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Prevalence of COVID 19 IGG among Cohort of SLE Egyptian Patients and Its Relation with SLE Disease Activity and Drug Intake Regimen

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Abstract

Background: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease that primarily impacts younger females and is defined by the generation of autoantibodies targeting nuclear and cytoplasmic antigens. Concurrently, coronavirus disease 2019 (COVID-19) is an infection designated as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

Objective: To detect the prevalence of COVID 19 IgG antibody among cohort of SLE Egyptian patients and its relation with disease activity and drug intake regimen.

Patients and methods: This study was conducted on a cohort of 100 SLE patients. Clinical data, counting medical history, physical examination findings, and laboratory investigation results were collected. The study assessed IgG COVID-19 antibody levels and analyzed their relationship with disease activity and the patients' drug regimens. Statistical analyses, including non-parametric tests and correlation analyses, were performed.

Results: COVID IgG antibodies were found to be positive in 91% of SLE patients who reported mild symptoms of COVID affection and there was significant relation between the history of fever and sore throat with the positivity of COVID IgG. No relation was found between patients on Hydroquine (HCQ), prednisone, mycophenolate or other immunosuppressants and COVID-19 IgG positivity.

Conclusion: These results offer reassurance regarding patients' capacities to produce a suitable antibody response following infection and their potential recurrence prevention with similar SARS-CoV-2 strains.

Keywords: Systemic lupus erythematosus, Autoimmune diseases, Coronavirus disease 2019, severe acute respiratory syndrome coronavirus 2.

INTRODUCTION

Systemic lupus erythematosus (SLE) is a chronic, systemic autoimmune disease that exhibits a predominant effect on younger females. The defining characteristic of SLE is the aberrant trigger of autoantibodies that are specifically aimed at nuclear and cytoplasmic antigens within the body. Although the exact etiology of this complex disease is not yet fully elucidated, a considerable number of genetic, epigenetic, and environmental risk factors identified as contributing to its pathogenesis [(1)].

The illness induced by a novel coronavirus, now officially known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2; previously referred to as 2019-nCoV), is denoted as coronavirus disease 2019 (COVID-19) [(2)]. The virus was initially detected during an outbreak of respiratory diseases in Wuhan City, located in Hubei Province, China. An initial report was submitted to the World Health Organization (WHO) by the end of 2019.

In January 2020, the WHO acknowledged the COVID-19 outbreak a global health emergency, and later

it was further classified as a global pandemic, marking the first declaration since H1N1 influenza pandemic [3]. It is reported that the main way COVID-19 spreads is human-to-human, through respiratory droplets or direct contact with infected people [4].

The infection itself can affect patients both with and without underlying diseases, although the majority of fatalities have been observed in older patients or those with significant comorbidities. The clinical presentations of COVID-19 have ranged widely, from completely asymptomatic or mild symptomatic cases to severe illness and death [5]. The most commonly reported symptoms have included fever, a persistent cough, and shortness of breath. Other frequently described symptoms encompass a general feeling of malaise, muscle pain, headaches, a sore throat, anosmia (loss of smell), severe fatigue, sputum production, diarrhea, and respiratory distress [6].

Aside from the initial symptoms, SARS-CoV-2 infection led to significant secondary complications. This encompasses the emergence of acute respiratory distress syndrome (ARDS), acute cardiac injury, and an increased vulnerability to subsequent secondary bacterial or fungal infections. The significance of these complications is evident in the substantial percentage of patients—data shows this figure can be as high as 23%—who have needed to be admitted to the intensive care unit (ICU) for advanced medical assistance. This underscores the virus's potential to inflict serious, multi-organ damage beyond the usual respiratory illness, given the gravity of their condition [7].

The detection of IgM and IgG antibodies through rapid testing can be a valuable tool for identifying both potential asymptomatic infections and past exposures to the virus. Specific IgM antibodies to SARS-CoV-2 typically become detectable in the bloodstream 3 to 5 days after the onset of symptoms, although the strength and timing of this immune response can exhibit considerable variability among different patients [8]. This variability underscores the need for a multifaceted diagnostic approach.

IgG antibodies develop in most patients at around 2 weeks after infection and remain in the blood after you have recovered although we don`t presently know how long it may persist and it is unknown at this point how much protection it provides [9].

The primary objective of this investigation was to thoroughly evaluate and determine the prevalence of COVID-19 IgG antibodies within a specific cohort of Egyptian patients with systemic lupus erythematosus (SLE). A key secondary aim of the study was to explore the potential correlations between the seroprevalence of these antibodies and two critical factors: the patients' disease activity and their specific pharmacological treatment regimens.

PATIENTS AND METHODS

This study included a total of 100 adult patients diagnosed with systemic lupus erythematosus (SLE) who were recruited from the Rheumatology Outpatient Clinic and the Internal Medicine and Rheumatology Inpatient departments at Ain Shams University Hospitals between January and September 2020. The primary objective was to determine the prevalence of IgG COVID-19 antibodies among Egyptian SLE patients and to explore its relationship with disease activity and their medication regimens. The diagnosis of SLE was confirmed based on the 2012 Systemic Lupus International Collaborating Clinics (SLICC) classification criteria [10].

