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COMPLEMENT PROFILE, ANA TEST, AND ANTI-DSDNA IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) PATIENTS TREATED AT DR. SOETOMO GENERAL HOSPITAL SURABAYA 2022–2023

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Abstrak

Sistem komplemen merupakan bagian penting dari sistem kekebalan bawaan yang terdiri atas beberapa protein yang berperan dalam pertahanan tubuh terhadap infeksi, perbaikan jaringan, dan pembersihan kompleks imun. Komponen C3 dan C4 merupakan bagian utama dari sistem ini yang dapat menggambarkan aktivitas respon imun pada penyakit autoimun seperti Lupus Eritematosus Sistemik (LES). Penelitian ini bertujuan engetahui profil kadar komplemen (C3 dan C4), hasil ANA Test, dan kadar anti-dsDNA pada pasien Lupus Eritematosus Sistemik (LES) yang dirawat di Unit Rawat Inap RSUD Dr. Soetomo Surabaya periode 2022–2023. Penelitian ini menggunakan desain deskriptif retrospektif dengan data sekunder dari rekam medis pasien LES yang dirawat di RSUD Dr. Soetomo Surabaya. Variabel yang dianalisis meliputi karakteristik pasien (usia, jenis kelamin, pekerjaan), hasil pemeriksaan kadar komplemen C3 dan C4, hasil ANA Test, serta kadar anti-dsDNA. Hasil penelitian menunjukkan dari 1.978 data pasien LES, sebanyak 274 pasien memenuhi kriteria inklusi penelitian. Sebagian besar pasien berjenis kelamin perempuan (81%) dengan rentang usia terbanyak 15–19 tahun (28,1%). Pemeriksaan kadar komplemen menunjukkan bahwa 57,6% pasien memiliki kadar C3 di bawah normal, sedangkan 51,1% pasien memiliki kadar C4 dalam batas normal. Hasil ANA Test positif ditemukan pada 52,6% pasien, sementara 26,6% pasien menunjukkan kadar anti-dsDNA positif. Analisis korelasi Spearman menunjukkan hubungan negatif yang bermakna antara kadar anti-dsDNA dengan kadar C3 ($r = –0,498$; $p < 0,001$) dan C4 ($r = –0,561$; $p < 0,001$), yang berarti peningkatan kadar anti-dsDNA diikuti dengan penurunan kadar komplemen. Mayoritas pasien LES di RSUD Dr. Soetomo Surabaya merupakan perempuan usia produktif. Sebagian besar pasien menunjukkan penurunan kadar komplemen dan peningkatan kadar anti-dsDNA yang berkorelasi dengan aktivitas penyakit.

Kata Kunci: *Lupus Eritematosus Sistemik, komplemen, ANA Test, anti-dsDNA*

Abstract

The complement system is an important part of the innate immune system, consisting of several proteins that play a role in defending the body against infection, tissue repair, and immune complex clearance. Components C3 and C4 are major parts of this system that can describe immune response activity in autoimmune diseases such as systemic lupus erythematosus (SLE). This study aims to determine the complement levels (C3 and C4), ANA test results, and anti-dsDNA levels in patients with systemic lupus erythematosus (SLE) treated at the Dr. Soetomo General Hospital in Surabaya during the period 2022–2023. This study used a retrospective descriptive design with secondary data from the medical records of SLE patients treated at Dr. Soetomo General Hospital in Surabaya. The variables analyzed included patient characteristics (age, gender, occupation), C3 and C4 complement levels, ANA test results, and anti-dsDNA levels. The results showed that out of 1,978 SLE patient data, 274 patients met the inclusion criteria for the study. Most patients were female (81%) with the highest age range being 15–19 years (28.1%). Complement level tests showed that 57.6% of patients had below-normal C3 levels, while 51.1% of patients had normal C4 levels. Positive ANA test results were found in 52.6% of patients, while 26.6% of patients showed positive anti-dsDNA levels. Spearman's correlation analysis showed a significant negative correlation between anti-dsDNA levels and C3 levels ($r = –0.498$; $p < 0.001$) and C4 levels ($r = –0.561$; $p < 0.001$), meaning that an increase in anti-dsDNA levels was followed by a decrease in complement levels. The majority of SLE patients at Dr. Soetomo General Hospital in Surabaya were women of childbearing age. Most patients showed decreased complement levels and increased anti-dsDNA levels, which correlated with disease activity.

Keywords: *Systemic Lupus Erythematosus, complement, ANA Test, anti-dsDNA*

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INTRODUCTION

Systemic Lupus Erythematosus (SLE) is a complex systemic autoimmune disease involving multiple systems in the body. This disease has various phenotypes with varying clinical manifestations, ranging from mild symptoms to severe complications involving vital organs such as the kidneys, heart, and central nervous system. The development of SLE is influenced by various immunopathogenic pathways that interact with each other and cause immune system dysregulation (Vaillant, 2023).

Immunopathologically, SLE is characterized by the loss of immune tolerance to self-antigens, particularly to nuclear antigens released from cells undergoing apoptosis. This process promotes the formation of various autoantibodies against nuclear components, which then bind to form immune complexes and cause chronic inflammation. One of the main autoantibodies that plays an important role in this mechanism is the Antinuclear Antibody (ANA). ANA testing plays an important role in establishing the diagnosis of SLE because this antibody is the main immunological marker indicating an autoimmune reaction against nuclear components (Fanouriakis et al., 2021). In addition to serving as a diagnostic indicator, the presence of ANA also reflects excessive immune activity and the involvement of the adaptive immune system, which contributes to the process of tissue damage.

In addition to ANA, anti-double-stranded DNA (anti-dsDNA) antibodies are more specific immunological markers for SLE and are closely related to disease severity and activity. These antibodies react to double-stranded DNA in the cell nucleus and form immune complexes with endogenous DNA, which then induce systemic inflammation and cause tissue damage. These antibodies not only play a role in diagnosis but also serve as indicators of disease activity and clinical progression in SLE patients (Infantino et al., 2023; Ghirardello et al., 2023).

Beyond their diagnostic value, anti-dsDNA antibodies also have significant pathogenic significance in the course of SLE. Research by Ramos-Casals et al. (2023) explains that these antibodies play a role in the process of NETosis or the formation of neutrophil extracellular traps, which can exacerbate inflammation and accelerate tissue damage. Complement system activation induced by anti-dsDNA immune complexes with DNA enhances the inflammatory response and causes a decrease in complement protein levels, particularly C3 and C4, which are often used as parameters for assessing disease activity.

