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Mapping the viral battlefield: SARS-CoV-2 infection dynamics among healthcare workers in Brazil

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Abstract

Background Understanding the dynamics of SARS-CoV-2 viral infection and factors associated with in-hospital transmission rates among healthcare workers (HCW) is crucial for their protection. Brazil experienced high mortality rates due to COVID-19, and limited data are available on transmission of SARS-CoV-2 infection among HCW. This cohort study aimed to assess the dynamic of SARS-CoV-2 infections in HCW from two tertiary hospitals in central Brazil, one of them a Reference Hospital for COVID-19.

Methods From May 2020 to January 2021, 554 HCW directly involved with COVID-19 care were followed through 12 biweekly visits. During these visits, blood, nasal, and oropharyngeal samples were collected, and participants underwent interviews. SARS-CoV-2 detection was carried out using RT-qPCR, while the assessment of seroprevalence was based on IgG detection. Additionally, 35 positive samples underwent viral whole-genome sequencing.

Results The infection prevalence, as per RT-qPCR, was 28.5% (24.9–32.4), reflecting an overall attack rate ranging from 0.5% to 9.5%, marked by two peaks in August and December 2020. Oligosymptomatic and asymptomatic infections accounted for 14% of prevalent infections. The seroprevalence rate stood at 25.8%. The hospitalization rate was 8.2%, with a fatality rate of 1.3%. Risk factors associated with a positive diagnosis of COVID-19 included being male, working at the referral hospital, having a graduate-education level, and using hydroxychloroquine and zinc for prevention or treatment. One reinfection was identified. Absenteeism was 56.6%. The infection dynamics mirrored the pattern observed in the general population.

Conclusion One-third of the professionals in the followed cohort were infected. Being male, working in a COVID-19 referral center, having a low level of education, and using medications for preventive treatment represented risk

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factors. Healthcare workers at the COVID-19 referral hospital exhibited a higher incidence rate compared to those at the non-referral hospital, increasing the plausibility that some of the infections occur in the hospital environment. **Keywords** COVID-19, SARS-CoV-2, Healthcare worker, Asymptomatic infection, Epidemiology

Background

"The COVID-19 pandemic has reminded all of us of the vital role health workers play to relieve suffering and save lives" said the WHO Director-General in 2020, on World Patient Safety Day [1]. Despite the high risk of contracting COVID-19, healthcare workers (HCW) continue to provide services under immense work pressure and negative emotional stress [2]. This unpredictable and stressful environment and traumatic situations not only affect HCW, but also their family members, friends, and colleagues [3]. During the first waves of the pandemic, there was a high number of infections and deaths among HCW worldwide, resulting in significant pressure on human resources [4].

To inform occupational health policy and strategy, understanding the dynamics of SARS-CoV-2 infection among HCW is critical. The prevalence of infection among HCW varies depending on the pandemic phase and the diagnostic modality (molecular versus serology), differences in the target HCW population, as well as methodological approach [5, 6]. Hospital infection among HCW can be reduced through early detection, isolation, understanding of individual protection measures and guidelines, adequate education/training, availability of personal protective equipment (PPE), and high-risk group stratification [7, 8]. It is unclear whether new infections among HCW were contracted in the workplace or in the community, which is important for the formulation of control strategies. Country such as US, Mexico, China, Denmark, and Italy are among the countries that have reported the highest SARS-CoV-2 infections among HCW, while Austria, Egypt, and Canada reported the lowest [5].

Brazil has experienced one of the highest mortality rates of COVID-19 in the world, with over 702 116 deaths recorded as of May 2024 [9]. Despite the significant impact of COVID-19 on HCW, there have been few studies reporting on the incidence and prevalence rates of SARS-CoV-2 infection as well as its dynamics during the most lethal period of the pandemic, particularly prior to the introduction of COVID-19 vaccination[10–15]. Brazil has not yet published follow-up studies that provide a comprehensive overview of prevalence, incidence, absenteeism, reinfection, circulation of strain types, and their similarities with the general population's circulation. Therefore, the aim of this study is to explore the early scenario and dynamics of COVID-19 among Brazilian HCWs.

Methods

Study type, location and period

This is a quantitative observational cohort study which used the STROBE (Strengthening the reporting of observational studies in epidemiology) checklist for reporting (https://www.strobe-statement.org/checklists/) (Supplementary File 1). Its prospective primary data were collected in two tertiary hospitals in Campo Grande, a capital city with 898 100 inhabitants [16] in the Central-West Region of Brazil, from May 2020 to January 2021. Reference Hospital allocated 100% and non-general Hospital allocated 20% of their beds to COVID-19 patients during the study period.

Sampling and inclusion criteria

Non-probabilistic sampling was utilized to select participants. The inclusion criteria were as follows: (1) being a healthcare professional working in any department of the Reference Hospital (Hospital A) or the Non-Reference Hospital (Hospital B) who provides services or has contact with suspected or confirmed COVID-19 patients; (2) being 18 years of age or older; (3) not having a previous diagnosis of COVID-19 and (4) signing the informed consent.

