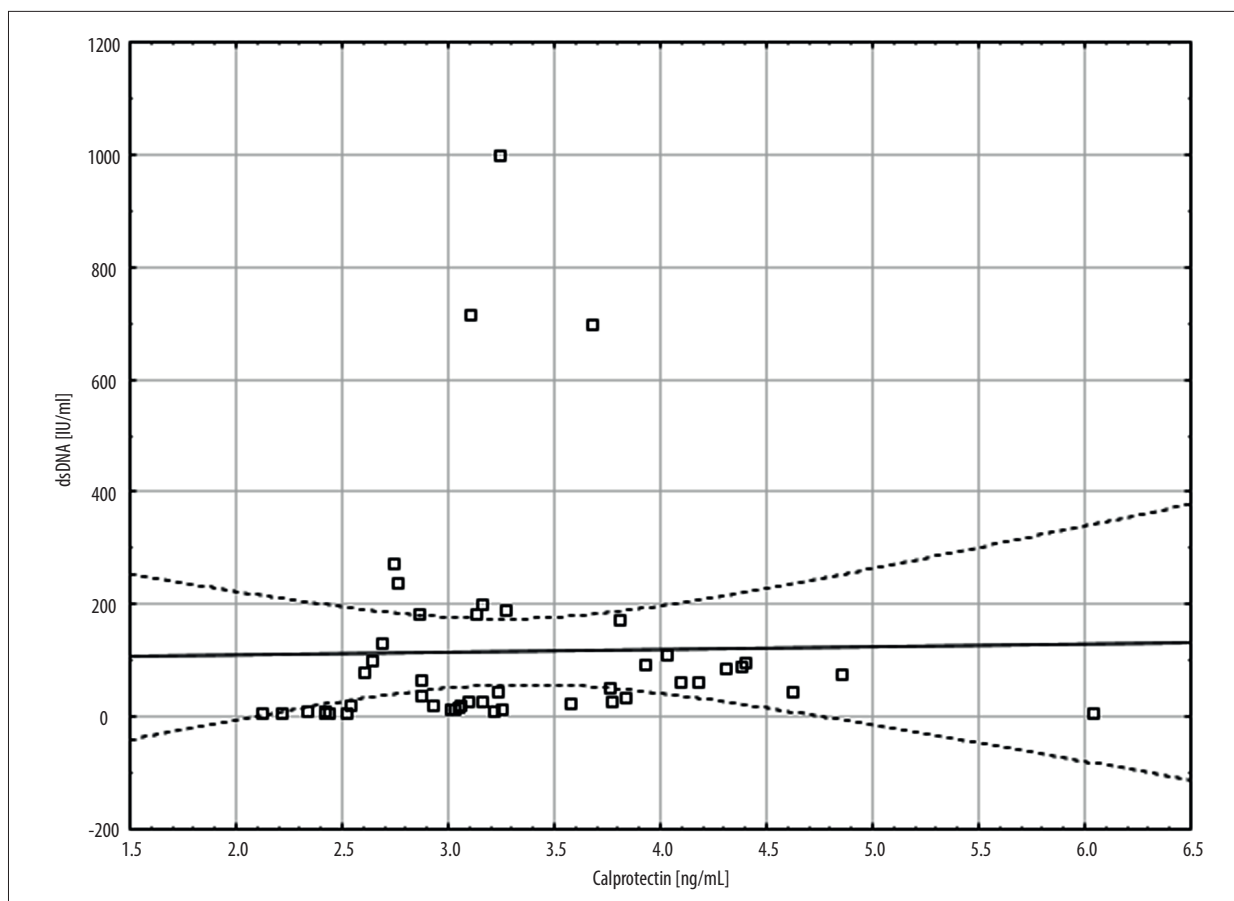
Variable	n	rho	p
Age (years)	59	-0.146	0.2664
Duration of the disease (years)	58	0.0388	0.7695
SLEDAI – Mild vs moderate and severe	59	0.167	0.2056
SLEDAI – Mild and moderate vs severe	59	0.0523	0.6942
RBC [ $10^6/\mu\text{l}$ ]	59	-0.122	0.3515
HGB [g/dl]	59	-0.0108	0.9343
WBC [ $10^3/\mu\text{l}$ ]	59	-0.236	0.0726
NEUTR [ $10^3/\mu\text{l}$ ]	59	-0.171	0.1934
LYM [ $10^3/\mu\text{l}$ ]	59	-0.227	0.0833
PLT [ $10^3/\mu\text{l}$ ]	59	-0.114	0.3867
ESR [mm/h]	58	-0.122	0.3562
CRP [mg/l]	59	0.0625	0.6342
Total protein [g/dl]	41	0.259	0.1016
Creatinine [mg/dl]	59	-0.223	0.0899
GFR [ml/min/1.73 m <sup>2</sup> ]	59	0.130	0.5435
dsDNA	59	0.325	0.0277*
C3	59	-0.429	0.0012*
C4	28	-0.291	0.1375
IgG [mg/dl]	23	0.395	0.0637
IgM [mg/dl]	23	0.0356	0.8674
IgA [mg/dl]	26	0.0005	0.9982