Disease activity was assessed using the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) [11], which was categorized into five levels: inactive (SLEDAI = 0), mild (SLEDAI = 1-5), moderate (SLEDAI = 6-10), severe (SLEDAI = 11-19), and very high (SLEDAI > 20).

Patients with other autoimmune diseases or any co-existing chest diseases were excluded.

Laboratory investigations:

These included a complete blood count (CBC), erythrocyte sedimentation rate (ESR) measured by the Westergren method, and C-reactive protein (CRP) via ELISA. Complement proteins C3 and C4 were analyzed with a latex agglutination test. Standard renal and liver function tests were performed, including urine analysis, 24-hour urinary protein, creatinine clearance, liver enzymes (AST and ALT), serum creatinine, and uric acid level. The prevalence of COVID-19 IgG antibodies was assessed using a microparticle-based ELISA, with the test strips coated with S1, S2, and whole spike proteins. The

antibody concentration, proportional to the signal intensity, was measured photometrically after detection with alkaline phosphatase-labeled secondary antibodies.

Positive results were defined by a COVID-19 IgG antibody titer greater than 10 U/ml, while negative results had a titer less than 10 U/ml.

Ethical approval: The research protocol for this study underwent a rigorous review and obtained ethical approval from the **Ethical Committee of Ain Shams University**, with the assigned IRB number 000017585. The entire investigation was carried out in compliance with the ethical principles outlined in the **Declaration of Helsinki**, a globally recognized standard for medical research involving human subjects. Prior to their enrollment in the study, all participants were required to provide their **written informed consent**. This crucial step ensured that their participation was both voluntary and fully informed, thereby upholding the fundamental rights and autonomy of all individuals involved. Data collection from the patients commenced only after this consent was secured and the study had received all necessary ethical committee approvals, thereby ensuring the protection and autonomy of all individuals involved.

Statistical analysis:

Statistical analyses were conducted with IBM SPSS Statistics software, version 20 (IBM Corp., Armonk, NY, USA). Descriptive statistics were leveraged to compile the data. Continuous variables were displayed as means ± standard deviations for data that were normally distributed, and as medians with interquartile ranges for data with a skewed distribution. Categorical variables were summarized using frequencies and percentages. To evaluate relationships among variables, a series of statistical tests were employed. The chi-square ($\chi 2$) test was leveraged for comparing categorical variables, with Fisher's exact test serving as an alternative when the expected cell count in any cell was less than 5, thereby ensuring the validity of the statistical analysis in cases involving small sample sizes. For comparing continuous variables between two distinct groups, the Mann-Whitney U test, a non-parametric method, was used when the data did not satisfy the assumptions of normality. Conversely, the independent samples t-test, a parametric test, was applied when the data met the assumptions of normality and equal variances. For the correlation analysis, Spearman's rank correlation coefficient (ρ) was calculated to rigorously evaluate the monotonic relationship between two continuous variables. This non-parametric method was specifically chosen for its suitability when the data did not conform to a normal distribution. To determine the statistical significance of all tests, a two-sided p-value was utilized. A p-value greater than 0.05 was interpreted as not statistically significant. Conversely, a p-value less than 0.05 was considered to be statistically significant, while a p-value less than 0.01 was designated as highly statistically significant. These specific thresholds were applied to ensure the reliability and interpretability of the study's findings.

RESULTS

- A total of 100 SLE patients were included in the study; aged between 18-56 years old of which 94 were females and 6 males of which 4% were diabetics and 32% were hypertensive, 5 % 0f the studied patients were cigarette smokers, SLE disease duration ranged from8 months to 16 years.
- Positive COVID IgG antibody was positive in 91% of the studied SLE patients. 10% of SLE patients in our study were known to be COVID infected and this was confirmed by PCR.

Comparative analyses were performed to investigate the differences between SLE patients with positive and negative COVID-19 IgG antibody results. The study systematically compared the two groups based on the duration and clinical manifestations of their SLE (Table 1), their complete drug history (Table 2), and a full set of laboratory parameters (Table 3).

Table (1): Comparison between SLE patients with positive and negative COVID IgG antibody results regarding the duration and manifestation of SLE

		COVID IgG antibodies by Elisa		**T-Test**		**significance**
		Negative	**Positive**	**t**	**P-value**	
Duration of SLE(years)	**Range**	1 - 12	0.08 - 16	-0.404	0.687	N.S