We excluded participants with a positive test for COVID-19 by RT-PCR or antibodies to SARS-CoV-2, as well as professionals exclusively working in primary care, exclusively in administrative areas, or exclusively in another hospital other than Hospital A or B.

The sample was determined by order of registration until reaching the maximum number of participants. The cohort was defined based on the availability of voluntary workforce to meet the daily demand of patient care from the beginning to the end of the study performed nonprobabilistic sample of 600 was established, as only 600 tests were available due to the absence of diagnostic tests in Brazil and worldwide at the time.

Study procedures

Eligible HCW were followed through 12 visits conducted every 14 days. Additionally, an online symptom surveillance was conducted every 3 days. HCW who fulfilled the inclusion criteria answered questions regarding demographic characteristics, habits, and health status. BCG vaccine scar assessment was performed by a trained research assistant. The study was conducted according to the guidelines of the Declaration of Helsinki and approved by Research Ethics Committee; Federal University of Mato Grosso do Sul (CAAE number 31411920.4.0000.0021). Informed consent was obtained from all subjects involved in the study. All collected data were recorded and managed using REDCap[®] (Research Electronic Data Capture), a browser-based, metadatadriven electronic data capture software, ensuring efficient and secure data storage and analysis [17, 18].

Definitions

Oligosymptomatic infection. Report of only mild symptoms possibly characteristic of COVID-19, including headache, sore throat, irritability/confusion, nausea/vomiting, conjunctival congestion, enlarged lymph nodes, and skin lesions.

Symptomatic infection. Report of mild symptoms associated with one or more severe symptoms such as adynamia, anosmia, dysgeusia, fever/feeling feverish, chills, runny nose, diarrhea, difficulty swallowing, difficulty breathing, myalgia, sputum production, cough, and/or nasal congestion.

Reinfection. Infection by a new strain, confirmed by complete genome sequencing of viral isolates.

Molecular screening by RT-qPCR

All nasopharyngeal and oropharyngeal swab samples were processed for molecular testing of SARS-CoV-2 using a specific reverse transcription real-time PCR (RTqPCR). Firstly, nucleic acids were extracted from samples using the QIAamp Viral RNA Mini Kit (Qiagen, Hilden, Germany) according to the manufacturer's instructions.

Serological screening for anti-SARS-CoV-2 IgG

All samples underwent qualitative detection of IgG antibodies for SARS-CoV-2 using the Chemiluminescent Microparticle Immunoassay (CMIA) methodology according to the manufacturer's instructions (ARCHI-TECT, Abbott).

Complete viral genome sequencing

Thirty-five samples with high viral load (Cycle of quantification (C_t) value < 25 for both N1 and N2 genes) were selected for whole-genome sequencing (WGS). RNA was extracted from nasopharyngeal swabs using the Mag-MAX Viral Pathogen Nucleic Acid Isolation Kit (Thermo Fisher Scientific, USA, Accession Number: MN908947.3) [19].

Quality control of the generated reads was performed using the SARS-CoV-2 Coverage Analysis plugin (v5.16). Reference-guided assembly was conducted using the Iterative Refinement Meta-Assembler (IRMA) [20], annotation was performed using COVID19AnnotateSnpEff (v1.3.0.2) [21] and a nomenclature system [22]. The consensus sequences produced for each sample were deposited in the GenBank and GISAID databases under the accession numbers OL442124 to OL442158 and EPI-ISL-6633631 to EPI-ISL-6633842, respectively.

Data analysis

Data analysis was performed using Stata SE software, version 13 (StataCorp LP, College Station, USA). The Chi-square test (χ 2) or Fisher's exact two-tailed test were used to assess differences between proportions for categorical variables., Student's t-test was used to compare means of continuous variables. The incidence rate of RT-qPCR positivity and a 95% confidence interval (CI) were calculated. Odds ratios (OR), adjusted odds ratios (aOR), and 95% confidence intervals (CI) were used to identify potential predictors of SARS-CoV-2 infection (RT-qPCR positivity for SARS-CoV-2 RNA). Variables with a *p*-value < 0.20 were included in the multiple logistic regression analysis. Stepwise variable selection was performed for the final model, considering the number of events per variable (EPV). Collinearity among selected variables was assessed through bivariate analysis. The Hosmer-Lemeshow test was employed to evaluate the model that best fits the regression equation. Correlation analyses were conducted using the Spearman's rank correlation test. The analysis of participant retention in the study was conducted using the Kaplan-Meier test. A *p*-value < 0.05 was considered statistically significant.

Results

Participants

The study included a population of 554 HCW. Most participants were female (77.10%), with a median age of 38 years (range 21–69). The population was predominantly characterized by the absence of comorbidities (74.70%). A body mass index (BMI) above normal values was observed in 65.17%, a visible scar from the BCG vaccine was present in 91.69%, 58.31% worked in Reference Hospital. Complete data are shown in Table 1.

The participant adherence in this prospective cohort study was above 80%, and the highest frequency of collections was observed among professionals belonging to non-reference hospital (Supplementary File 2).