\* Statistically significant results. C3 – complement component 3; C4 – complement component 4; CRP – C reactive protein; dsDNA – double-stranded DNA; GFR – glomerular filtration rate; HGB – haemoglobin; IgA – immunoglobulin A; IgG – immunoglobulin G; IgM – immunoglobulin M; LYM – lymphocytes; n – number; NEUTR – neutrophils; ESR – erythrocyte sedimentation rate; PLT – platelets; RBC – red blood cells; SLEDAI – Systemic Lupus Erythematosus Disease Activity Index; WBC – white blood cells.

specificity (82.46%) in the detection of patients with moderate and severe SLE assessed using SLEDAI. We also performed basic morphological and biochemical tests on our patients, which are used for diagnosis and monitoring of the disease. We noted a statistically significant but weak negative correlation between the level of calprotectin and the concentration of complement component 3 (C3) protein. We also found a statistically significant but weak positive correlation between the level of calprotectin S100A8 protein and dsDNA.

The increased concentration of this protein is observed in SLE as well as in other autoimmune diseases, such as psoriasis and rheumatoid arthritis [3,28-30]. Significantly higher levels of calprotectin were detected in patients with SLE. Sumova et al evaluated the levels of S100A4, S100A8/9, and S100A12 proteins in 44 patients with SLE and 43 healthy volunteers. In the case of calprotectin, they obtained similar results and demonstrated a significantly higher level of calprotectin in patients

with SLE [9]. Soyfoo et al also showed that serum calprotectin level were significantly higher in patients with SLE compared to healthy controls [24]. Moreover, Haga also showed a higher concentration of calprotectin in patients with SLE (n=100) compared to healthy controls (n=80) (3661.25  $\mu\text{g/l}$  vs 1050.83  $\mu\text{g/l}$ ;  $P<0.001$ ). Haga et al also found a significant correlation between calprotectin and CRP ( $r=0.42$ ,  $P<0.001$ ) as well as disease activity ( $r=0.28$ ;  $P<0.01$ ) in patients with SLE [31]. In the course of SLE diagnosis and monitoring, in addition to basic morphological and biochemical tests, the standard procedure involves determination of the levels of dsDNA as well as C3 and C4 complement components, and the disease activity is assessed using SLEDAI. The level of calprotectin was significantly higher in patients with SLE in whom dsDNA level was very high compared to those in whom the level of dsDNA remained normal. In addition, we observed a positive correlation between calprotectin concentration and dsDNA and C3 levels in patients with SLE. Tyden et al demonstrated that



**Figure 5.** A scatter plot showing the correlation between double-stranded DNA (dsDNA) (IU/ml) and calprotectin concentration (ng/ml).