The complement system itself is an important component of the innate immune system, consisting of various plasma proteins with functions to defend the body against infection, repair tissues, and clear immune complexes. In addition, the complement system also plays a role in regulating the adaptive immune response through interaction with lymphocytes, as evidenced by the finding of C3 receptors on lymphocytes, which indicates the involvement of complement in adaptive immune mechanisms (Triggianese et al., 2023). Excessive activation of the immune system in SLE patients causes an increase in the formation of immune complexes that bind complement proteins such as C3 and C4. As a result, there is excessive consumption of complement proteins, which causes a decrease in serum complement levels, which in turn can reflect the level of disease activity (Yuliasih, 2020).

The aim of this study was to determine the characteristics of SLE patients treated at Dr. Soetomo General Hospital in 2022–2023 and to determine the complement level profile in SLE patients with organ manifestations of lupus nephritis, CNS lupus, hematology, and unspecified lupus treated at Dr. Soetomo General Hospital in 2022–2023, to determine the ANA test results in SLE patients treated at Dr. Soetomo General Hospital in 2022–2023, To determine the Anti-dsDNA levels in SLE patients treated at Dr. Soetomo General Hospital in 2022–2023, and to determine the correlation between Anti-dsDNA and complement levels in SLE patients treated at Dr. Soetomo General Hospital in 2022–2023.

Thus, complement level testing, ANA testing, and anti-dsDNA testing are important immunological tests in assessing the immunological status and disease activity in SLE patients. These tests not only aid in establishing a diagnosis but also have prognostic value in monitoring disease progression and treatment efficacy. Based on this, this study was conducted to determine the complement levels, ANA test results, and anti-dsDNA levels in patients with systemic lupus erythematosus (SLE) treated at the Inpatient Unit of Dr. Soetomo General Hospital in Surabaya in 2022–2023.

METHODS

This research design is a descriptive study using a retrospective approach. The data collected is secondary data from the medical records of LES patients treated at Dr. Soetomo General Hospital in 2022–2023. The data collected is data that meets the inclusion criteria and is not included in the exclusion criteria. The population studied in this research was all LES patients who received treatment at the Internal Medicine Inpatient Unit of Dr. Soetomo General Hospital in Surabaya. Meanwhile, the sample in this study was all LES patients in the Inpatient Unit of Dr. Soetomo General Hospital in 2022–2023. The sample size of this study was all LES patient data that met the inclusion criteria, so the sample size estimate used the total sampling method. This study design used the consecutive total sampling technique, meaning that each sample must meet the inclusion criteria and not meet the exclusion criteria. The inclusion criteria for this study were patients with a primary diagnosis of SLE, while the exclusion criteria included patients with SLE who did not have complete and accurate medical records. The variables in this study consisted of classification criteria, complement levels, ANA tests, and dsDNA.

The instrument used in this study was secondary data in the form of medical records of SLE patients treated at Dr. Soetomo General Hospital in Surabaya in 2022–2023. This study was

conducted at the Internal Medicine Inpatient Unit of Dr. Soetomo General Hospital in Surabaya. This study began with the preparation of a proposal from April to June 2024. Then, it was followed by data preparation and collection, which was carried out from January to August 2025. Data analysis was performed using descriptive statistical analysis and then processed using Microsoft Excel software.

Research Ethics Aspects

a. Confidentiality: This principle requires researchers to maintain the confidentiality of data and information collected from research subjects. In this study, all patient data collected from medical records will be kept confidential.

b. Non-Maleficence: This principle emphasizes the importance for researchers

to ensure that the use of medical records will not harm or cause harm to research subjects. In this study, researchers are responsible for ensuring that patient data remains secure and is used wisely, responsibly, and without causing harm.

RESULT AND DISCUSSION

The results of this study are a report of secondary data observations in the form of medical records of Systemic Lupus Erythematosus patients in the Inpatient Unit of Dr. Soetomo General Hospital, Surabaya, from 2022 to 2023. The initial data received was 1,978 patients, consisting of 691 patients with a first diagnosis of Systemic Lupus Erythematosus and 1,287 patients admitted to the hospital not due to a flare-up of Systemic Lupus Erythematosus, but due to other conditions unrelated to lupus disease activity.

Of the 691 patients, 416 were outpatients and 275 were inpatients. One patient out of the 275 was excluded due to clinical manifestations that did not meet the inclusion criteria.

Therefore, the sample size for this study was 274 patients. The results presented describe patient profiles, complement profiles, ANA tests, and anti-dsDNA. The correlation between anti-dsDNA levels and complement levels in these patients was also investigated.

Age, Gender, and Occupation of SLE Patients

Based on the analyzed data, the age distribution of the 274 Systemic Lupus Erythematosus patients studied was 77 (28.1%) in the 15-19 age range, and 12 (4.4%) in the 1-4 age range. Furthermore, 16 (5.8%) patients were found in the 5-9 age range, 60 (21.9%) in the 10-14 age range, 26 (9.5%) in the 20-24 age range, 25 (9.1%) in the 25-29 age range, and 58 (21.2%) in the 29 age range. The gender of the Systemic Lupus Erythematosus patients studied was significantly higher in female patients than male patients. There were 222 female patients (81%) and 52 male patients (19%). The occupational distribution of the Systemic Lupus Erythematosus patients studied was predominantly underage (students), with 147 (53.6%) being the most common. 85 (31%) were employed, and 42 (15.3%) were unemployed.