Identification of factors associated with positivity in the RT-qPCR molecular test

Out of the total 554 participants, 158 (28.5%) (95% CI: 24.9–32.4) tested positive for the presence of the SARS-CoV-2 virus on RT-qPCR. Demographic characteristics associated with positivity in the molecular test were male

 Table 1
 Comparison of the main demographic characteristics among healthcare professionals in the study, according to the RT-qPCR results for SARS-CoV-2

| Characteristics | Positive n (%) 158 (28.52) | Negative n (%) 396 (71.48) | Total n (%) 554 (100.00) | p | Odds ratio (OR) | p | Adjusted OR (aOR) |
|-------------------------------------|----------------------------------|----------------------------------|--------------------------------|------------------------|-----------------------|-------|---------------------|
| | | | | | | | |
| Female | 114 (26 70) | 313 (73 30) | 427 (100 00) | | 1 | _ | _ |
| Male | 44 (34.65) | 83 (65.35) | 127 (100.00) | 0.083 (1) | ' 1.45 (0.95–2.22) | 0.011 | 2.00 |
| Race/ethnicity | | | | | | | (|
| White | 89 (27.99) | 229 (72.01) | 318 (100.00) | | 1 | - | - |
| Non-white | 69 (29.24) | 167 (70.76) | 236 (100.00) | 0.747 ⁽¹⁾ | 1.06 (0.73–1.54) | - | - |
| Age group | | | | | | | |
| 20 to 40 years | 93 (25.83) | 267 (74.17) | 360 (100.00) | | 1 | | |
| 41 years or older | 65 (33.51) | 129 (66.49) | 194 (100.00) | 0.057 ⁽¹⁾ | 1.45 (0.99–2.12) | 0.540 | 1.13 (0.71–1.80) |
| Body mass index (BMI) | | | | | | | (0.71 1.00) |
| Overweight (25.0–29.9) | 67 (31.90) | 143 (68.10) | 210 (100.00) | 0.055 (1) | 1.54 (0.99–2.40) | 1.21 | (0.71–2.05) |
| Underweight and normal (< 24.9) | 45 (23.32) | 148 (76.68) | 193 (100.00) | | 1 | - | - |
| Obese I and II (30.0–39.9) | 31 (29.81) | 73 (70.19) | 104 (100.00) | 0.222 ⁽¹⁾ | 1.40 (0.82–2.39) | 0.79 | (0.41-1.53) |
| Obese III (>40) | 15 (31.91) | 32 (68.09) | 47 (100.00) | 0.224 ⁽¹⁾ | 1.54 (0.77–3.10) | 0.71 | (0.31-1.66) |
| Comorbidities | | | | | | | |
| No | 118 (28.50) | 296 (71.50) | 414 (100.00) | | 1 | - | - |
| Yes | 40 (28.57) | 100 (71.43) | 140 (100.00) | 0.988 ⁽¹⁾ | 1.00 (0.66–1.53) | - | - |
| Continuous medication use | | | | | | | |
| No | 105 (27.56) | 276 (72.44) | 381 (100.00) | | 1 | - | - |
| Yes | 53 (30.64) | 120 (69.36) | 173 (100.00) | 0.457 (1) | 1.16 (0.78–1.72) | - | - |
| BCG vaccine scar ^(a) | | | | | | | |
| Yes | 139 (27.36) | 369 (72.64) | 508 (100.00) | | 1 | - | - |
| No | 14 (43.75) | 18 (25.25) | 32 (100.00) | 0.050 ⁽¹⁾ | 2.06 (1.00–4.26) | 0.142 | 1.94 (0.84–4.46) |
| Not answered | | | 14 | | | | |
| Habits | | | | | | | |
| None | 144 (28.74) | 357 (71.26) | 501 (100.00) | | 1 | - | - |
| Smoking | 4 (15.38) | 22 (84.62) | 26 (100.00) | 0.149 ⁽²⁾ | 0.45 (0.15–1.33) | 0.23 | (0.07–0.77) |
| Alcoholism | 6 (33.33) | 12 (66.67) | 18 (100.00) | 0.673 ⁽²⁾ | 1.24 (0.46–3.37) | 1.42 | (0.41-4.88) |
| Smoking and alcoholism | 4 (44.44) | 5 (55.56) | 9 (100.00) | 0.313 ⁽²⁾ | 1.98 (0.52–7.49) | 1.19 | (0.24–5.82) |
| Workplace | | | | | | | |
| COVID-19 reference hospital (A) | 113 (34.98) | 210 (65.02) | 323 (100.00) | < 0.001 ⁽¹⁾ | 2.22 (1.49–3.31) | 0.001 | 2.51 (1.50–4.21) |
| Non-COVID-19 reference hospital (B) | 45 (19.48) | 186 (80.52) | 231 (100.00) | | 1 | - | - |
| Education | | | | | | | |
| Postgraduate | 65 (21.59) | 236 (78.41) | 301 (100.00) | | 1 | - | - |
| Technical level | 51 (39.53) | 78 (60.47) | 129 (100.00) | 0.009 ⁽¹⁾ | 1.86 (1.17–2.95) | 0.056 | 1.85 (1.08–3.17) |
| Undergraduate | 42 (33.87) | 82 (66.13) | 124 (100.00) | < 0.001 ⁽¹⁾ | 2.37 (1.52–3.71) | 0.025 | 1.82 (1.02–3.26) |
| Professional category | | | | | | | |
| Nursing | 109 (31.78) | 234 (68.22) | 343 (100.00) | 0.462 ⁽¹⁾ | 1.31 (0.63–2.71) | 0.415 | 1.46 (0.47–4.47) |
| Physician | 22 (21.57) | 80 (78.43) | 102 (100.00) | 0.549 ⁽¹⁾ | 0.78 (0.33–1.78) | 0.886 | 0.98 (0.29–3.29) |
| Physical therapist | 16 (23.88) | 51 (76.12) | 67 (100.00) | 0.786 ⁽¹⁾ | 0.88 (0.36–2.15) | 0.783 | 1.00 (0.28–4.48) |