the presence of anti-dsDNA antibodies was associated with increased calprotectin concentration, hypothesizing that the autoantibodies that attack dead cell elements contribute to elevated serum calprotectin levels by increasing phagocytosis and PMN activation, which is commonly observed in SLE [11]. However, Sumova et al did not report similar correlations [9]. On the other hand, Soyfo et al showed a weak, positive correlation between the level of calprotectin and disease activity assessed using SLEDAI [24]. Calprotectin had 89.85% sensitivity and 53.85% specificity in differentiating between SLE patients and healthy volunteers. When differentiating between patients with severe or moderate and mild SLE according to SLEDAI, the sensitivity of calprotectin was 100% and the specificity was 82.46%. Sumova et al tested the discriminatory qualities of the calprotectin level, finding that calprotectin had 63.6% sensitivity and 64.1% specificity [9]. The above results suggest the potential utility of calprotectin as a biomarker of SLE.

The limitations of the study include a relatively small study group and its heterogeneity in terms of disease exacerbation (assessed according to SLEDAI). To confirm our results, further research is needed. Other limitations include the single-center design and the observational nature of the study. Moreover,

we did not analyze the correlation between calprotectin and some other supplementary laboratory parameters used in the diagnostics of SLE.

Studies using animal models of such autoimmune diseases as multiple sclerosis, SLE, RA, and inflammatory bowel disorders have shown that low molecular weight inhibitors of calprotectin lead to reduction in disease activity due to blocking of this particle [7]. NETs are recognized as being involved in the pathogenesis of autoimmune diseases. This information may help researchers to develop new therapies and establish new markers of disease development, assessment of its stage of progression, and the monitoring of treatment [3,32].

## Conclusions

Patients with SLE demonstrate significantly higher serum calprotectin level as compared to healthy people. Calprotectin correlates with known markers of SLE exacerbation. Consistent with previous studies, serum calprotectin level was revealed to have potential as a rapid diagnostic biomarker of disease activity in patients with SLE.



**Table 5.** Differences in calprotectin value depending on clinical manifestation of SLE in the study group.

Variable	Median	p	Variable	Median	p
Form of disease			Arthralgia		
Kidney	3.05	0.3768	Yes	3.12	0.0942
Articular	3.18		No	3.01	
Dermal	3.08		Pleurisy		0.1416
Neuropsychiatric	3.82		Yes	3.92	
Haematological	3.16		No	3.09	
Photosensitivity			Pericarditis		
Yes	3.10	0.7673	Yes	3.06	0.8921
No	3.10		No	3.11	
Skin changes			Epilepsy		
Yes	3.10	0.7673	Yes	3.47	0.4510
No	3.11		No	3.10	
Erosions of the mucous membranes			Seizures		
Yes	3.17	0.3572	Yes	3.94	0.0938
No	3.10		No	3.10	
Tiredness			Psychosis		
Yes	3.11	0.3173	Yes	3.83	–
No	3.02		No	3.10	
Fever			Proteinuria		
Yes	3.16	0.1618	Yes	3.06	0.0711
No	3.06		No	3.21	
Raynaud's syndrome			Hematuria		
Yes	3.25	0.4392	Yes	3.05	0.4687
No	3.09		No	3.11	
Chair loss			Chronic kidney disease		
Yes	3.22	0.4097	Yes	3.04	0.3191
No	3.06		No	3.11	
Myopathy			Hepatomegaly		
Yes	3.94	0.0277*	Yes	3.76	0.3272
No	3.09		No	3.10	
Vasculitis			Splenomegaly		
Yes	3.25	0.1049	Yes	3.43	0.2922
No	3.06		No	3.11	
Arthritis			Lymphadenopathy		
Yes	3.10	0.9454	Yes	3.45	0.4022
No	3.10		No	3.10	

\* Statistically significant results.

### Declaration of Figures' Authenticity

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