Complement C3 Level Profile

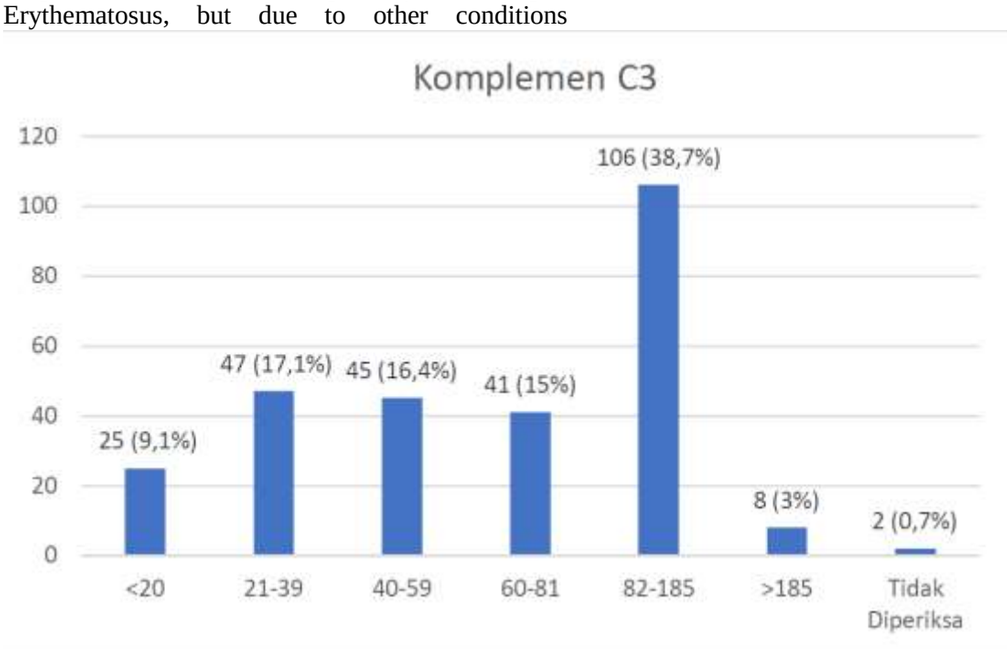

Figure 1. Bar Chart of Complement C3 Level Distribution in Systemic Lupus Erythematosus Patients in the Inpatient Unit of Dr. Soetomo Regional General Hospital, Surabaya 2022 – 2023.

Figure 1 shows the results of complement C3 levels in the studied patients with systemic lupus erythematosus. The normal complement C3 level range is 82-185 mg/dL, with 106 patients (38.7%) having elevated levels. Furthermore, 158 patients (57.6%) had decreased complement C3 levels, which were further categorized into several ranges. Eight patients (3%) had elevated complement levels (greater than 185 mg/dL), and two patients (0.7%) did not have their complement C3 levels measured. Therefore, the majority of patients experienced decreased C3 levels. Then, from all the complement C3 levels studied, the median result was 66 mg/dL.

Complement C49 Level Profile

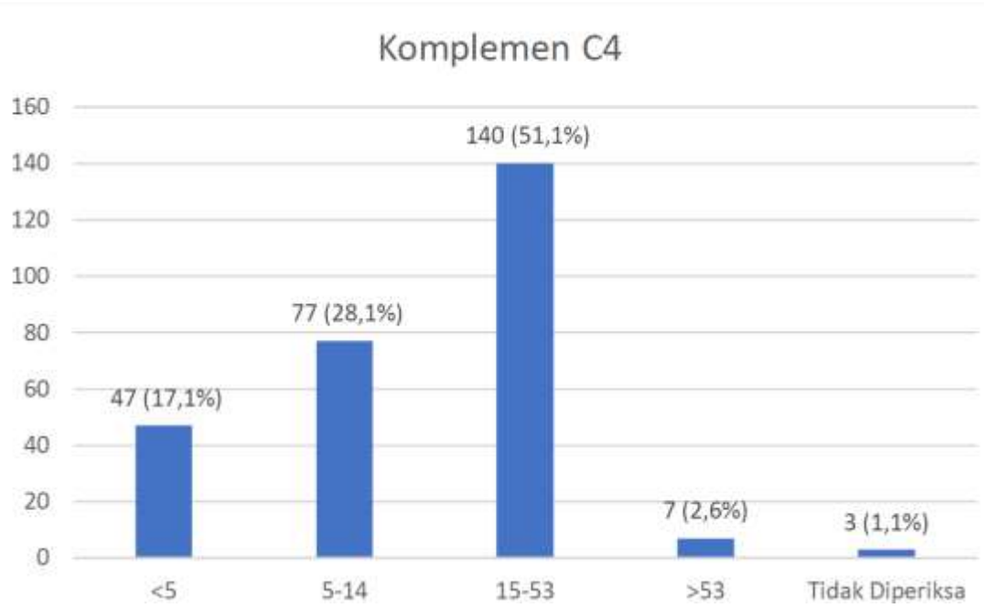

Figure 2. Bar Chart of Complement C4 Level Distribution in Systemic Lupus Erythematosus Patients in the Inpatient Unit of Dr. Soetomo Regional General Hospital, Surabaya, 2022 – 2023.

Based on Figure 2, the results of the complement C4 levels in the Systemic Lupus Erythematosus patients studied. The normal range of complement C4 levels is 15-53 mg/dL with a total of 140 patients (51.1%), then patients who experienced decreased complement C4 levels were 124 patients (45.2%), which were further categorized into 2 ranges of values. There were patients with complement C4 levels above normal (more than 53 mg/dL) namely 7 patients (2.6%), finally patients who did not undergo complement C4 level examination were 3 patients (1.1%). Thus, the largest number is patients with complement C4 levels within the normal range. Based on the overall complement C4 data, the median data was 16 mg/dL.

Range of Complement C3 and C4 Levels in Clinical Manifestations of CNS Lupus, Hematology, Lupus Nephritis, and Unspecified Lupus

Table 1. Distribution of Complement C3 and C4 Levels in Clinical Manifestations of CNS Lupus, Hematology, Lupus Nephritis, and Unspecified Lupus in Systemic Lupus Erythematosus Patients in the Inpatient Unit of Dr. Soetomo General Hospital, Surabaya, 2022–2023.

Clinical Manifestations		CNS Lupus	Hematology	Lupus Nephritis	Unspecified
Frequency (%)		18 (6,6%)	40 (14,6%)	139 (50,7%)	77 (28,1%)
Range C3	<20	3	5	12	5
	21-39	1	10	23	13
	40-59	4	11	17	13
	60-81	2	6	24	9
	82-185	7	7	58	34
	>185	-	-	5	3
	Not checked	1	1	-	-
Range C4	<5	3	14	18	12
	5-14	3	19	35	20
	15-53	12	6	82	40
	>53	-	-	3	4
	Not checked	-	1	1	1

Based on Table 1, complement C3 and C4 levels were studied in CNS lupus, hematologic lupus, lupus nephritis, and unspecified systemic lupus erythematosus patients. Of the 274 patients studied, the most common clinical manifestations were in lupus nephritis patients (139 patients) (50.7%), followed by unspecified SLE patients (77 patients) (28.1%), hematologic SLE patients (40 patients) (14.6%), and CNS lupus patients (18 patients) (6.6%). All clinical manifestations had a very low lower limit of complement C3 levels, 185 mg/dL. Furthermore, complement C4 levels were similar in that all four clinical manifestations had a relatively low lower limit, 53 mg/dL.