	Mean ±SD	5.444 ± 3.745		6.051 ± 4.342				
Chi-Square		**N**	**%**	**N**	**%**	**X^2**	**P-value**	
Arthritis	**No**	0	0	4	4.40	0.412	0.521	N.S
	Yes	9	100	87	95.60			
Renal affection	**No**	7	77.78	35	38.46	5.197	**0.023***	**S**
	Yes	2	22.22	56	61.54			
neurological affection	**No**	8	88.89	77	84.62	0.117	0.732	N.S
	Yes	1	11.11	14	15.38			
Cutaneous	**No**	0	0	11	12.09	1.222	0.269	N.S
	Yes	9	100	80	87.91			
Oral and nasal ulcers	**No**	7	77.78	41	45.05	3.514	0.061	N.S
	Yes	2	22.22	50	54.95			
Alopecia	**No**	4	44.44	31	34.07	0.388	0.533	N.S
	Yes	5	55.56	60	65.93			
Hematological affection	**No**	6	66.67	49	53.85	0.544	0.461	N.S
	Yes	3	33.33	42	46.15			
Leucopenia	**No**	8	88.89	71	78.02	0.583	0.445	N.S
	Yes	1	11.11	20	21.98			
Anemia	**No**	8	88.89	53	58.24	3.233	0.072	N.S
	Yes	1	11.11	38	41.76			
Thrombocytopenia	**No**	9	100	78	85.71	1.478	0.224	N.S
	Yes	0	0	13	14.29			
Cardiac affection	**No**	7	77.78	58	63.74	0.710	0.400	N.S
	Yes	2	22.22	33	36.26			
Serositis	**No**	6	66.67	61	67.03	0.000	0.982	N.S
	Yes	3	33.33	30	32.97			
Antiphospholipid	**No**	8	88.89	71	78.02	0.583	0.445	N.S
	Yes	1	11.11	20	21.98			

N.S: not significant S: significant

Table (2): Comparison between SLE patients with positive and negative COVID IgG antibody results regarding drug history

		COVID IgG antibodies by Elisa				**Chi-Square**		**significance**
		Negative		**Positive**				
		N	**%**	**N**	**%**	**X^2**	**P-value**	
Steroids	**No**	0	0	1	1.10	0.100	0.752	N.S
	Yes	9	100	90	98.90			
T-Test						**t**	**P-value**	
Steroids Dose(mg)	**Range**	10 - 30		5 - 60		-0.726	0.469	N.S
	Mean ±SD	22.222 ± 6.667		24.444 ± 8.914				
Chi-Square		**N**	**%**	**N**	**%**	**X^2**	**P-value**	
Hydroxychloroquine	**No**	0	0	17	18.68	2.026	0.155	N.S
	Yes	9	100	74	81.32			
T-Test						**t**	**P-value**	
Hydroxychloroquine Dose(mg)	**Range**	200 - 400		200 - 400		0.483	0.630	N.S
	Mean	377.77 ± 66.66		364.86 ± 76.62				

	±SD	8	7	5	8			
Chi-Square		**N**	**%**	**N**	**%**	**X^2**	**P-value**	
Azathioprine	**No**	4	44.44	41	45.05	0.001	0.972	N.S
	Yes	5	55.56	50	54.95			
T-Test						**t**	**P-value**	
Azathioprine Dose(mg)	**Range**	100 - 100		100 - 400		-0.625	0.534	N.S
	Mean ±SD	100 ± 0		117 ± 60				
Chi-Square		**N**	**%**	**N**	**%**	**X^2**	**P-value**	
Mycophenolate mofetil	**No**	5	55.56	62	68.13	0.586	0.444	N.S
	Yes	4	44.44	29	31.87			
T-Test						**t**	**P-value**	
Mycophenolate mofetil Dose (gm)	**Range**	2 - 2		1 - 3		0.434	0.667	N.S
	Mean ±SD	2 ± 0		1.897 ± 0.470				
Chi-Square		**N**	**%**	**N**	**%**	**X^2**	**P-value**	
Cyclophosphamide	**No**	7	77.78	61	67.03	0.435	0.510	N.S
	Yes	2	22.22	30	32.97			
T-Test						**t**	**P-value**	
cyclophosphamide Dose (gm)	**Range**	4 - 6		1 - 6		1.234	0.227	N.S
	Mean ±SD	5 ± 1.414		3.233 ± 1.977				
Chi-Square		**N**	**%**	**N**	**%**	**X^2**	**P-value**	
Calcium	**No**	0	0	2	2.20	0.202	0.653	N.S
	Yes	9	100	89	97.80			
T-Test						**t**	**P-value**	
Calcium Dose(mg)	**Range**	1500 - 1500		1500 - 1500		-	-	N.S
	Mean ±SD	1500 ± 0		1500 ± 0				
Chi-Square		**N**	**%**	**N**	**%**	**X^2**	**P-value**	
Vitamin D	**No**	0	0	2	2.20	0.202	0.653	N.S
	Yes	9	100	89	97.80			
Proton pump inhibitors	**No**	0	0	2	2.20	0.202	0.653	N.S
	Yes	9	100	89	97.80			

Mg: milligram

Table (3): Comparison between SLE patients with positive and negative COVID IgG antibody results regarding SLEDAI score

		COVID IgG antibodies by Elisa				**T-Test**		**significance**
		Negative		**Positive**		**t**	**P-value**	
SLEDAI score	**Range**	2 - 8		0 - 29		-1.457	0.148	N.S
	Mean ±SD	4 ± 2		6.912 ± 5.938				
Chi-Square		**N**	**%**	**N**	**%**	**X^2**	**P-value**	
SLEDAI Degree	**Mild**	8	88.89	51	56.04	3.776	0.151	N.S
	Moderate	1	11.11	28	30.77			
	Severe	0	0	12	13.19			

N.S: not significant, SLEDAI : systemic lupus erythromatousus disease activity index

Furthermore, a direct comparison of SLE disease activity was conducted using the SLEDAI score for both patient groups (Table 4).

