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Since the global emergence of Sars-Cov2 at the end of 2019, a special concern has raised regarding patients with rheumatic and inflammatory diseases, such as systemic lupus erythematosus (SLE) [1]. Indeed, many treated SLE patients are immunocompromised and often suffer from chronic kidney or cardiovascular diseases [2]. Recently, anti-interferon antibodies have been implicated in severe Sars-Cov2 infection [3] while it has been known for decades that SLE patients may produce such autoantibodies [4]. Although available data from short SLE series are reassuring [5,6], large-scale nation-wide studies are still needed to assess the risk of developing severe Sars-Cov2 infection in SLE.

We therefore used the French healthcare database system called "Programme de Médicalisation des Systèmes d'Information" (PMSI) - which contains hospitalization data of all inpatients in France - to analyse the SLE population that had at least one stay in a French hospital between March and October 30th, 2020 (Supplementary Material). On this population, we compared SLE patients with or without Sars-Cov2 infection (SLE/COVID-19^{+}, SLE/COVID-19^{-}). Among SLE/COVID-19^{+}, we distinguished patients with poor outcome after Sars-Cov2 infection and patients with good outcome after COVID-19. We defined poor outcome as admission to Intensive Care Unit (ICU) or death. We also compared the in-hospital mortality associated with Sars-Cov2 infection in SLE and in the total population in France.

Based on the 10th International Classification of Diseases "M32" and "L93" diagnosis code, we identified 11 055 SLE patients who had at least one stay in a French hospital between March 1st and October 31st, 2020 (Supplementary materials, Figure S1). Among them, 1 411 (12.8%) also had a COVID-19 diagnosis code. Characteristics of SLE/COVID-19^{+} and SLE/COVID-19^{-} patients are given Table 1. These 1 411 SLE/COVID-19^{+} patients experienced 1 721 hospital stays during the period of study.

Among these SLE/COVID-19^{+} stays, 293 (17 %) took place in Intensive Care Unit (ICU). The mean Simplified Acute Physiology Score (SAPS) II at admission was 35.4+/-16.8. In ICU, 78 (26.7%) and 71 (24.7%) SLE/COVID-19^{+} patients required invasive or non-invasive mechanical ventilation, respectively. Overall, 134 (9.5 %) SLE patients admitted for COVID-19 died. The in-hospital mortality rate was almost 4 times higher in SLE/COVID-19^{+} as compared to SLE/COVID-19^{-} patients admitted during the same period (9.5 % vs 2.4 %, p <0.001). Interestingly, while the overall mortality rate was lower in SLE/COVID-19^{+} patients as compared to the total population admitted for Sars-Cov2 infection in France during the same period (9.5 % vs 15.7%, p <0.0001), the mortality rate at a younger age appeared higher in SLE patients after stratification according to the age (Supplementary materials, Figure S2).

Our study based on a comprehensive nationwide database confirms that patients with SLE are more likely to develop severe Sars-Cov2 infection when they have comorbidities already identified as risk factors of severe infection in the general population, such as older age, male gender, and hypertension [1]. Poor outcome was associated with chronic kidney disease (CKD) status thus confirming that CKD increases the risk for severe infection in SLE and is a major predictor of mortality and morbidity in these patients[2].

Given the importance of male sex as a poor prognosis factor of COVID-19, the lower mortality rate observed among SLE population may be explained by an unbalanced sex ratio (F/M 8.5:1.5). On the other hand, the mortality of SLE/COVID-19^{+} patients seems higher in the youngest patients as compared to the general population with Sars-Cov2 infection. Because lupus activity and the need for immunosuppressive drugs decline with age, the higher mortality rate observed in younger patients suggests that SLE disease impact COVID-19 outcome. This finding argues for prioritizing vaccination studies and policies in the youngest patients with SLE.

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AUTHOR CONTRIBUTIONS

AM designed and conducted analysis and wrote the manuscript. GA, NC, DG and TP were involved in the project development and edited the manuscript. KS and JFT directed the project and wrote the manuscript.

PATIENT AND PUBLIC INVOLVEMENT

Patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of our research

TABLE

Table 1 Characteristics of SLE inpatients in France with and without COVID-19 infection between March and October 2020.

	SLE/COVID-19 $^{-}$	SLE/COVID-19^{+}		p*
		good outcome	poor outcome	
	n= 9644	n= 1070	n= 341	
Age, years (mean +/-sd)	52.1+/-17.2	55.8+/-18.7	61.5+/-17.6	<0.0001
Male gender, n (%)	1 144 (16 .1)	171 (16.0)	96 (28.2)	<0.0001
Chronic kidney disease, n (%)	1312 (13.6)	184 (17.2)	108 (31.7)	<0.0001
Diabetes, n (%)	1251 (13.0)	173 (16.2)	72 (21.1)	0.03
High blood pressure, n (%)	3404 (35.3)	480 (44.9)	215 (63.1)	<0.0001
Obesity, n (%)	1811(18.8)	240 (22.4)	86 (25.2)	0.29
Chronic pulmonary disease, n (%)	1275 (13.2)	240 (22.4)	102 (29.9)	0.005
Cardiovascular event history, n (%)	2050 (22.8)	291 (28.5)	140 (43.8)	<0.0001
Lupus nephritis history, n (%)	1271 (13.2)	158 (14.8)	77 (22.6)	0.0007
Sjögren syndrome, n (%)	1088 (11.3)	124 (11.6)	38 (11.1)	0.8
Antiphospholipid syndrome, n (%)	803 (8.3)	107 (10.0)	144 (12.9)	0.13
Solid organ transplantation, n(%) **	212 (2.2)	22 (2.1)	14 (4.1)	0.04

* Level of significance for the difference between SLE/COVID-19^{+} with good outcome vs SLE/COVID-19^{+} with poor outcome. Student's T test was performed for quantitative variables and chi-square test was used for categorical variables.

** Solid organ transplantation during the last 10 years.