ANA Test Profile and Anti-dsDNA Profile

ANA test results in the Systemic Lupus Erythematosus patients studied. The majority of patients had a positive ANA test, at 144 (52.6%). A positive result is obtained if the antibody level is greater than or equal to 40 IU/mL. Furthermore, 82 patients (29.9%) had a negative ANA test, which is obtained if the antibody level is less than 40 IU/mL. Forty-eight patients (17.5%) did not undergo an ANA test. Meanwhile, the results of the Anti-dsDNA test in the Systemic Lupus Erythematosus patients studied. Anti-dsDNA is considered positive if the level is greater than or equal to 30 IU/mL. Of the 274 patients studied, 73 patients (26.6%) had a positive anti-dsDNA result, which is further categorized into several value ranges. Anti-dsDNA is declared negative if the Anti-dsDNA level is less than 30 IU/mL, there are 76 patients (27.8%) who have negative Anti-dsDNA results and are categorized into 2 value ranges. Of the 149 Anti-dsDNA level data studied, the median value was 23.65 IU/mL. However, the examination of Anti-dsDNA levels was not fully carried out because there were still 125 patients (45.6%) who did not undergo Anti-dsDNA level examination.

Anti-dsDNA Level Range in Clinical Manifestations of CNS Lupus, Hematology, Lupus Nephritis, and Unspecified Lupus

Table 2. Distribution of Anti-dsDNA Levels in Clinical Manifestations of CNS Lupus, Hematology, Lupus Nephritis, and Unspecified Lupus Erythematosus Patients in the Inpatient Unit of Dr. Soetomo General Hospital, Surabaya, 2022–2023.

Clinical Manifestations	Frequency (%)	<15	15-29	30-100	101-400	400-800	>800
CNS Lupus	6 (4,03%)	2	1	1	-	2	-
Hematology	16 (10,73%)	6	1	-	4	5	-
Lupus Nephritis	102 (68,46%)	47	7	19	6	21	2
Unspecified	25 (16,78%)	8	4	3	3	7	-

Based on Table 2, Anti-dsDNA levels in clinical manifestations of CNS Lupus, Hematology, Lupus Nephritis, and Unspecified Systemic Lupus Erythematosus patients were studied. Of the 149 patient data that underwent Anti-dsDNA level examination, 73 patients had positive Anti-dsDNA results, with a distribution of 3 patients with clinical manifestations of CNS Lupus, 9 patients with Hematology, 48 patients with Lupus Nephritis, and 13 patients with Unspecified. In addition, 76 patients had Negative Anti-dsDNA results, with a distribution of 3 patients with clinical manifestations of CNS Lupus, 7 patients with Hematology, 54 patients with Lupus Nephritis, and 12 patients with Unspecified. Therefore, the four clinical manifestations have diverse Anti-dsDNA level examination results.

Correlation of Anti-dsDNA Levels with Complement C3 and C4 Levels in Systemic Lupus Erythematosus Patients

	Kolmogorov-Smirnov[a]		
	Statistic	df	Sig.
KadarC3	.103	136	.001
KadarC4	.114	136	<.001
Anti-dsDNA	.360	136	<.001

a. Lilliefors Significance Correction

Figure 3. Results of the Normality Test of Complement C3, C4, and Anti-dsDNA Levels in Systemic Lupus Erythematosus Patients in the Inpatient Unit of Dr. Soetomo Hospital, Surabaya, 2022-2023.

Based on Figure 3, the results of the normality test for the complement variables C3, C4, and Anti-dsDNA show that all variables had significance values below 0.05 in the Kolmogorov-Smirnov test. This indicates that the three variables were not normally distributed. Because the data did not meet the assumption of normality, the analysis of the relationship between the variables was performed using a non-parametric test, namely the Spearman correlation test.

Table 3. Spearman Correlation Test Results Between Anti-dsDNA and C3 and C4 in Systemic Lupus Erythematosus Patients in the Inpatient Unit of Dr. Soetomo Hospital, Surabaya, 2022-2023.

		C3 levels	C4 levels	Anti-dsDNA
C3 levels	Sig. (2-tailed)	-	<0,001	<0,001
	N	137	137	136
C4 levels	Sig. (2-tailed)	<0,001	-	<0,001
	N	137	137	136
Anti- dsDNA	Correlation Coefficient	-0,498	-0,561	-
	Sig. (2-tailed)	<0,001	<0,001	-

N	136	136	136

*** Correlation is significant at the 0,01 level (2-tailed).*

Table 3 shows the results of the Spearman correlation test between Anti-dsDNA and complement C3 and Anti-dsDNA and complement C4. A significant negative correlation was found between Anti-dsDNA levels and complement C3 levels, with a correlation coefficient of r = -0.498 and a significance value of p < 0.001. These results indicate that increasing Anti-dsDNA levels are inversely proportional to complement C3 levels. In other words, as Anti-dsDNA levels increase, C3 levels tend to decrease.

Furthermore, the relationship between Anti-dsDNA and complement C4 levels also showed a significant negative correlation, with r = 0.561 and p < 0.001. This coefficient value indicates that the negative correlation between these two variables is stronger than the relationship between Anti-dsDNA and C3. This means that increasing Anti-dsDNA levels are associated with a more significant decrease in complement C4 levels.

Overall, the results of this analysis show that Anti-dsDNA levels have a statistically significant relationship with complement C3 and C4 levels, where an increase in Anti-dsDNA levels tends to be followed by a decrease in the levels of both complements in Erythematosus (SLE) patients.

Discussions

Systemic Lupus Systemic Lupus Erythematosus (SLE) is a systemic autoimmune disease that affects various organs in the body. This study used secondary data obtained from the medical records of SLE patients in the Inpatient Unit of Dr. Soetomo General Hospital in Surabaya during the period 2022–2023, which were analyzed and reported qualitatively. Of the total 1,978 patient data obtained, 691 patients had a first diagnosis of SLE, while the other 1,287 patients were hospitalized not because of a flare-up of systemic lupus erythematosus, but due to other conditions unrelated to lupus disease activity. Of the 691 patients, 416 were outpatients and 275 were inpatients. One patient from the inpatient group was then excluded because they did not meet the inclusion criteria, so the final sample used in this study was 274 patients.

This study focused on evaluating various aspects related to SLE patients. These aspects included patient profiles covering age, gender, and occupation, C3 and C4 complement levels, ANA test results, Anti-dsDNA levels, and clinical manifestations. In addition, this study also examined the relationship between Anti-dsDNA levels and C3 and C4 complement levels.

Age, Gender, and Occupation of SLE Patients

Based on the results of the study, of the 274 SLE patient data, the largest sample was in the 15 19 age group (28.1%). This shows that the majority of patients are of productive age.

These findings are consistent with previous studies, which show that Systemic Lupus Erythematosus (SLE) predominantly affects individuals of productive age. A study (Yanih, 2016) conducted in Surabaya showed that all respondents were SLE patients aged 18–37 years with an average age of 34 years, clearly falling within the productive age category. Similar findings were reported in Slovakia, where the first symptoms appeared on average at the age of 28 and the diagnosis was confirmed around the age of 29, with more than 80% of patients being in the 30–59 age range, which is classified as working age (Macejova et al., 2020). Furthermore, data from the RELESSER national registry in Spain showed that 84.4% of patients were classified as early-onset with an average age of diagnosis of 28.6 years, confirming that SLE most often appears before the age of 50 (Riveros Frutos et al., 2021). Overall, these three studies reinforce the evidence that SLE often occurs during productive age, which has a significant impact on the quality of life, daily activities, and work capacity of sufferers.