Table (4): Comparison between SLE patients with positive and negative COVID IgG antibody results regarding laboratory data

		COVID IgG antibodies Elisa		T-Test		
		Negative	Positive	t	P-value	
Total leucocytic count(10^3/uL)	**Range**	3.5 - 7.9	1.7 - 18.5	-1.341	0.183	N.S
	Mean ±SD	5.167 ± 1.556	6.625 ± 3.214			
Neutrophils(10^3/uL)	**Range**	2 - 5	1 - 11.9	-1.502	0.136	N.S
	Mean ±SD	3.022 ± 1.087	4.099 ± 2.116			
Lymphocytes(10^3/uL)	**Range**	1 - 2.5	0.2 - 4.6	0.515	0.608	N.S
	Mean ±SD	1.700 ± 0.497	1.563 ± 0.783			
Hemoglobin(10^3/uL)	**Range**	7 - 14	5 - 14.7	2.603	**0.011***	**S**
	Mean ±SD	12.111 ± 2.205	10.385 ± 1.868			
Platelets(10^3/uL)	**Range**	154 - 451	10 - 458	0.866	0.389	N.S
	Mean ±SD	270.889 ± 111.252	241.538 ± 95.666			
Erythrocyte sedimentation rate(mm/hour)	**Range**	14 - 60	5 - 140	-2.217	**0.029***	**S**
	Mean ±SD	29.889 ± 17.961	54 ± 32.036			
C- reactive protein (mg/l)	**Range**	4 - 20	0.6 - 278	-1.198	0.234	N.S
	Mean ±SD	6.556 ± 5.126	20.856 ± 35.604			
Complement 3 (C3)	**Range**	54 - 98	30 - 205	1.011	0.314	N.S
	Mean ±SD	81.778 ± 14.507	72.385 ± 27.397			
Complement 4 (C4)	**Range**	7 - 33	2 - 93	1.465	0.146	N.S
	Mean ±SD	19.556 ± 9.409	14.054 ± 10.861			
24hr urinary protein (mg/day)	**Range**	50 - 1500	25 - 7685	-1.551	0.124	N.S
	Mean ±SD	318.556 ± 465.743	1202.246 ± 1695.426			
Aspartate amino transferase (IU/L)	**Range**	7 - 30	7 - 226	-1.060	0.292	N.S
	Mean ±SD	14.556 ± 7.650	24.242 ± 27.202			
Alanine amino transferase (IU/L)	**Range**	8 - 45	7 - 152	-0.491	0.624	N.S
	Mean ±SD	20 ± 11.990	23.286 ± 19.651			
Serum Creatinine (mg/dl)	**Range**	0.4 - 1.3	0.5 - 8.1	-0.899	0.371	N.S
	Mean ±SD	0.833 ± 0.269	1.132 ± 0.988			
Serum Uric acid (mg/dl)	**Range**	3 - 6	1.7 - 12.7	-2.11	**0.037***	**S**
	Mean ±SD	4.333 ± 1	5.843 ± 2.115			

						1		
Urinary pus cells (H.P.F)	**Range**	0 - 25		0 - 100		-0.696	0.488	N.S
	Mean ±SD	3.889 ± 7.944		7 ± 13.132				
Urinary RBCs (H.P.F)	**Range**	1 - 10		0 - 35		-0.712	0.478	N.S
	Mean ±SD	2.333 ± 2.915		3.736 ± 5.823				
Chi-Square		**N**	**%**	**N**	**%**	**X^2**	**P-value**	
Urinary Casts(L.P.F)	**No**	8	88.89	80	87.91	0.007	0.931	N.S
	Yes	1	11.11	11	12.09			

N.S: not significant S: significant (IU/L): International units per litre (mg/l): milligrams per liter (mm/hour): millimeters per hour (mg/day):milli gram per day (mg/dl): Milligrams per decilitre (H.P.F): high power field (L.P.F): Low-pass filter (g/dL): Grams per decilitre (10^3/uL): 1000/unit litre

A separate correlation analysis was also performed to examine the relationship between the SLEDAI score after RIF and other relevant parameters, with the findings documented in a dedicated table (Table 5).

Table (5): Correlations between COVID IgG antibody titre and duration of SLE, SBP, DBP, different used drugs doses in SLE treatment, SLEDAI score and variable lab data

