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Healthcare-associated infections related to COVID-19 in intensive care unit patients

Infecção relacionada à assistência hospitalar associada ao COVID-19 em pacientes de unidade de terapia intensiva

Infección asociada a la atención de la salud relacionada con COVID-19 en pacientes de la unidad de cuidados intensivos

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ABSTRACT

Introduction: The COVID-19 pandemic, caused by the SARS-CoV-2 virus, has precipitated a global health crisis, potentially amplifying healthcare-associated infections (HAIs). **Aim**: To observe the impact of HAIs on COVID-19 patients admitted to the ICU of a hospital in Southern Maranhão. **Design**: This study is descriptive, retrospective, and quantitative, based on primary data from hospital records spanning June to November 2020. **Results**: The study encompassed 274 patients, with an average age of 63 years (range: 18-97 years). A low incidence of HAIs in COVID-19 patients in the ICU (2.91%) was observed during the study period. The utilization rate of invasive devices was 33.21%, with CVD (97.8%) being the predominant type. CVD-associated urinary tract infection (UTI) caused by *Candida sp.* accounted for 50% of diagnosed HAIs. The mortality rate attributable to HAIs in COVID-19 patients in the ICU is 1.46%, whereas the rate among those without HAIs is 25.91%. **Implications**: The study reveals a limited impact of HAIs on the clinical outcomes of COVID-19 patients admitted to the ICU, suggesting the need to promoting complete COVID-19 vaccination.

DESCRIPTORS
COVID-19; Cross Infection; Intensive Care Units.

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INTRODUCTION

The COVID-19 pandemic, initiated by the SARS-CoV-2 virus and officially declared by the WHO in March 2020, has profoundly impacted the healthcare systems of various countries and disrupted global socio-economic dynamics.[1] The first wave of the COVID-19 epidemic in Brazil occurred from February 23 to November 1, 2020, spanning the 9th to the 45th epidemiological week.[2]

During the study period, Brazil has recorded a total of 30,701,900 cases and 664,987 deaths from COVID-19 until May 2022. Maranhão boasts the lowest national mortality rate from COVID-19, with 153.9 deaths per 100,000 inhabitants.[3] Despite this achievement, Maranhão ranks second to last among Brazilian states in the Human Development Index (HDI),[4] with high rates of morbidity and mortality from other diseases and inadequate medical-hospital care, having the second lowest rate of physicians per thousand inhabitants in the country.[5]

Due to the vast expanse of Brazilian territory and socio-economic disparities among states, there was an urgent need for a greater quantity of Intensive Care Unit (ICU) beds during the pandemic, capable of meeting the functional and structural requirements for quality healthcare due to the high demand from patients. Temporary healthcare units for hospital care, known as Field Hospitals, were implemented to address the emergency needs of COVID-19 patients.[6]

Throughout the pandemic, various protocols advocated for early treatment using antimicrobials without clinical evidence of bacterial infection associated with COVID-19, such as azithromycin. This antibiotic was widely publicized and used both within and outside of hospitals[7-8] and was even recommended as early treatment for COVID-19 by the Brazilian Ministry of Health through the so-called "COVID Kit”.[9,7]

Other antibiotics and medications were also excessively and abusively used, with consumption reaching up to 90% in some regions,[10] potentially resulting in increased microbial selection and elevated side effects, particularly in intensive care patients.[11-12] Additionally, the Brazilian population already exhibits high antibiotic resistance, making it even more susceptible to healthcare-associated infections (HAIs).[13]

Furthermore, the high demand for intensive care beds and the exacerbated working hours of healthcare professionals often required unprepared manpower within hospital services during the pandemic.[14-15] Coupled with these factors is the global shortage of hospital supplies, which affected the purchase and distribution of Personal Protective Equipment (PPE) used in COVID-19 management and prevention. Additionally, the lack of adherence to intra-hospital protocols for disease prevention may have contributed to increased microbial infections.[16] This context may have led to the rise in the number of HAIs as well as related complications and deaths.[17]

Healthcare-Associated Infections (HAIs) are contracted in hospital environments, with diagnostic criteria well-established by Anvisa, following patient hospitalization or invasive procedures. Notably, the use of invasive devices in the ICU includes the Indwelling Urinary Catheter (IUC), Central Venous Catheter (CVC), and Mechanical Ventilation (MV), which are associated with Urinary Tract Infections (UTIs), Primary Bloodstream Infections (PBSIs), and Ventilator-Associated Pneumonia (VAP), respectively. These infections are typically diagnosed after a patient has spent 3 days in the Intensive Care Unit, among other specific diagnostic requirements.[18]

Invasive procedures serve as potential entry points for microorganisms, primarily bacteria and fungi, and may entail a high risk of in-hospital mortality.[19] Globally, the primary culprits responsible for HAIs are the "ESKAPE" pathogens - *Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Enterobacter* species.[20]