Research conducted by Charras et al. (2025) explains the causes of SLE, which generally appears during productive age. It explains that a high genetic burden can accelerate the onset of the disease, so that symptoms are often detected from adolescence to young adulthood. This is supported by research by Dai, Fan, and Zhao (2025), which places puberty to pre-menopause as the period with the highest incidence of SLE, making productive age the most vulnerable phase.

Then, in terms of gender, the results showed that of the 274 SLE patients studied, the number of female patients was far greater than that of male patients, namely 222 patients (81%). The results of this study support previous studies conducted both in Indonesia and other parts of the world. Yanih's (2016) study in Surabaya reported that the majority of LES patients were in the 15–45 age range, with a risk ratio of 9:1 for women to men, meaning that it was nine times more common in women. Then, on the island of Kalimantan, the results of a study by Aswin et al. (2023) in East and North Kalimantan also found a similar pattern, where almost all respondents in the study were women (98.1%).

Not only in Indonesia, this epidemiological picture was also seen in the RELESSER multicenter study in Spain by Riveros Frutos et al. (2021), which noted that most SLE patients were women with the onset of the disease occurring mainly in the second to fourth decades of life. The results of these various studies confirm that the predominance of women in SLE cases is not just a local phenomenon, but a recurring pattern in various parts of the world.

The reason why women dominate LES cases is explained through biological mechanisms closely related to the immune system and hormonal influences. Research by Sachdeva and Pal (2022) explains that the hormones estrogen and prolactin have immunostimulatory effects that strengthen B cell activation and increase autoantibody production, a mechanism that plays a direct role in the pathogenesis of SLE. Meanwhile, testosterone, which functions as an autoimmunity suppressor, is found at lower levels in women, thereby failing to

provide optimal protection against the onset of autoimmune diseases. This combination of hormonal factors makes women more susceptible to SLE than men, especially during their reproductive years.

In addition to hormonal factors, genetic predisposition also plays an important role in explaining the high incidence of SLE in women. Charras et al. (2025) reported that individuals with a high genetic burden tend to experience earlier onset of SLE and exhibit more severe symptoms, a condition more commonly observed in female patients. Another study by Dai, Fan, and Zhao (2025) also confirmed that globally, SLE occurs most frequently in women from puberty to menopause, reinforcing the understanding that women are the group at highest risk. Thus, it can be concluded that the predominance of women in the epidemiology of SLE is the result of a complex interaction between hormonal factors that increase immune system activity and genetic predisposition that accelerates the onset of symptoms, making women the group most vulnerable to this disease.

In terms of occupation, the study found that the most common occupation among SLE patients was underage (students) (53.6%). Not many previous studies have explicitly stated that certain types of work have a significant influence on the emergence of SLE. This is because SLE is not caused by external factors such as work, but by complex autoimmune mechanisms within the body. This process is more influenced by genetic, hormonal, and biological environmental factors than by a person's type or workload. However, previous studies have shown that SLE disease activity has an effect on the productivity of sufferers.

Blomjous et al. (2025) found that 63% of SLE patients who stopped working cited disease symptoms as the cause, with fatigue, pain, and the fluctuating nature of the disease proven to reduce work productivity and make it difficult for patients to maintain their jobs. Other factors such as longer disease duration and organ damage are also closely related to an increased risk of work disability. These results confirm that clinical symptoms play a major role in determining the continuity of employment status for SLE patients.

Additionally, research by Utset et al. (2015) showed that 31% of SLE patients experienced work disability, and 88% of them stated that their inability to work was due to their health condition. Pain, fatigue, depression, and cognitive impairment were found to be the main factors that increased the risk of absenteeism and reduced productivity (presenteeism). Meanwhile, Groot et al. (2021), who studied patients with childhood-onset SLE, found that 52% of working adults experienced decreased productivity, and 39% of them directly cited the disease as the cause. Symptoms such as chronic fatigue and organ damage from a young age greatly influence educational and career choices, causing many patients to stop working at a productive age.

Complement C3

This study shows that in the examination of complement C3 levels, the largest number of patients had decreased C3 levels, namely 158 patients (57.6%). Of these 158 patients, 41 patients had complement C3 levels in the range of 60-81 mg/dL, 45 patients with C3 complement levels in the range of 40-59 mg/dL, 47 patients in the range of 21-39 mg/dL, and 25 patients in the range of C3 complement levels below 20 mg/dL. These results indicate that the majority of SLE patients treated at Dr. Soetomo General Hospital in Surabaya from 2022 to 2023 tended to experience a decrease in C3 complement levels, with quite a range of C3 complement levels. These ranged from quite extreme decreases to below 20 mg/dL to decreases that were not too significant (60-81 mg/dL). Additionally, the distribution of patients across each category was relatively balanced, with approximately 40–50 patients in each category, except for the extreme decrease category (below 20 mg/dL), which only had 25 patients.

These results are in line with several previous studies. One of them is a study by Abas et al. (2021) at Dr. Soetomo General Hospital in Surabaya, Indonesia, which reported that 48% of SLE patients had low C3 levels and that this condition was significantly negatively correlated with disease activity. The study also showed that patients with normal C3 levels were more likely to be in remission, while patients with low C3 levels were more likely to experience moderate to severe flares. Ayano and Horiuchi (2023) in Japan also confirmed that hypocomplementemia or decreased complement levels were found in 50–89% of patients from the onset of SLE diagnosis, and a progressive decrease in complement levels could predict future relapses.

Furthermore, Rossi et al. (2022), who conducted a multicenter study in Italy (Parma University Hospital) and the United States (NIH and Johns Hopkins Hospital), showed that persistent isolated low C3 (PI-LowC3) is a strong predictor of the progression of lupus nephritis to end-stage renal failure, confirming that low C3 levels not only reflect disease activity but also serve as a prognostic biomarker. Finally, Sandhu and Quan (2017), through a literature review in Canada, wrote that many studies have proven a decrease in C3 in active SLE patients, although this is not always consistent in all cases due to individual variations in complement production and consumption. Thus, the findings of this study reinforce the evidence that decreased C3 levels are a common phenomenon in SLE patients, relevant both as an indicator of disease activity and as a predictor of long-term prognosis.