Correlations			**Significance**
	IgG Titre		
	R	**P-value**	
Duration of SLE	0.092	0.609	N.S
Systolic blood pressure	-0.143	0.426	N.S
Diastolic blood pressure	-0.084	0.642	N.S
Steroids Dose	-0.290	0.107	N.S
Hydroquinone Dose	-0.192	0.337	N.S
Azathioprine Dose	-0.256	0.399	N.S
Mycophenolate mofetil Dose	0.339	0.199	N.S
cyclophosphamide Dose	-0.172	0.613	N.S
SLEDAI score	-0.101	0.577	N.S
Total leucocytic count(10^3/uL)	0.140	0.436	N.S
Neutrophils(10^3/uL)	0.153	0.394	N.S
Lymphocytes(10^3/uL)	-0.004	0.984	N.S
Hemoglobin level(g/dl)	0.020	0.910	N.S
Platelets(10^3/uL)	-0.120	0.508	N.S
Erythrocyte sedimentation rate(mm/hour)	-0.030	0.866	N.S
C-reactive proteins(mg/l)	-0.227	0.203	N.S
Complement 3 (C3)	-0.066	0.715	N.S
Complement 4 (C4)	-0.092	0.612	N.S
24hr urinary protein(mg/day)	-0.027	0.882	N.S
Aspartate amino transferase(IU/L)	0.000	1.000	N.S
Alanine amino transferase(IU/L)	-0.153	0.395	N.S
Creatinine(mg/dl)	-0.091	0.614	N.S
Uric acid(mg/dl)	0.025	0.890	N.S
Urine pus(H.P.F)	-0.253	0.156	N.S
Urine RBCs(H.P.F)	-0.289	0.102	N.S

N.S: not significant (IU/L): International units per litre (mg/l): milligrams per liter (mm/hour):

millimeters per hour (mg/day):milli gram per day (mg/dl): Milligrams per decilitre (H.P.F): high power field (L.P.F): Low-pass filter (g/dL): Grams per decilitre (10^3/uL): 1000/unit litre.

DISCUSSION

Systemic lupus erythematosus (SLE) is an autoimmune disorder marked by a breakdown in immunological self-tolerance, leading to the generation of nuclear autoantigens and immune complexes that trigger inflammation across various organ systems. The global pandemic of Corona Virus Disease-19 (COVID-19), caused by the novel Severe Acute Respiratory Syndrome Corona Virus 2 (SARS-CoV-2), presents a diverse range of clinical outcomes, from asymptomatic to severe conditions like pneumonia [12, 13]. Early in the pandemic, it was hypothesized that individuals with autoimmune rheumatic diseases (AIRDs) such as SLE and rheumatoid arthritis (RA) might face a higher risk of SARS-CoV-2 infection due to an impaired immune defense, either from their disease or its treatment. This supposition was based on historical data from previous SARS and MERS outbreaks, which linked immunosuppression to delayed viral clearance and an increased incidence of secondary infections [14].

Our study's primary objective was to determine the seroprevalence of COVID-19 IgG antibodies in a cohort of 100 Egyptian SLE patients and to assess any correlation between antibody status, SLE disease activity, and their prescribed therapeutic regimens. The cohort, comprising patients aged 18 to 60, was recruited from both the outpatient and inpatient departments of Rheumatology at Ain Shams University Hospital. All participants provided informed consent, and their SLE diagnosis was confirmed using established clinical criteria. Patients with other autoimmune conditions were excluded. Each participant underwent a comprehensive medical history review, including a detailed inquiry about any past COVID-19 symptoms, and a thorough clinical examination.

The results demonstrated a high seropositivity rate, with 91% of the SLE patients testing positive for COVID-19 IgG antibodies via ELISA, while only 9% were seronegative. This finding stands in contrast to the study by **Saxena et al.** [15], which reported a positive SARS-CoV-2 IgG antibody test in only 16% (51 of 329) of their SLE patient cohort. The high seroconversion rate observed in our population suggests that the immune response in the majority of lupus patients is robust enough to combat the SARS-CoV-2 virus, even in the context of ongoing immunosuppressive therapy [15].

10% of the studied SLE patients were confirmed to be COVID positive by PCR this is in contrast to study done on SLE patients on Lombardy region by **Ramirez et al.** [16] where 12 out of 417 patients (2.8%) only were confirmed to be COVID positive by PCR, also **Espinosa et al.** [17] found that only 1.0% out of 150 SLE patients in Catalonia were classified as confirmed cases of COVID-19.

In this study there was significant relation between history of lupus nephritis and the presence of COVID IgG antibodies among SLE patients, as in the IgG positive 61.54% had lupus nephritis while negative group 22.22% with **P value 0.023**

In contrast, the study reported by **Ramirez et al.** [16] showed that patients had higher prevalence of neuropsychiatric symptoms.

In this study there was no significant relation between COVID IgG antibody titre and the SLEDAI score, while **Zonana et al.** [18] who performed his study on 200 Mexican SLE patients reported that there was significant relation between infections in SLE and SLEDAI score.

The difference between our study results and the other studies regarding SLEDAI score was because most of the patients involved in our research were evident to be COVID IgG positive reflecting past infection of COVID and not being in acute infection.

In this study there was no significant relation between the positivity of COVID IgG antibodies and intake of steroids, hydroxychloroquine (HCQ) and other immune suppressive drugs this is in concordance with results published by **Ramirez et al.** [16] who showed that no relation was found among patients on HCQ, prednisone and COVID IgG antibodies.

Also, **Konig et al.** [19] reported that rheumatic medications do not overly increase the risk of COVID-19.

According to **Mitja et al.** [20], the evidence for hydroxychloroquine's effectiveness as a prophylactic treatment was largely negative, making it an unlikely factor for the lower seroprevalence observed. This indicates that while the medication does not appear to affect the presence of COVID-19 IgG antibodies, its use may be linked to milder COVID-19 symptoms.

