The continuous increase in the number of systemic lupus erythematosus cases in Brazil in the COVID-19 era

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Abstract: This study aims to reevaluate and compare the data from the Brazilian Unified Health System (SUS) on the number of diagnoses of systemic lupus erythematosus (SLE) in the pre-pandemic period with those in the pandemic period, as well as to compare the first year (2020) of the COVID-19 pandemic in Brazil with the last year (2021), to update the data, and to verify whether SLE disease control measures were effective in 2021. There was a consistent and significant increase in the incidence of SLE cases all over Brazil between the first and second pandemic years and between the pre-pandemic triennium and the second pandemic year. Therefore, it is inescapable to have larger clinical studies with different populations to better understand the relationship between these two conditions and find measures to improve the control of this disease.

Keywords: COVID-19; Lupus Erythematosus, Systemic; Autoimmune Diseases.

Introduction

As the Coronavirus 2019 (COVID-19) pandemic goes on around the world, clinical and epidemiological evidence of the incidence and increase in the number of systemic lupus erythematosus (SLE) continues to be discussed, but the real association between SLE and the risk factors associated with worse COVID-19 outcomes in this population are not well established.[1,2] Even with the expansion of vaccination in Brazil, with full immunization of 171 million (80.6%) people, COVID-19 variants such as OMICRON have impacted and increased COVID-19 cases. Brazil has experienced approximately 34 million cases of COVID-19 and over 682,358 deaths to date (August 19, 2022) (https://covid.saude.gov.br/).

This scenario still represents a cause for concern about the management of patients with autoimmune diseases, such as SLE. Ugarte-Gil et al.[1] demonstrated that more severe COVID-19 outcomes in individuals with SLE are largely driven by factors such as untreated or active SLE. Patients on glucocorticoids also have more severe outcomes. The concern becomes even greater when studies conducted during the pandemic showed a decrease in the hospitalization rate of patients with SLE but an increase in the mortality rate due to the measures implemented

to mitigate the pandemic, such as negligence in medical assistance for other diseases.[2,3]

A number of orofacial manifestations have also been reported in patients with SLE, such as nonspecific ulcerations, involvement of salivary glands, and temporomandibular joint disorders.[4] A recent study has highlighted the difficulties and damage from the current COVID-19 pandemic to dental services in general and to oral medicine and oral pathology particularly, which makes the possible number of undiagnosed SLE cases even more concerning.[5]

Methodology

The data on the number of diagnoses of SLE in 2017 – 2019, 2020, and 2021 from five Brazilian regions (north, northeast, southeast, south, and midwest), representing 26 states and the Federal District were extracted from SISAB (Health Information System for Primary Care), a public database maintained by the Brazilian Ministry of Health (https://sisab.saude.gov.br/paginas/acessoRestrito/relatorio/federal/saude/RelSauProduc Re.xhtml).

Statistical analyses were performed using the BioEstat 5.0 statistical software (Biostatistical Institute of Science and Technology). The number of diagnoses of SLE was compared between the pre-pandemic period and the pandemic period. The number of diagnoses of SLE in the first year (2020) of the COVID-19 pandemic in Brazil was compared with the last year (2021). The study also aimed to update the data and verify whether SLE disease control measures were effective in 2021. In addition, binomial regression was used to analyze the longitudinal associations between the impact of the COVID-19 pandemic and the number of diagnoses. Percentage changes were calculated by dividing the change in value by the original value and then multiplying the obtained value by 100. In all analyses, the data were disaggregated by Brazilian regions.

Results

Table 1 presents the previous study by the same research group[6] and shows an increase in the number of SLE diagnoses in all Brazilian regions in 2020, compared to the mean number of the pre-pandemic triennium (2017–2019). The increase ranged from +23.4% in the south to +108.9% in northeastern region. The overall Brazilian average increase amounted to 55.9%, corresponding to 13,107 more cases in the first year of the pandemic period.

Table 2 shows the comparison of the second year of the pandemic period (2021) initially with the first year of the COVID-19 pandemic (2020) and then with the pre-pandemic period. There was a trend towards an increase in the number of SLE cases in the second year of the pandemic throughout Brazil (+ 20.4%), giving special attention to the southern region, the least affected in the first study and now the one with the largest increase (+ 28.1%) during the pandemic. When comparing the subsequent period of the pandemic (2021) with the mean number in the pre-pandemic period (2017–2019), the increase in the number of SLE cases was higher compared to the previous study, showing the northeastern

Table 1. Average number of diagnosed systemic lupus erythematosus cases across Brazilian geographical macroregions in different periods (2017–2019 *vs.* 2020). Previous study – *Martelli-Junior et al., 2021.*

Macroregions of Brazil	2017-2019 - n	2020 - n	Difference - n (%)
North	1,296	2,221	+ 925 (71.3)
Northeast	5,119	10,697	+ 5,578 (108.9)
Southwest	10,32	14,526	+ 4,206 (40.7)
South	4,75	5,863	+ 1,113 (23.4)
Midwest	1,957	3,242	+ 1,285 (65.6)
Total	23,442	36,549	+ 13,107 (55.9)

Source: Health Information System for Primary Care – SISAB (https://sisab.saude.gov.br/paginas/acessoRestrito/relatorio/federal/saude/RelSauProducRe.xhtml).