In SLE patients, decreased C3 complement levels are primarily caused by excessive consumption due to complement system activation. Pickering & Botto (2024) explain that the formation of immune complexes from anti-nuclear autoantibodies triggers activation of the classical pathway, which then depletes C3 along with C4 and causes hypocomplementemia as a characteristic serological feature of the disease. This statement reinforces the research conducted by Weinstein et al. (2021), which emphasizes that low C3 levels are not due to reduced production but rather to hypercatabolism caused by repeated activation. The main evidence is seen in the

increased levels of degradation fragments such as iC3b and C3dg, as well as a significantly higher iC3b/C3 ratio in patients with active disease compared to those with inactive disease.

In addition to the classical pathway, the alternative pathway also plays a role in accelerating the decline in C3 levels. Ayano & Horiuchi (2023) mention that C3 is the convergence point of all complement activation pathways, so when C3 is low while C4 remains normal, it indicates the involvement of the alternative pathway. This explanation is consistent with the review by Sandhu & Quan (2017), who found that low C3 levels are often accompanied by a decrease in factor B, indicating increased C3 turnover through amplification of the alternative pathway. Thus, the pathophysiology of C3 reduction in SLE patients can be understood as a result of the combined effects of excessive activation of the classical pathway by immune complexes and amplification of the alternative pathway, both of which increase the consumption of C3 protein in the circulation.

Complement C4

Furthermore, this study found that in the complement C4 level test, the largest number of samples were patients with complement C4 levels within the normal range, namely 140 patients (51.1%). This number was not significantly different from the number of patients with decreased C4 levels, which was 124 patients, with 77 patients having complement C4 levels in the range of 5-14 mg/dL and 47 patients having complement C4 levels below 5 mg/dL. These results indicate that the majority of SLE patients treated at Dr. Soetomo General Hospital in Surabaya in 2022–2023 tended to have normal C4 complement levels. However, the number of patients with decreased C4 complement levels cannot be considered small, as it is almost equal to the number of patients with normal C4 levels. Therefore, it can be concluded that C4 complement levels in LES patients treated at Dr. Soetomo General Hospital in Surabaya in 2022–2023 varied greatly. These results are interesting because most previous studies tended to state that C4 complement levels in LES patients generally decreased beyond normal limits. However, some studies still showed that LES patients could have normal C4 levels.

Ayano and Horiuchi (2023) explain that C4 levels can remain within normal limits, especially when complement activation is dominated by the alternative pathway, which consumes more C3 than C4. This condition means that patients can exhibit clinical symptoms of lupus with normal C4 levels, so complement biomarker interpretation should not be done in isolation. Furthermore, variations in the number of C4 gene copies also play a role in determining serum C4 levels, so there are groups of patients who have normal or even low C4 levels without a direct link to disease activity (Ayano & Horiuchi, 2023).

Another study conducted by Takamatsu et al. (2022) in Japan reported 21 SLE patients with normal C3, C4, and CH50 levels at diagnosis. Interestingly, patients with normal complement levels still met the classification criteria for SLE and exhibited different clinical characteristics, namely a lower frequency of kidney involvement and less frequent anti-dsDNA positivity compared to the group with hypocomplementemia. The study also showed that normal complement levels did not prevent the occurrence of typical lupus clinical symptoms and did not significantly affect prognosis (Takamatsu et al., 2022). Thus, it can be understood that the existence of SLE patients with normal C4 levels is a real phenomenon, and this needs to be considered in clinical evaluation for a more comprehensive assessment of the disease.

The cause of this phenomenon can be explained through pathophysiological mechanisms involving complement system activation, genetic factors, and physiological variations in the body. Activation of the classical pathway by immune complexes often results in excessive consumption of C4, thereby reducing its levels in the circulation. However, some patients maintain normal C4 levels due to genetic capacity and adequate complement protein synthesis. Weinstein et al. (2021) emphasize that complement levels can be chronically low or chronically normal, so they do not always correlate with disease activity, as they are influenced by variations in gene copy number and protein metabolism (“serum complement levels did not change over time and were chronically low or chronically normal”) (Weinstein et al., 2021). In some cases, the body can compensate for C4 degradation by increasing synthesis by hepatocytes after the complement system is activated. This mechanism serves to maintain the homeostasis of the immune system, so that C4 levels can return to near-normal values despite excessive consumption due to the formation of immune complexes.

From a genetic perspective, research by Pereira et al. (2019) shows that a low number of C4 gene copies, particularly C4A, significantly increases the risk of developing SLE and exacerbates the course of the disease. Patients with a low number of gene copies more often experience decreased C4 levels, while those with a normal or high number of gene copies are able to maintain C4 levels within the normal range even when the disease is active. These findings confirm that genetic variation plays a major role in determining C4 levels, as stated that “The risk of developing SLE was 3.59 times higher in subjects with low C4A GCN compared to those with normal or high GCN” (Pereira et al., 2019). Thus, C4 levels in SLE patients are the result of an interaction between consumption due to immune system activation and production capacity determined by genetic factors, so it is reasonable to find patients with normal or decreased C4 levels.

Range of Complement C3 and C4 Levels in Clinical Manifestations of CNS Lupus, Hematology, Lupus Nephritis, and Unspecified

This study shows the range of complement C3 and C4 levels in clinical manifestations of CNS Lupus, Hematology, Lupus Nephritis, and Unspecified. In all four manifestations, there are differences in complement C3 and C4 levels, as complement C3 and C4 levels vary among individuals, depending on disease activity or the amount of complement circulating in the systemic circulation.

In hematological clinical manifestations, C3 and C4 complement levels were predominantly decreased, consistent with findings in the literature described by Perge et al. (2024), who also found that C3 and C4 levels in patients with hematological manifestations of SLE tended to be lower than in patients without hematological disorders. This decrease in C3 and C4 is closely associated with increased disease activity, and reflects the high consumption of complement that occurs as part of an excessive immune response. Additionally, Huang et al. (2023) also reported that decreased C3 and C4 levels frequently occur in SLE patients with hematological manifestations, indicating the role of complement in the hematological pathogenesis of SLE and serving as a potential biomarker for assessing disease severity.

The decrease in C3 levels indicates higher complement consumption due to excessive immune complex formation, a characteristic feature of disease activity in SLE. This indicates stronger inflammation in the hematological system, leading to a decrease in red blood cells and platelets. Furthermore, the decrease in C4 levels indicates higher immune system activation, which plays a role in immune complex formation and inflammation in platelets and red blood cells. This shows that not only C3 is affected, but C4 also plays a role in hematological clinical manifestations.