This study found no statistically significant association between the presence of COVID IgG antibodies and either leukopenia or thrombocytopenia. This finding, however, stands in contrast to the results of other investigations. For instance, **Ramirez et al.** [16] reported a high prevalence of leukopenia, particularly lymphopenia, among their cohort of patients with systemic lupus erythematosus and COVID-19. Specifically, their data indicated that 36% of these patients presented with leukopenia and 28% with thrombocytopenia, highlighting a potential difference in outcomes based on patient population characteristics.

Evidence indicates that lymphocytes possess the ACE2 receptor on their cell surface, which allows SARS-CoV-2 to directly infect these cells [21]. This infection may ultimately lead to the lysis of the lymphocytes, contributing to lymphopenia observed in COVID-19.

Our study showed no significant relation between the positivity of COVID IgG antibodies and C-reactive protein.

This is in contrast with **Lippi & Plebani** [22] who performed his study on 470 COVID patients showed that C-reactive protein increased in 75-93% of patients with acute COVID-19 infection particularly in severe disease.

The elevated levels of C-reactive protein (CRP) observed in patients with severe COVID-19 may be directly linked to the excessive production of pro-inflammatory cytokines. While these cytokines are integral to the host's defense against pathogens, an uncontrolled, hyperactive immune response can result in significant damage to vital organs, particularly lung tissue. As a consequence, CRP production is triggered not only by the systemic inflammatory cytokines but also by the direct tissue destruction that characterizes severe COVID-19 [23]. The relationship between CRP and inflammation is also relevant in other systemic diseases. For example, in a study by **Wang et al.** [24] that evaluated the diagnostic utility of C-reactive protein and procalcitonin in 177 SLE patients, it was found that CRP levels were higher in patients with inactive SLE who had a co-existing infection compared to those with inactive SLE who were not infected. This highlights CRP's role as a marker for systemic inflammation beyond baseline disease activity.

The difference between our study results and the other studies regarding CRP level was because most of the patients included in our study were evident to be COVID IgG positive reflecting past infection of COVID and not being in acute infection.

In this study there was significant relation between the positivity of COVID IgG antibodies and ESR with P value 0.029.

COVID-19 might precipitate alterations in the morphology of erythrocytes or the biochemical properties of plasma, through a yet-to-be-defined mechanism. This process is hypothesized to result in an increased erythrocyte sedimentation rate (ESR) [25], a biomarker commonly associated with inflammation and infection.

These results may be attributed to the presence of significant relation between the positivity of COVID IgG antibodies and anemia which is usually associated with high ESR in addition to significant correlation between COVID IgG antibodies and lupus nephritis in our study which also may explain the significance of high ESR as high ESR reflect active nephritis**.**

Hou et al. [26] who performed his study on 173 SLE patients to evaluate the clinical characteristics and infections in SLE patients**,** reported that ESR rises more in infected SLE patients than non-infected SLE patients, Also **Schäfer et al.** [27] who performed his study on 371 SLE patients 48 of them had infection, reported that there was significant relation between ESR and infections in SLE patients

In this study, a statistically significant difference was observed in hemoglobin levels between the two cohorts of patients with systemic lupus erythematosus. Specifically, the group of patients who tested

positive for COVID IgG antibodies had a lower mean hemoglobin level than the group who tested negative for the antibodies. This finding was supported by a p-value of 0.011, which indicates a strong statistical association.

The findings of this study are consistent with a meta-analysis conducted by **Taneri et al.** [28], which demonstrated that hemoglobin levels were significantly reduced in patients afflicted with **COVID-19**. Further support is provided by **Bellman et al.** [29], who additionally documented that a considerable proportion of COVID-19 patients, specifically 24.7%, presented with anemia upon hospital admission. This collective evidence points to a consistent hematological abnormality associated with the disease.

This is explained by our study which showed significant relation between the Positivity of COVID IgG antibodies and lupus nephritis. Along with the study published by **Guo et al.** [30] who performed his study on 82 SLE patients with lupus nephritis confirmed by renal biopsy showed that 64 of 82 lupus nephritis patients were found to be anemic showing significant correlation between lupus nephritis and anemia.

A consistent observation in more severe COVID-19 cases is the presence of lower hemoglobin levels. This phenomenon may be related to a number of contributing factors, including pre-existing underlying medical conditions, a state of malnutrition, or the presence of a coagulopathy [31]. These variables can collectively lead to a reduction in hemoglobin concentration in critically ill patients.

In this study there was significant correlation between serum uric acid level and SLE patients with COVID IgG antibodies with P value 0.037 this is attributed to the high percentage of lupus nephritis in our studied SLE patients and the significant relation between lupus nephritis and the positivity of COVID IgG antibodies.

The findings from **Fang et al.** [32] indicate a significant correlation between elevated serum uric acid levels and the severity of COVID-19. The potential increase in serum uric acid among COVID-19 patients is thought to be a consequence of SARS-CoV-2 targeting the kidneys and gut, which are the principal sites for uric acid excretion. This viral-induced disruption of metabolic regulation likely affects serum uric acid concentrations [33]. Furthermore, pro-inflammatory cytokines have been shown to influence uric acid excretion and contribute to elevated serum levels [9].