Table 1 (continued)

| Characteristics | Positive n (%) | Negative n (%) | Total n (%) | p | Odds ratio (OR) | p | Adjusted OR (aOR) |
|--|-------------------|-------------------|----------------|----------------------|------------------|-------|---------------------|
| | 158 (28.52) | 396 (71.48) | 554 (100.00) | | | | |
| Other* | 11 (26.19) | 31 (73.81) | 42 (100.00) | | 1 | _ | _ |
| Work sector | | | | | | | |
| Intensive care unit | 40 (19.32) | 167 (80.68) | 207 (100.00) | 0.072 ⁽¹⁾ | 0.48 (0.21–1.07) | 0.431 | 0.60 (0.18–1.97) |
| Outpatient clinic | 42 (28.38) | 106 (71.62) | 148 (100.00) | 0.572 ⁽¹⁾ | 0.79 (0.35–1.78) | 0.929 | 1.03 (0.31–3.40) |
| Emergency room | 60 (28.52) | 83 (58.04) | 143 (100.00) | 0.364 ⁽¹⁾ | 1.45 (0.65–3.21) | 0.214 | 2.14 (0.63–7.22) |
| Surgical room | 5 (21.74) | 18 (78.26) | 23 (100.00) | 0.348 ⁽¹⁾ | 0.56 (0.16–1.89) | 0.386 | 0.44 (0.08–2.44) |
| Other** | 11 (33.33) | 22 (66.67) | 33 (100.00) | | 1 | - | - |
| Have you received training for the use and removal of personal protective equipment? | | | | | | | |
| Yes | 144 (27.75) | 375 (72.25) | 519 (100.00) | | 1 | - | - |
| No | 5 (41.67) | 7 (58.33) | 12 (100.00) | 0.296 ⁽²⁾ | 1.86 (0.58–5.96) | - | - |
| How many training sessions? | | | | | | | |
| One | 36 (24.83) | 109 (75.17) | 145 (100.00) | 0.095 ⁽¹⁾ | 0.62 (0.36–1.09) | 0.961 | 1.02 (0.53–1.94) |
| Тwo | 36 (20.57) | 139 (79.43) | 175 (100.00) | 0.011 ⁽¹⁾ | 0.49 (0.28–0.85) | 0.324 | 0.74 (0.40–1.35) |
| Three | 34 (39.08) | 53 (60.92) | 87 (100.00) | 0.530 ⁽¹⁾ | 1.21 (0.67–2.19) | 0.467 | 1.27 (0.67–2.40) |
| More than three | 35 (34.65) | 66 (65.35) | 101 (100.00) | | 1 | - | - |
| Not answered | | | 46 | | | | |

*HCW without direct and continuous patient contact, such as pharmacists, internal laboratory staff, and administrative staff

**Areas without direct and continuous patient contact, such as administrative offices, internal laboratory, and laundry facilities

^(a) The total represents the number of individuals who answered the question

⁽¹⁾ Chi-square test

(2) Fisher's exact test

participants (aOR = 2.00, 95% CI: 1.18–3.41), individuals working at Reference Hospital (aOR = 2.51, 95% CI: 1.50–4.21), and those holding a degree (p = 0.025; aOR = 1.82, 95% CI: 1.02–3.26). The data are shown in Table 1.

No statistical difference was observed between the groups that received training in using PPE. Among the participants who tested positive, 36 (20.57%) reported having received two (2) training sessions, while 36 (24.83%) reported having received one training session (Table 1).

The clinical manifestations associated with positivity in the molecular test were cough (aOR=3.16, 95% CI: 1.33–7.48), myalgia/arthralgia (aOR=3.55, 95% CI: 1.47–8.55), headache (2.24, 95% CI: 1.24–4.06), loss of smell or taste (aOR=10.52, 95% CI: 2.49–44.42), and fever or feeling feverish (aOR=3.30, 95% CI: 1.31–8.34). Complete data are presented in Supplementary File 3.

Our detection of 7 out of 158 (4.44%) asymptomatic cases and 15 out of 158 (9.49%) oligosymptomatic.