Furthermore, complement levels in the clinical manifestations of Lupus Nephritis show that the majority of patients experience a decrease in C3 and C4 complement levels. These results are in line with research by Gasparotto et al. (2020). The study explains that lupus nephritis is the most common and most serious manifestation in SLE patients, with a prevalence of around 40% and generally appearing within the first five years after diagnosis. Gasparotto et al. also emphasized that kidney involvement is a major determinant of morbidity and mortality, as patients with lupus nephritis are at high risk of developing end-stage renal failure despite receiving modern therapy (Gasparotto et al., 2020). Not only that, research in Indonesia conducted by Hustrini et al. (2025) further reinforces this by showing that the prevalence of lupus nephritis reaches 40–60% in SLE patients, with class IV being the most commonly found type (39.6%). The researchers highlighted that delayed diagnosis, limited kidney biopsy facilities, and limited access to immunosuppressive therapy further worsened the prognosis of patients. This condition shows that lupus nephritis is not only dominant globally but also very significant in the Indonesian population (Hustrini et al., 2025).

Then, in unspecified clinical manifestations, the majority of C3 levels were below the normal range, but some patients with unspecified manifestations showed C4 levels that remained within the normal range. This is in line with the findings in a study by Huang et al. (2023), which showed that in SLE patients with nonspecific manifestations, decreased C3 levels were often found, even though C4 could remain within normal limits. This decrease in C3 indicates higher complement consumption caused by systemic inflammation, even though there is no specific organ involvement.

These results are also supported by research by Tan & Zhao (2021), which noted that in the group of patients with unspecified manifestations, decreased C3 levels were often found, while C4 levels in some patients remained within the normal range. This decrease in C3 levels indicates the formation of immune complexes and high immune activity, which are characteristic of SLE. Although the clinical manifestations do not point to specific organs, decreased C3 and C4 levels can be used as useful indicators of disease activity in monitoring the progression and therapy of SLE patients with unspecified manifestations.

Finally, CNS Lupus clinical manifestations yield different results compared to the previous three clinical manifestations. CNS Lupus patients do not experience a significant decrease in C3 levels like other clinical manifestations. Meanwhile, most patients show normal C4 levels. These results align with research by Khormi et al. (2023), where patients experiencing neurological symptoms as early signs of SLE, C4 levels remain within the normal range despite the presence of severe neurological disorders. This differs from other manifestations of SLE, in which C4 tends to show a significant decrease as an indicator of increased disease activity.

These findings reinforce the understanding that in CNS lupus manifestations, C3 and C4 levels often do not show a significant decrease, unlike other organ manifestations that exhibit more pronounced complement reduction. Therefore, even though neurological symptoms in CNS lupus can be very severe, C3 and C4 complement levels may remain within the normal range, indicating that complement level testing needs to be considered within a broader clinical context (Huang et al., 2023; Ragab et al., 2022).

ANA Test Results

Research shows that in ANA tests conducted on SLE patients treated at Dr. Soetomo General Hospital in 2022-2023, the most common result was a positive ANA test, with 144 patients (52.6%). A positive result was obtained if the antibody level was greater than or equal to 40 IU/mL. This result is in line with previous studies showing that the majority of patients with SLE generally have positive ANA test results as part of the main diagnostic criteria for this disease.

Research by Alsaed et al. (2021) in Qatar found that the ANA test, using both ELISA and IIF methods, showed high positive rates in SLE patients. This indicates that the ELISA-based method is superior in detecting nuclear antibodies in lupus patients (Alsaed et al., 2021).

Similar results were also obtained by Li et al. (2022) in China, who studied 617 newly diagnosed SLE patients. Of these, 604 patients (97.89%) were ANA positive, while only 13 patients (2.11%) were ANA negative. The researchers emphasized that this very high ANA positivity rate is consistent with various other research cohorts reporting ranges from 96.8% to 99.8%. Thus, ANA positivity remains a serological hallmark in most SLE patients (Li et al., 2022).

Finally, a study by Zakeri et al. (2023) in Iran involving 668 patients with suspected SLE showed that 15.42% of them were ANA positive with an average level of 36.44 U/mL, which was much higher than the negative group (3.34 U/mL). This study also found a significant correlation between positive ANA and anti-dsDNA levels, confirming that positive ANA is not only a serological phenomenon but is also closely related to the immunopathological activity of the disease (Zakeri et al., 2023).

The cause of positive ANA results in SLE patients can be explained by impaired immune tolerance, particularly in B cells, which leads to the production of autoantibodies against various nuclear components. These autoantibodies then form immune complexes with circulating nuclear antigens and deposit in tissues, triggering systemic inflammatory responses, tissue damage, and exacerbating disease activity (Zanussi et al., 2023). This mechanism is reinforced by abnormal B cell activation, accompanied by impaired T cell regulation and the important role of the type I interferon pathway in maintaining autoimmune activation (Li et al., 2022). Therefore, the high prevalence of ANA positivity in lupus not only serves as a diagnostic indicator but also reflects the complex pathophysiological basis of the disease (Al-Mughales, 2022).

Anti-dsDNA Profile

This study showed that of the 274 patients who underwent anti-dsDNA testing, 125 (45.6%) did not undergo anti-dsDNA testing. This represents the largest sample size. The remaining 149 patients were divided into 76 with negative anti-dsDNA results and 73 with positive anti-dsDNA results. Anti-dsDNA levels were considered positive if the anti-dsDNA level was greater than or equal to 30 IU/mL. These 73 patients with positive anti-dsDNA were further divided into several categories: 30-100 IU/mL (23 patients), 101-400 IU/mL (14 patients), 401-800 IU/mL (34 patients), and more than 800 IU/mL (2 patients). Higher anti-dsDNA levels indicate more severe disease activity. Therefore, it appears that SLE patients who test positive for anti dsDNA have varying levels and disease activity.

However, because the majority of samples were patients who did not undergo specific anti dsDNA testing, it is important to understand the results of other studies that can explain this. One study that explains this phenomenon is the study by Rojo et al. (2023). They stated that although anti dsDNA is an important classification criterion for SLE, this test has limitations due to antibody heterogeneity and a lack of standardization between testing methods, so its use is primarily focused on patients with clear clinical indications. This supports the finding that some patients are not tested for anti-dsDNA levels because the ANA test is the initial reference before further testing.

In addition to clinical factors and medical indications, the low number of anti-dsDNA tests may also be influenced by economic factors and policies in place at healthcare facilities. Anti dsDNA testing is a specific immunological test with a relatively high cost compared to the ANA test, so its implementation is often prioritized for patients with strong clinical indications or in cases requiring further monitoring. Furthermore, another possibility that needs to be considered is that some patients had undergone anti-dsDNA testing at other healthcare facilities before being admitted to Dr. Soetomo Regional General Hospital, so the testing was not repeated during the treatment period. Therefore, in addition to medical factors, economic aspects, financing policies, and the history of previous healthcare facility examinations also contributed to the low proportion of anti-dsDNA testing in Systemic Lupus Erythematosus (SLE) patients at the hospital.