Table 2. Difference between the number of diagnosed systemic lupus erythematosus cases reported by the Brazilian public health system in all geographical regions in 2020 (previous study) compared to 2021 and comparison of the average number of SLE cases in the pre-pandemic and pandemic periods.

Macroregions of Brazil	2020 (n)	2021 (n)	2017-2019 (n)	Difference (%) 2020 vs 2021	Difference (%) 2017-2019 vs 2021
North	2,221	2,772	1,296	+ 551 (24.8)	+ 1,476 (113.9)
Northeast	10,697	12,716	5,119	+ 2,019 (18.9)	+ 7,597 (148.4)
Southeast	14,526	17,122	10,32	+ 2,596 (17.9)	+ 6,802 (65.9)
South	5,863	7,508	4,75	+ 1,645 (28.1)	+ 2,758 (58.1)
Midwest	3,242	3,874	1,957	+ 632 (19.5)	+ 1,917 (98)
Total	36,549	43,992	23,442	+ 7,443 (20.4)	+ 20,550 (87.7)

2020: Previous study (Martelli-Junior et al., 2021); 2017-19: Pre-pandemic period; 2021: Pandemic period (This study).

Table 3. Incidence of systemic lupus erythematosus per million people in Brazilian macroregions in 2017–2019 *vs.* 2021 and 2020 *vs.* 2021.

Regions of Brazil	2017–2019 Incidence rate (95%CI)	2020 Incidence rate (95%CI)	2021 Incidence rate (95%CI)	Incidence ratio* (95%CI)	p-value
North	72.2 (68.4– 76.3)	123.8 (118.7–129.1)	154.5 (148.8 – 160.6)	(1.80 –2.06)	< 0.001
Northeast	97.4 (93.1–107.4)	186.8 (183.3–190.4)	222.1 (218.3 – 226.0)	(2.21–2.36)	< 0.001
Southeast	48.4 (44.8–51.9)	167.1 (164.4–169.8)	196.9 (194.0 – 199.9)	(1.49–1.57)	< 0.001
South	160.2 (155.7–164.9)	197.8 (192.7–202.9)	253.3 (247.6 – 259.1)	(1.35–1.46)	< 0.001
Midwest	123.3 (117.9–128.9)	204.2 (197.4–211.4)	244.0 (236.4–251.8)	(1.72–1.91)	< 0.001
Total	112.9 (111.4–114.3)	176.0 (174.2–177.8)	221.8 (209.9–213.8)	(1.69–1.74)	< 0.001

*Comparison between the average figures for post-pandemic (2020-2021) and pre pandemic (2017-2019) periods.

region was the most widely affected (148.4%), in addition to an increase of 20,550 cases throughout Brazil (+ 87.7%).

Table 3 shows the comparison of the incidence rate adjusted per million people for the five Brazilian regions and throughout the country. There was a consistent and significant increase in the incidence rate all over Brazil between the first and second pandemic years and between the pre-pandemic triennium and the second pandemic year.

Discussion

SLE is clearly an important risk factor for the development of more severe COVID-19.[2,7] Patients with SLE develop more severe manifestations of COVID-19, especially when they have other comorbidities and predisposing factors, including smoking, obesity, and chronic use of medications, such as immunosuppressants.[2] It has been suggested that SARS-CoV-2 could act as a triggering factor for the development of rapid autoimmune and/ or autoinflammatory dysregulation due to similar pathogenic mechanisms and clinico-radiological aspects in hyperinflammatory diseases and COVID-19.[2,8]

At the beginning of the pandemic period, telemedicine came into use because of health service restrictions, having a positive impact for patients who sought rheumatology care.[9] Nevertheless, it is still unclear why SLE cases continue to increase during the pandemic even after the adoption of these preventive measures and the decrease in COVID-19 cases.[1,2]

The fear of patients of seeking medical services during the pandemic, difficulties related to technology and telemedicine, routine care cancellations,

difficulties in accessing healthcare, and pandemic-related stress seem to contribute to the physical deterioration of SLE patients and might also have increased the number of patients diagnosed with the disease.[10]

Conclusion

Therefore, given the increase of rheumatic diseases, such as SLE,[9] described in the literature during the pandemic and demonstrated in this paper, it is inescapable to have larger clinical studies with different populations to better understand the relationship between these two conditions and find measures to improve the control of this disease.

Acknowledgements

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