Positivity in the RT-qPCR test for SARS-CoV-2 was associated with the use of hydroxychloroquine (aOR=3.17, 95% CI: 1.31-7.66) and zinc (aOR=3.35, 95% CI: 1.18-9.51). Complete data are presented in Table 2.

Dynamic of incidence and attack rates

The overall attack rate ranged from 0.51% to 9.52%, with two peaks identified in August and December 2020 (Fig. 1). The incidence rate curves of both hospitals showed similar dynamics, except for August 2020, when general hospital experienced a decrease in the number of HCW with positive RT-qPCR (3.88%). In September 2020, both hospitals had similar incidences, followed by a decline in the number of cases until October 2020. Throughout the follow-up period, the attack rate at the Reference Hospital exceeded that of the Non-Reference Hospital and the highest peaks were observed in August 2020 (14.42%) and December 2020 (7.33%).

Table 2 Comparison of the use of drug to prevent SARS-CoV-2 infection among healthcare professionals in the study, according to the RT-qPCR results for SARS-CoV-2

| Characteristics | Positive n (%) | Negative n (%) | Total n (%) | p | Odds ratio (OR) | p | Adjusted OR (aOR) |
|---|-------------------|-------------------|----------------|-------------|---------------------|-------|-------------------|
| Antipyretic use | | | | | | | |
| No | 115 (22.77) | 390 (77.23) | 505 (100.00) | | 1 | - | - |
| Yes | 43 (87.76) | 6 (12.24) | 49 (100.00) | 0.000 (1) | 24.30 (10.09–58.54) | - | - |
| Use of any medication/substance to prevent or treat COVID-19? | | | | | | | |
| No | 76 (23.10) | 253 (76.90) | 329 (100.00) | | 1 | | - |
| Yes | 82 (36.44) | 143 (63.56) | 225 (100.00) | 0.001 (1) | 1.91 (1.31–2.77) | 0.079 | 0.37 (0.12–1.11) |
| Ivermectin | | | | | | | |
| No | 312 (76.10) | 98 (23.90) | 410 (100.00) | | 1 | | - |
| Yes | 84 (58.33) | 60 (41.67) | 144 (100.00) | < 0.001 (1) | 4.01 (1.52-3.40) | 0.952 | 1.02 (0.44–2.39) |
| Hydroxychloroquine | | | | | | | |
| No | 130 (25.59) | 378 (74.41) | 508 (100.00) | | 1 | | - |
| Yes | 28 (60.87) | 18 (39.13) | 46 (100.00) | < 0.001 (1) | 4.73 (2.42-8.45) | 0.011 | 3.17 (1.31–7.66) |
| Vitamin D | | | | | | | |
| No | 89 (23.54) | 289 (76.46) | 378 (100.00) | | 1 | | |
| Yes | 69 (39.20) | 107 (60.80) | 176 (100.00) | < 0.001 (1) | 3.76 (1.43-3.08) | 0.651 | 1.27 (0.46–3.54) |
| Zinc | | | | | | | |
| No | 89 (22.53) | 306 (77.47) | 395 (100.00) | | 1 | | |
| Yes | 69 (43.40) | 90 (56.60) | 159 (100.00) | < 0.001 (1) | 2.64 (1.78–3.90) | 0.023 | 3.35 (1.18–9.51) |

⁽¹⁾ p-value using Chi-square test



Fig. 1 Incidence rates of SARS-CoV-2 infection and the seroprevalence of SARS-CoV-2-specific IgG among HCW in two tertiary hospitals located in the city of Campo Grande, Brazil, from May 2020 to January 2021. In light blue, the figure presents the incidence rate of SARS-CoV-2 infection. The dark blue, the figure presents the seroprevalence of SARS-CoV-2-specific IgG. Correlation analyses were conducted using the Spearman's rank correlation test

From November 2020 onwards, the attack rate continued to decline at Hospital B (1.63%, 1.10%, and 0.00%,

respectively). In contrast, at Reference Hospital, there was an increase in the number of infections, with a new

peak in December 2020 and a decline only in January 2021 (0.96%), the last month of the follow-up period.

Identification of circulating variants

A total of 35 out of 158 samples (22.15%) underwent complete viral genome sequencing, revealing the presence of four strains of the SARS-CoV-2 virus: P.2 (n=12), B.1.1.28 (n=13), B.1.1.33 (n=9), and N.4 (n=9). The temporal distribution of these lineages revealed that B.1.1.28 and B.1.1.33 were the predominant lineages from May to August 2020. In November and December 2020, only the P.2 lineage was identified. The N.4 lineage was observed solely in July 2020. A decline in the number of cases was observed starting from August 2020, followed by a significant increase in October 2020, where the predominant variant of SARS-CoV-2 identified was P2.

Incidence of COVID-19 among HCW and the community, by epidemiological week

Population positivity data for the city of Campo Grande, Brazil, were obtained from the Epidemiological Bulletins published by the State Department of Health of Mato Grosso do Sul. The infection dynamics among HCW from Reference Hospitals and General Hospital were similar to that of the population of Campo Grande, MS, as shown in Fig. 2A. Two pandemic waves were observed during the study period, from epidemiological weeks 22 to 42 in 2020 and from weeks 43/2020 to 03/2021. There was a positive correlation between the number of cases among HCW in our study and the number of cases in the local population for both the first wave (r=0.82; CI_{95%} 0.59–0.93) and the second wave (r=0.81; CI_{95%} 0.47–0.9).