Anti-dsDNA Level Ranges in Clinical Manifestations of CNS Lupus, Hematologic, Lupus Nephritis, and Unspecified Lupus

Distribution of anti-dsDNA levels in clinical manifestations of CNS lupus, hematologic, lupus nephritis, and unspecified lupus. It appears that each clinical manifestation has a relatively low lower range and a very high upper range. While this data could be expanded if more patients were tested for anti-dsDNA levels, it does provide a useful indication of how anti-dsDNA levels influence disease activity in each clinical manifestation.

In patients with positive anti-dsDNA test results, this phenomenon is supported by research by Damoiseaux & van Beers (2023). They reported that positive anti-dsDNA results were found in approximately 60% of SLE patients, particularly those with severe organ involvement such as lupus nephritis. This is supported by research by Wang et al. (2022) stated that this antibody is strongly correlated with kidney, skin, and central nervous system damage, as it forms immune complexes that deposit in target tissues and trigger complement activation and the release of pro-inflammatory cytokines.

However, Orme et al.'s (2022) study explains that variations in testing methods, such as ELISA, CLIFT, or CLIA, produce differences in sensitivity and specificity, which may explain why not all SLE patients test positive. This supports the negative anti-dsDNA results in SLE patients.

Regardless of whether the results are positive or negative, Yeo et al. (2024) found that fluctuating anti-dsDNA levels can predict disease flares, while persistently negative or positive levels have limited value for routine monitoring. Mechanistically, anti-dsDNA production stems from impaired clearance of dead cells, leading to overexposure of nuclear antigens to the immune system. This process activates dendritic cells, TLR7/TLR9, and the differentiation of autoreactive B cells, which produce pathogenic autoantibodies (Wang et al., 2022). These autoantibodies then bind to DNA or other cross-reactive antigens such as α actinin or NMDAR, triggering kidney tissue inflammation and nerve damage (Wang et al., 2022).

Therefore, the study's findings that the majority of patients did not undergo anti-dsDNA testing do not completely contradict the literature. However, they do reinforce the understanding that anti-dsDNA testing is not a universal test for all SLE patients, but rather is recommended in specific circumstances based on clinical suspicion and the

need to monitor disease activity. Furthermore, the fact that only about a quarter of patients in this study tested positive, consistent with previous reports, confirms that anti-dsDNA sensitivity is not 100% and is highly dependent on the testing method and the heterogeneity of SLE clinical subtypes (Damoiseaux & van Beers, 2023; Orme et al., 2022).

Correlation between Anti-dsDNA Levels and Complement C3 and C4

The study found that Anti-dsDNA levels had a weak negative (inverse) correlation with complement C3 and C4. Spearman's correlation test showed a correlation between Anti-dsDNA levels and C3 (rho = –0.498; $p < 0.001$) and C4 (rho = 0.561; $p < 0.001$). These results indicate that the majority of SLE patients treated at Dr. Soetomo General Hospital in 2022-2023 experienced increased Anti-dsDNA levels, followed by decreased C3 and C4 levels.

These correlation results align with the study by Ricchiuti et al. (2025) which compared five anti-dsDNA detection methods. Researchers found a consistent negative correlation between anti-dsDNA levels and both C3 and C4, with the ELISA method showing the strongest correlation (ρ = –0.81 for C3 and –0.65 for C4). This confirms that higher anti-dsDNA levels result in lower complement levels due to overconsumption as disease activity increases (Ricchiuti et al., 2025).

A study by Cai et al. (2022) also provided additional evidence for this relationship. They revealed that anti-dsDNA-positive patients had significantly higher levels of C3a fragments than controls, and there was a positive correlation between C3a and the SLEDAI score. These findings suggest that excessive complement activation due to anti-dsDNA immune complexes leads to an increase in C3 degradation products (C3a), while total C3 decreases. Thus, high anti-dsDNA levels are pathophysiologically associated with complement consumption, characterized by decreased C3 and C4 (Cai et al., 2022).

Giles and Boackle (2013) further strengthened this mechanism by explaining that anti-dsDNA antibodies form immune complexes with nuclear antigens, activating the classical complement pathway. This activation triggers the consumption of large amounts of C3 and C4, resulting in decreased levels during disease flares. They emphasized that this negative correlation is not merely laboratory-based but also reflects the pathogenesis of SLE, specifically tissue damage due to immune complex deposition (Giles & Boackle, 2013).

Finally, a study by Dhason et al. (2017) provided strong empirical evidence through an analysis of 300 SLE patients. The results showed a significant negative correlation between anti-dsDNA levels and C3 ($r = –0.432$; $p < 0.001$) and C4 ($r = –0.608$; $p < 0.001$). Furthermore, patients with very low C3 and C4 levels had higher SLEDAI scores, indicating more severe disease activity. Researchers concluded that the combination of anti-dsDNA testing along with C3 and C4 is the most useful serological marker in assessing lupus disease activity (Dhason et al., 2017).

CONCLUSION

Based on research conducted, the number of patients with systemic lupus erythematosus (SLE) treated at the Dr. Soetomo General Hospital Surabaya Inpatient Unit in 2022–2023 was 274 patients, with the most common age group being 15–19 years old (28.1%), with the majority being female (81%) and students (45.3%). The most common clinical manifestation in SLE patients was lupus nephritis (50.7%), with the most common complement C3 level test result being a decrease (57.6%) and complement C4 levels within the normal range (51.1%). ANA test results showed that most patients were positive (≥ 40.0 IU/mL) (52.6%). Anti-dsDNA testing showed that 73 patients (26.6%) were positive for Anti-dsDNA and 76 patients (27.8%) were negative.

The Spearman correlation test results showed a weak negative correlation between Anti dsDNA levels and C3 and C4 complement levels in SLE patients treated at Dr. This study has limitations in the data collection process, particularly regarding the completeness of patient medical records. The researchers encountered difficulties in obtaining complete laboratory test data, particularly for the Anti-dsDNA variable, so not all patients could be included in the comprehensive analysis. Therefore, the researchers suggest that further research be conducted with the support of more complete medical record data.

In addition, the electronic medical record (EMR) system is expected to not only contain diagnoses based on ICD-10, but also include other symptoms experienced by patients, because there are still ICD-10 diagnoses that are not in accordance with the symptoms experienced by patients. This will greatly help in improving the accuracy and completeness of research data. The implementation of this system is expected to facilitate the analysis process and enrich the research results.

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