This link between high uric acid and inflammatory disease is also observed in other conditions; for example, **Calich et al.** [34] reported significantly higher serum uric acid in lupus nephritis patients with normal kidney function. Elevated serum uric acid may endorse the stimulation of inflammatory pathways, as well as the development of autoantibodies in the kidneys, resulting in a decrease in the glomerular filtration rate [35]. Other mechanisms that may contribute to this association include polymorphisms in urate transporters, metabolic syndrome, and the consumption of certain medications like diuretics, beta-blockers, and the immunosuppressant cyclosporine, all of which can increase uric acid levels by reducing the glomerular filtration rate or through other pathways that diminish renal excretion [36].

Uric acid can also induce renal microvascular disease, leading to subsequent renal ischemia, infiltration of T-cells and macrophages, development of renal vasoconstriction, and a drop in renal function [1]. Ultimately, persistently high serum uric acid levels may contribute to the progressive nature of chronic kidney disease and the gradual damage of kidney function. The underlying pathological mechanisms are thought to involve a cascade of destructive changes, including glomerular and tubular damage, and eventual interstitial fibrosis. Clinically, this is manifested by the presence of proteinuria and an elevation in serum creatinine levels [37].

CONCLUSION

- 91% of SLE patients were found to have COVID IgG antibodies.
- There was relation between the positivity of COVID IgG antibodies and the presence of lupus nephritis, high ESR, anemia and high uric acid.
- Different medications used or disease activity don`t affect the presence of COVID antibodies.

These findings provide reassurance about patients' abilities to generate an appropriate antibody response after infection and their possible protection against re-infection with similar strains of SARS-CoV-2.

DECLARATIONS

- **ASU Ethical Committee approval code/license**: The ASU Ethical Committee regulations approved all experimental protocols.
- **Conflict of interest**: I declare that all authors have no competing interests as defined by Nature Research, or other interests that might be perceived to influence the results and/or discussion reported in this paper.
- **Consents for publication:** not applicable
- **Available Data:** The datasets used and/or analyzed in the current study are available from the corresponding author. Data sharing applies to this article, as datasets were generated and analyzed during the current study.
- **Author's contributions:**

Arafa S.G., Farouk H.M. and El-Azizi N.O. conceived and designed the study. Mohammed T.E. and Arafa S.G. contributed to data collection. Arafa S.G., El-Azizi N.O, and Lotfy N.M. analyzed and interpreted the data. Mohammed M.M. drafted the manuscript. Arafa S.G., Mohammed M.M., Farouk H.M carefully revised it. All authors have read and approved the final manuscript.

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REFERENCES

1. **Wang H, Ren Y, Chang J et al. (2018):** A systematic review and meta-analysis of prevalence of biopsy proven lupus nephritis. Arch. Rheumatol., 33(1):17-25.
2. **World Health Organization (2020):** Naming the coronavirus disease (COVID-19) and the virus that causes it. Braz. J. Implantol. Health Sci., 2(3). Available from: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/naming-the-coronavirus-disease-(covid-2019)-and-the-virus-that-causes-it
3. **World Health Organization (2022):** A year without precedent: WHO's COVID-19 response. [Internet]. Available from: https://www.who.int/news-room/spotlight/a-year-without-precedent-who-s-covid-19-response
4. **Jin Y, Yang H, Ji W et al. (2020):** Virology, epidemiology, pathogenesis and control of COVID-19. Viruses, 12(4):372.
5. **Morawska L, Milton D (2020):** It is time to address airborne transmission of COVID-19. Clin. Infect. Dis., 71(9):2311-2313.
6. **Spinato G, Fabbris C, Polesel J et al. (2020):** Alterations in smell or taste in mildly symptomatic outpatients with SARS-CoV-2 infection. JAMA, 323(20):2089-2090.
7. **Wang Y, Liu Y, Liu L et al. (2020):** Clinical outcome of 55 asymptomatic cases at the time of hospital admission infected with SARS-Coronavirus-2 in Shenzhen, China. J. Infect. Dis., 221(8):764-768.
8. **Ruano-Gallego D, García-Villadangos M, Moreno-Paz M et al. (2021):** A multiplex antigen microarray for simultaneous IgG and IgM detection against SARS-CoV-2 reveals higher seroprevalence than reported. Microb. Biotechnol., 14(3):1228-1236.
9. **Wu V, Huang J, Hsueh P et al. (2005):** Renal hypouricemia is an ominous sign in patients with severe acute respiratory syndrome. Am. J. Kidney Dis., 45(1):88-95.
10. **Petri M, Orbai A, Alarcon G et al. (2012):** Derivation and validation of systemic lupus international collaborating clinics classification criteria for systemic lupus erythematosus. Arthritis Rheum., 64(8):2677-2686.

11. Gladman D, Ibanez D, Urowitz M (2002): Systemic lupus erythematosus disease activity index 2000. J. Rheumatol., 29(2):288-291.