Furthermore, the dynamics of the number of COVID-19 cases among HCW in Campo Grande were similar to the number of cases in the general population of the municipality (Fig. 2B). There was a positive correlation between the number of cases in both groups for the first wave (r=0.47; CI_{95%} 0.04–0.76) and the second wave (r=0.83; CI_{95%} 0.53–0.95). These findings suggest that the number of cases among HCW followed the trend of positive cases by RT-qPCR in the population local.

Seroprevalence and monthly serological incidence

Out of the 554 participants, 143 (25.81%) tested positive for IgG antibodies to the SARS-CoV-2 virus in the serology test at some point during the study (Fig. 1). The highest monthly incidence of seropositivity occurred in September, with a rate of 9.92% (49 out of 494 participants) (Fig. 1).

We identified 14 (8.86%) individuals who tested positive for SARS-CoV-2 on RT-qPCR, but did not develop detectable IgG antibodies throughout the study. Among these 14 individuals, nine were asymptomatic at the time of their positive RT-qPCR diagnosis for SARS-CoV-2. The mean age of this group was 38.5 years, ranging from 30 to 49 years, indicating a non-elderly population.

Work absences and hospitalizations

During the follow-up period of the study, the rate of work absences was 56.68% (314 out of 554 participants). Out of these, 13 (2.35%) reported belonging to a highrisk group, 173 (55.09%) reported absences exclusively due to flu syndrome, and 76 (24.20%) reported absences due to flu syndrome and other reasons. Among the 554 HCW, 38.09% (n=211) reported other reasons for their absences. These reasons included mental health issues such as anxiety, depression, panic disorder and stress, accounting for 10.42% (n=22) of the total. Orthopedic problems accounted for 7.11% (n=15), while surgical procedures accounted for 4.74% (n=10). Isolation due to contact was reported by 2.84% (n=6), pregnancy by 2.37% (n=5), accidents by 1.89% (n=4), and tonsillitis by 0.94% (n=2). Additionally, 9.00% (n=19) reported random reasons, and 61.61% (n=130), indicated absences for unspecified reasons. It is important to note that participants may have been absent from work for multiple reasons.

Hospitalizations were reported by 7.40% (41 out of 554) of the professionals, and in some cases, multiple reasons for hospitalization were observed. Among the reported reasons, COVID-19 accounted for 31.64% of the hospitalizations, followed by surgical procedures (17.08%) and flu syndrome with negative RT-qPCR results (5.06%). Random reasons were cited by 19.51%, and 29.26% did not provide the reason for their hospitalization.

Among the 13 professionals who reported hospitalization due to COVID-19, was 8.22% (13 out of 158), 23.07% required intubation, while 7.69% did not provide information on the interventions received. The average length of stay in the ward was 6.9 days, ranging from 1 to 25 days, and 23.07% did not report the duration of their hospital stay.

The average pulmonary impairment among hospitalized patients was 38.61%, with a range of 0% to 85%. In 23.07% of cases, the presence or absence of pulmonary impairment was not reported. The reported average oxygen saturation was 89.33%, ranging from 78 to 96%. Saturation values were not reported by 30.76% of the participants.

Mortality and fatality rate

The mortality rate in our study was 3.6 per thousand (2 out of 554), and the case fatality rate was 1.27% (2 out of 158). Both participants who passed away were in Reference Hospital and the Non-Reference Hospital, respectively. In Reference Hospital, the mortality rate was 3.09



Fig. 2 Dynamics of SARS-CoV-2 infection in HCWs (columns) versus confirmed cases of Covid-19 in the population of Campo Grande, Mato Grosso do Sul, Brazil (blue line). A Distribution of SARS-CoV-2 infection cases in the HCW cohort from the two evaluated hospitals in the present study. B Distribution of SARS-CoV-2 infection cases in HCWs from Campo Grande. Data expressed in absolute numbers per epidemiological week. Non-primary data were obtained from the Epidemiological Bulletins of the State Health Department of Mato Grosso do Sul during the study period. Correlation analyses were conducted using the Spearman's rank correlation test

per thousand (1 out of 323), while in General Hospital, it was 4.32 per thousand (1 out of 231). The case fatality rate in Reference Hospital was 0.88% (1 out of 113), and in Non-Reference Hospital, it was 2.22% (1 out of 45) (Fig. 3).

Reinfection identification

With the emergence of the second pandemic wave in October, all professionals who had previously tested

positive during the follow-up period were invited to undergo additional nasal and oropharyngeal swab collections, regardless of their symptoms.

Of the 158 professionals with a positive diagnosis, 13 (8.22%) withdrew from the follow-up after their initial positive result. In the last collection, 14 professionals (8.86%) tested positive again, two individuals (1.26%) unfortunately passed away, and 41 professionals (25.94%) declined to participate in the screening. Therefore,



Fig. 3 Mortality (‰) and lethality (%) rates of COVID-19 among HCW in two tertiary hospitals located in the city of Campo Grande, Brazil, from May 2020 to January 2021. Hospital A, which serves as a reference for COVID-19, and Hospital B, which is non-reference for COVID-19

reinfection was not investigated in 44.30% of the previously positive cases.

