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LETTER TO THE EDITOR

Continuous increase of herpes zoster cases in Brazil during the COVID-19 pandemic



To the Editor:

With the continuation of the coronavirus disease 2019 (COVID-19) pandemic throughout the world, clinical and epidemiologic evidence of the occurrence and increase in the number of other diseases, such as herpes zoster (HZ), continue to be discussed, but the real association between HZ and COVID-19 is not well established.

An important narrative review identified 27 cases of HZ after 1-2 weeks of COVID-19 in unvaccinated patients. Most patients showed a typical manifestation of HZ, clinically characterized by painful unilateral rash, compromising the patients' quality of life. Other cases, including patients with lymphopenia, exhibited atypical presentations of HZ, with necrotic tissue injuries and severe neurologic involvement. The authors suggest that T-cell dysfunction, such as lymphopenia and lymphocyte exhaustion, reactivates the varicella zoster virus (VZV), which causes the HZ disease.¹

Conversely, recent studies reported cases of VZV reactivation in patients who were vaccinated with mRNA or inactivated COVID-19 vaccines.²⁻⁵ The COVID-19 vaccines' most common adverse reactions are pain, local redness and swelling, fatigue, headache, fever, chills, nausea, and vomiting.^{3,5,6} These do not include the main clinical findings of VZV reactivation, which were painful multiple grouped vesicles on an erythematous base and pruritic lesions, which manifested in patients from 4 to 14 days after vaccination. These clinical manifestations of HZ may ensue spontaneously after activation by a trigger, such as fever and immunosuppression.²⁻⁴

To explore this issue further, this study aims to compare the data from the Brazilian Unified Health System (SUS) on the number of diagnoses of HZ from the prepandemic period with the data from pandemic period, as well as to compare the first 6 months of the COVID-19 pandemic in Brazil with the most recent 6 months, to update the data and verify if HZ disease control measures were effective in the following months.

The analyzed data were extracted from the public database (DATASUS) (<http://tabnet.datasus.gov.br/cgi/tabcgi.exe?sia/cnv/qauf.def>) of the Ministry of Health of Brazil. Table I presents the previous study by the same research group⁷ and shows an increase in the number of HZ diagnoses in all Brazilian regions in the months from March through August 2020 compared with the mean number in the same months in 2017-2019. The increases ranged from 24% in the Northwest to 77% in the Midwest. The overall Brazilian average increase reached 35%, corresponding to an average of more than 2274 excess cases.

Table II shows a comparison of the second half of the pandemic period (September 2020 through February 2021) with the first half of the COVID-19 pandemic (March–August 2020) and afterward with the same months before the pandemic. There was a trend toward an increase in the number of HZ cases in the second half of the pandemic throughout Brazil (+11%), with attention to the Northeast region, the least affected region in the first study and now the one with the biggest increase (+15%) during the pandemic. When comparing the following period of the pandemic (September 2020–February 2021) with the same months before the pandemic, the increase in the number of HZ cases was similar to that in the previous study, keeping the Midwest region as the most affected (+82%) and an increase of 3350 cases throughout Brazil (+53%).

Table III shows a comparison of the incidence rate adjusted per 1 million population for the 5 geographic regions of Brazil and throughout the whole country. There was a consistent and significant increase in the incidence rate all over Brazil between the first and second pandemic periods and between the prepandemic and second pandemic periods. Limitations of this article include lack of information regarding the criteria for confirmation of HZ diagnoses in the public database from the SUS and the unavailability of larger clinical COVID-19 versus HZ studies.

The relationship between the manifestation of HZ disease and COVID-19 remains to be established. Only case reports and case series have been published showing this coexistence until now, and this evidence is not sufficient to assert this association. However, we observed in this study a continued increase in HZ cases during the COVID-19 pandemic, with a tendency toward an increase in subsequent months, which may suggest a correlation between these diseases, as demonstrated in the

Table I. Difference between average of herpes zoster diagnoses reported by Brazilian public health system in all geographic regions between March and August in 2017-2019 compared with same period in 2020 (previous study Maia et al., 2021⁷)

Regions of Brazil	Mar-Aug 2017-2019 (n)	Mar-Aug 2020 (n)	Difference (n)	Difference (%)
North	562	708	+146	+26%
Northeast	2192	2709	+517	+24%
Southeast	2058	3003	+945	+46%
South	1141	1447	+305	+27%
Midwest	468	828	+360	+77%
Total	6421	8695	+2274	+35%

Table II. Difference between average of herpes zoster diagnoses reported by Brazilian public health system in all geographic regions between March and August 2020 (previous study) compared with September to February 2020/2021 and in pre-pandemic and pandemic periods

Regions of Brazil	Mar-Aug 2020 (n)	Sep-Feb 2020/2021 (n)	Sep-Feb 2017-2020 (n)	Difference (%) Mar-Aug 2020 Sep-Feb 2020/2021	Difference (%) Sep-Feb 2017-2020 Sep-Feb 2020/2021
North	708	751	719	+43 (6.1%)	+32 (4.5%)
Northeast	2709	3126	2128	+417 (15.4%)	+998 (46.9%)
Southeast	3003	3336	2086	+333 (11.1%)	+1250 (59.9%)
South	1447	1532	873	+85 (5.9%)	+659 (75.5%)
Midwest	828	909	498	+81 (9.8%)	+411 (82.5%)
Total	8695	9654	6304	+959 (11%)	+3350 (53.1%)

Mar-Aug 2020: previous study (Maia et al., 2021⁷); Sep-Feb 2017-20: pre-pandemic period; Sep-Feb 2020/2021: pandemic period (present study).

Table III. Incident cases of herpes zoster per 1 million population in Brazilian macroregions according to periods 2017-2019 vs 2020

Regions of Brazil	Pre-pandemic period incidence rate (95% CI)	First pandemic period incidence rate (95% CI)	Second pandemic period incidence rate (95% CI)	P value*	P value†
North	40.0 (37.2-43.1)	39.5 (36.6-42.5)	41.9 (38.9-44.9)	.77	.40
Northeast	37.2 (35.6-38.8)	47.3 (45.5-49.1)	54.6 (52.7-56.5)	<.001	<.001
Southwest	24.0 (22.9-25.1)	34.4 (33.3-35.8)	38.4 (37.0-39.7)	.052	<.001
South	29.5 (27.5-31.5)	48.8 (46.3-51.4)	51.7 (49.1-54.3)	<.001	<.001
Midwest	31.4 (28.7-34.2)	52.2 (48.7-55.8)	57.3 (53.6-61.1)		
Total	30.4 (29.6-31.1)	41.9 (41.0-42.8)	46.5 (45.6-47.5)		

*Comparison between first and second pandemic periods.

†Comparison between the pre-pandemic and second pandemic periods.

previous study.⁷ Furthermore, these new data suggest that measures to control the increase in HZ cases in the first period of the pandemic were not effective, including the assessment of access to

medicines, health care-seeking behavior, telemedicine consultations, awareness of practitioners about possible increased risk of HZ during the pandemic period, and the application of timely preventive and

therapeutic measures against HZ. Thus, it is necessary to have larger clinical studies with different populations to better understand the relationship between these 2 conditions and find measures to increase the control of HZ.

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