12. Hui D, Azhar E, Madani T et al. (2020): The continuing 2019-nCoV epidemic threat of novel coronaviruses to global health - The latest 2019 novel coronavirus outbreak in Wuhan, China. Int. J. Infect. Dis., 91:264-266. http://dx.doi.org/10.1016/j.ijid.2020.01.009

13. Azhar E, Hui D, Memish Z et al. (2019): The middle east respiratory syndrome (MERS). Infect. Dis. Clin. North Am., 33(4):891-905.

14. Auyeung T, Lee J, Lai W et al. (2005): The use of corticosteroid as treatment in SARS was associated with adverse outcomes: a retrospective cohort study. J. Infect., 51(2):98-102.

15. Saxena A, Guttmann A, Masson M et al. (2021): Evaluation of SARS-CoV-2 IgG antibody reactivity in patients with systemic lupus erythematosus: analysis of a multi-racial and multi-ethnic cohort. Lancet Rheumatol., 3(8):e585-e594.

16. Ramirez G et al. (2020): COVID-19 in systemic lupus erythematosus: data from a survey on 417 patients. Semin. Arthritis Rheum., 50(5):1150-1157.

17. Espinosa G, Prieto-González S, Llevadot M et al. (2021): The impact of SARS-CoV-2 coronavirus infection in patients with systemic lupus erythematosus from a single center in Catalonia. Clin. Rheumatol., 40(5):2057-2063.

18. Zonana-Nacach A, Cmargo-Coronel A, Yañez P et al. (2001): Infections in outpatients with systemic lupus erythematosus: a prospective study. Lupus, 10(7):505-510.

19. Konig M, Kim A, Scheetz M et al. (2020): Baseline use of hydroxychloroquine in systemic lupus erythematosus does not preclude SARS-CoV-2 infection and severe COVID-19. Ann. Rheum. Dis., 79(10):1386-1388.

20. Mitjà O, Corbacho-Monné M, Ubals M et al. (2021): A cluster-randomized trial of hydroxychloroquine for prevention of Covid-19. N. Engl. J. Med., 384(5):417-427.

21. Xu H, Zhong L, Deng J et al. (2020): High expression of ACE2 receptor of 2019-nCoV on the epithelial cells of oral mucosa. Int. J. Oral Sci., 12(1):8.

22. Lippi G, Plebani M (2020): The critical role of laboratory medicine during coronavirus disease 2019 (COVID-19) and other viral outbreaks. Clin. Chem. Lab. Med., 58(7):1063-1069.

23. Tian W, Jiang W, Yao J et al. (2020): Predictors of mortality in hospitalized COVID-19 patients: a systematic review and meta-analysis. J. Med. Virol., 92(10):1875-1883.

24. Wang J, Niu R, Jiang L et al. (2019): The diagnostic values of C-reactive protein and procalcitonin in identifying systemic lupus erythematosus infection and disease activity. Medicine, 98(33):e16798.

25. Sun P, Lu X, Xu C et al. (2020): Understanding of COVID-19 based on current evidence. J. Med. Virol., 92(6):548-551.

26. Hou C, Jin O, Zhang X (2018): Clinical characteristics and risk factors of infections in patients with systemic lupus erythematosus. Clin. Rheumatol., 37(10):2699-2705.

27. Schäfer V, Weiß K, Krause A et al. (2017): Does erythrocyte sedimentation rate reflect disease activity in patients with systemic lupus erythematodes? Ann. Rheum. Dis., 76:1239-1240.

28. Taneri P, Gómez-Ochoa S, Llanaj E et al. (2020): Anemia and iron metabolism in COVID-19: a systematic review and meta-analysis. Eur. J. Epidemiol., 35(8):763-773.

29. Bellmann-Weiler R, Lanser L, Barket R et al. (2020): Prevalence and predictive value of anemia and dysregulated iron homeostasis in patients with COVID-19 infection. J. Clin. Med., 9(8):2429.

30. Guo Q, Lu X, Miao L et al. (2010): Analysis of clinical manifestations and pathology of lupus nephritis: a retrospective review of 82 cases. Clin. Rheumatol., 29(10):1175-1180.

31. Zhou F, Yu T, Du R et al. (2020): Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet, 395(10229):1054-1062.

32. Fang L, Karakiulakis G, Roth M (2020): Are patients with hypertension and diabetes mellitus at increased risk for COVID-19 infection? Lancet Respir. Med., 8(4):e21.
33. Lin L, Jiang X, Zhang Z et al. (2020): Gastrointestinal symptoms of 95 cases with SARS-CoV-2 infection. Gut, 69(6):997-1001.
34. Calich A, Borba E, Ugolini-Lopes M et al. (2018): Serum uric acid levels are associated with lupus nephritis in patients with normal renal function. Clin. Rheumatol., 37(5):1223-1228.
35. Sato Y, Feig D, Stack A et al. (2019): The case for uric acid-lowering treatment in patients with hyperuricaemia and CKD. Nat. Rev. Nephrol., 15(12):767-775.
36. Ueno S, Hamada T, Taniguchi S et al. (2016): Effect of antihypertensive drugs on uric acid metabolism in patients with hypertension: cross-sectional cohort study. Drug Res., 66(12):628-632.
37. Ejaz A, Johnson R, Shimada M et al. (2019): The role of uric acid in acute kidney injury. Nephron, 142(4):275-283.