Reinfection was observed in only 1.13% of the professionals who agreed to follow up on swab collections (one out of 88). This reinfection case, confirmed by wholegenome sequencing (unpublished data), occurred in a professional from Non-Reference Hospital, who received a second diagnosis 113 days after the initial diagnosis.

Discussion

The present study is an original, prospective investigation that aimed to conduct virological surveillance of SARS-CoV-2. Relevant information was systematically collected from a well-characterized cohort of 554 HCW in Brazil during a pre-COVID-19 vaccine period. Our findings showed an overall prevalence of SARS-CoV-2 infection of approximately 28%, which is consistent with previous studies reporting high infection rates ranging from 11% to 51.7% among HCW [6, 23-25]. However, comparing our results with other published studies is challenging due to variations in study design, testing intervals, and pandemic dynamics. Asymptomatic infections were frequent early in the pandemic, 51.7% to 87.9% [26, 27]. Although it was much lower in our study (4.4% and 9.5%), performing virological surveillance regardless of symptoms was useful, as asymptomatic, individuals can still transmit the virus [28, 29]. Systematic screening of healthcare workers can thus reduce the risk of nosocomial transmission [30]. In our study, we may have missed some cases, as tests were performed every 14 days. However, we conducted symptom surveillance every 3 days online and anticipated sampling in the presence of symptoms.

Our findings indicate that the risk factors associated with a positive COVID-19 diagnosis include being male, working at the referral hospital, having a graduate-level education, and using hydroxychloroquine and zinc for prevention or treatment. An increased risk of COVID-19 infection among male healthcare workers, which is noteworthy, as existing literature predominantly associates male healthcare workers with higher risk in severe disease conditions [31, 32]. Our study, however, focused on the timing of infection rather than exposure-related severity, suggesting that our findings may reflect behavioral distinctions within this group, which were beyond the scope of our study parameters. Professionals working at the Reference Hospital in Campo Grande had more than the double risk of RT-qPCR-confirmed infection, which could be attributed to repeated and prolonged occupational exposure, long working hours, double exposure, stress, and fatigue. Although we did not observe a difference in the infection risk across professional categories, unlike previous studies [33-35], HCW with a graduated-level education had nearly twice the odds of a positive RT-qPCR result. Nurses, physical therapists, and physicians experienced more mental, physical, and time pressures in other studies [36, 37]. Among the drugs that have been used in the prevention or treatment of COVID-19, hydroxychloroquine, zinc, and azithromycin have been mentioned by the enrolled participants. We found that individuals who used hydroxychloroquine had a 3.17 times higher chance of testing positive, while those who used zinc had an odds ratio of 3.35. However, it is important to note that these results may be biased due to misinformation regarding the use of these medications at the time of the study, whose inefficacy has been demonstrated by several studies. Moreover, many healthcare workers used these drugs without proper medical indication and the study did not investigate the time of their treatment or the number of doses taken [38–40].

Our study also investigated the infection dynamics among healthcare workers, which mirrored those observed in the general community of Campo Grande, as reported in another study [41]. It is important to note that infections among healthcare workers can originate not only from patients, but also from other individuals, both within and outside the hospital setting [42].

Past infection among HCW was high in our study. One-fourth of HCW had been previously infected, according to the IgG serology. Although serology should not be used for current infection, its role as an indicator of prevalence has been widely employed in epidemiological surveys [43]. In different regions, the reported overall seroprevalence in healthcare workers varied from 1.8% to 18% [44–48]. Among the 158 HCW, we found that 9.49% did not develop IgG antibodies at any point during the study. A similar finding was reported in another study [49].

A global study published in 2020 identified 17 genetically confirmed cases of COVID-19 reinfection, since the first documented case in August of the same year [50]. In our study, a single case of reinfection was identified in Hospital B, where the individual received a second positive diagnosis in November 2020, as confirmed by genomic sequencing. This first diagnosis was associated with the B.1.1.28 strain, characterized by mutations D614G, S939S, and V1176F in the spike protein. The second diagnosis was linked to the P2 strain, characterized by mutations E484K/L, D614G, and V1176F in the spike protein. This highlights the importance of genomic surveillance of SARS-CoV-2 in understanding viral dynamics and contributing to disease control.

During our study period, the frequency of dominant lineages circulating in our sample aligned with the frequency of dominant lineages in Brazil at the time [51–53]. Initially, cases were predominantly driven by the B.1.1.28 and B.1.1.33 strains, which emerged in São Paulo in late February [54, 55] and marked the prevalence of healthcare worker infections during the first wave of the pandemic, spanning from May to October. The P.2 variant accounted for 100% of the positive and sequenced cases during the second wave of the pandemic, which occurred in our study between October 2020 and January 2021. This variant was characterized by a significant increase in the number of cases due to its higher transmission rate.

Our study revealed that the hospitalization rate among healthcare workers was similar to that reported in studies conducted in Brazil and in the United State [13, 56]. Both the mortality and fatality rates in our study were low, which falls within the range observed in other studies ranging from 0.5% to 14.7% [57, 58]. The low case lethality rate observed in our study may be associated with the age group of the participants, as 64.98% were 40 years or younger, and the absence of comorbidities in 74.72% of the cohort [59–61]. Furthermore, our cohort consisted mostly of female healthcare workers, and it has been reported that females tend to have lower mortality rates [62].

Limitations

The present study has several limitations that need to be considered. Firstly, hospital A imposed limitations on testing, requiring HCW to travel to a separate collection site located at a distance. This may have resulted in inconvenience and potential bias, as some HCW may have been unable or unwilling to undergo testing due to the logistical challenges involved. Secondly, the ongoing pandemic itself posed a significant limitation. The rapidly evolving nature of the COVID-19 situation, coupled with the overwhelming workload on HCW, may have impacted the accuracy and completeness of data collection. In addition to these specific limitations, there are other general limitations that should be acknowledged, such as the sample size of the study may have been insufficient to detect subtle differences or rare outcomes. Lastly, it is important to note that this study was conducted in a specific geographical location and may not be representative of HCW in other regions or healthcare settings. Therefore, caution should be exercised when extrapolating the findings to broader populations.

Conclusions

Our study provides valuable insights into virological surveillance of SARS-CoV-2, a strategy that, during pandemics, could be promoted for adoption to map the battlefield and understand infection dynamics among healthcare workers. This is the only Brazilian long-term study focusing on the incidence of infection among front-line HWC, which can help in the future pandemics. The infection dynamics among healthcare workers mirrored the pattern in terms of prevalence, incidence, circulating strains, reinfection, hospitalization rate, mortality, and lethality, as well as a reduction in the workforce due to absenteeism. Although it is not possible to assert that the infection is community-based or nosocomial, it is possible to corroborate that there is dual exposure in conditions of high susceptibility.

Abbreviations

| aOR BCG BMI CAAE (acronym in Portuguese) | Adjusted odds ratios Bacille Calmette–Guerin Body mass index Certificate of Presentation for Ethical Consideration |
|---|--|
| CI | Confidence interval |
| CMIA | Chemiluminescent microparticle immunoassay |
| COVID-19 | Coronavirus disease-19 |
| Ct | Cycle of quantification |
| EPV | Events per variable |
| HCW | Healthcare workers |
| lgG | Immunoglobulin G |
| IRMA | Iterative Refinement Meta-Assembler |
| OR | Odds ratios |
| PCR | Polymerase chain reaction |
| PPE | Personal protective equipment |
| REDCap | Research Electronic Data Capture |
| RI-qPCR | Reverse transcription real-time PCR |
| STROBE | strengthening the reporting of observa- |
| WGS | Whole-genome sequencing |
| WHO | World Health Organization |
| χ2 | Chi-square test |

Supplementary Information

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| Supplementary Material 1. |
|---------------------------|
| Supplementary Material 2. |
| Supplementary Material 3. |

Author contributions

ALDBG participated in the conceptualization of the study, data collection, data curation, data analysis, drafting of the manuscript, and manuscript revision. SVBG participated in data collection, data analysis and revision of the manuscript, WMSS participated in data collection, sample curation, and revision of the manuscript, DGS participated in data collection, data analysis and revision of the manuscript, TASC participated in data collection, data analysis and revision of the manuscript. LMP participated in data collection, data analysis and revision of the manuscript. WSF participated in data collection, data analysis and revision of the manuscript. FPR participated in data collection, data analysis and revision of the manuscript. CS participated in data collection, data analysis and revision of the manuscript. AOF participated in data collection, data analysis and revision of the manuscript. ATGG participated in data collection, data analysis and revision of the manuscript. CAM participated in data collection, data analysis and revision of the manuscript. EFL participated in data collection, data analysis and revision of the manuscript. CCMG participated in the conceptualization of the study, data analysis, and revision of the manuscript. CABJ participated in data collection, data analysis and revision of the manuscript. RPF participated in data collection, data analysis and revision of the manuscript. JC participated in data analysis and revision of the manuscript. APL participated in data collection, data analysis and revision of the manuscript. CS participated in data collection, data analysis and revision of the manuscript. TNM participated in data collection, data analysis and revision of the manuscript. KRNS participated in data collection, data analysis and revision of the manuscript. AMTF participated in data collection, data analysis and revision of the manuscript. ACGN participated in data collection, data analysis and revision of the manuscript. AMMP participated in conceptualization of the study, data analysis and revision of the manuscript, ARCMC participated in conceptualization of the study, data analysis and revision of the manuscript. JV participated in financial management, data curation, data analysis, drafting of

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Availability of data and materials

Due to individual privacy and ethical constraints, the dataset underlying this analysis cannot be made publicly available. The entire data are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate

This study was approved by the Institutional Review Board of Federal University of Mato Grosso do Sul (CAAE number 31411920.4.0000.0021).

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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