Recent studies on the hospitalization of COVID-19 patients have more frequently identified *A. baumannii*, *K. pneumoniae*, *P. aeruginosa*, and *E. coli* with multidrug-resistant characteristics within the ICU environment.[21] This fact is likely linked to the increased profile of bacterial resistance, given the intimate association with the indiscriminate and empirical use of antibiotics during the pandemic.[22] Hence, there's a pressing need for investment in prevention and appropriate clinical management, achieved through the implementation of Hospital Infection and Antimicrobial Control, including the establishment of an Antimicrobial Stewardship Program (ASP)[11] adapted to the realities of the Brazilian healthcare system.[23]

In light of these circumstances, the present study examines the relationship between HAIs and COVID-19 in a Field Hospital in a city within the interior of Maranhão. This investigation is especially pertinent as the region faces challenges such as low HDI and limited access to healthcare. The study aims to demonstrate the mortality rates of COVID-19 patients associated with HAIs in the ICU of the Field Hospital and, despite the region's underdevelopment, compare the findings with studies conducted in national and international healthcare facilities of reference.

METHOD

This study adopts a cross-sectional, descriptive, retrospective design with a quantitative approach. The sample comprises convenience sampling of COVID-19 patients admitted to the ICU of the Field Hospital from June to November 2020, coinciding with the monitoring period of the Hospital Infection Control Committee (HICC). The analysis is based on medical records available in the HICC of the Regional Mother and Child Hospital, located in Imperatriz-MA, which, as per Ordinance No. 1,514, was tasked with the functional management of the COVID-19 Field Hospital.[6]

The Field Hospital under scrutiny is one of the key healthcare facilities in the Southern region of Maranhão, providing outpatient and Intensive Care Unit services for COVID-19 patients.

Initially, data from 381 patients were examined, with 107 excluded due to incomplete medical records or inconsistencies with the research's inclusion and exclusion criteria. Consequently, information from 274 patients was included in the study.

Data collection involved the scrutiny of hospital records and utilization of the National Anvisa database to validate information. Patient identification was coded numerically to maintain confidentiality, and researchers had no direct contact with the subjects. Data were tabulated and analyzed using Microsoft Excel 2019, facilitating total values, percentage calculations, and arithmetic means. Statistical tests were deemed inapplicable for this sampling method.

Inclusion criteria stipulated patients aged 18 years or older of any gender, admitted to the COVID-19 ICU of the Field Hospital during the specified period, and undergoing a confirmatory microbiological examination for HAIs after 72 hours of hospitalization. Exclusion criteria encompassed patients without positive COVID-19 confirmation in rapid antigen tests and/or RT-PCR, those with surgical infection HAIs, and individuals diagnosed with bacterial infections associated with COVID-19 upon hospital admission.

Data analysis considered independent variables such as age, sex, and use of invasive devices (Mechanical Ventilation (MV), Indwelling Urinary Catheter (IUC), Central Venous Catheter (CVC)), alongside dependent variables including HAIs documented by the hospital's HICC according to diagnostic criteria from the National Health Surveillance Agency (ANVISA).[23] HAIs encompassed ventilator-associated pneumonia, urinary tract infection, bloodstream infection, and case outcomes, including deaths.

As all data are non-public, the study underwent ethical review and approval by the Research Ethics Committee of HUUFMA, following guidelines outlined in CNS Resolution No. 466/2012 and Operational Standard No. 001 of 2013 of CNS, under opinion 5,339,824. Additionally, authorization was granted by the School of Public Health of the State of Maranhão - ESP/MA under Letter No. 2719/2021. Risks to participants included breaches of confidentiality in physical records, which were mitigated through strict control over data manipulation and storage on password-protected computers, complemented by antivirus software. Patient information remained confidential among the article's contributors, and no conflicts of interest were declared.

RESULTS

In Table 1, we observe the epidemiological profile, including age and sex, and the outcomes of patients admitted to the ICU. The majority of admitted patients are over 35 years old, with a predominance of elderly patients (> 65 years), with those aged over 65 (49.63%) being the most frequently admitted to the healthcare service. The average age is 63 years (range: 18-97 years). No significant difference between sexes is observed regarding the admission rate. A decrease in ICU admissions is noted over the analyzed period.

Table 1. Profile and clinical outcomes of COVID-19 patients admitted to the ICU of a Hospital in Southern Maranhão, between June 2020 and November 2020. (n=274)

Month	Jun	Jul	Aug	Sep	Oct	Nov	n	(%)
Total Cases	67	56	51	40	28	31	274	(100)
Gender								
Male	33	33	26	21	10	13	137	(49.8)
Female	34	24	25	19	18	18	138	(50.2)
Age								
≤ 20	1	1	0	0	2	0	4	(1.45)
21 a 35	1	3	9	4	2	4	22	(8.03)
36 a 50	12	10	5	7	7	4	45	(16.42)
51 a 65	18	15	11	8	5	11	67	(24.45)
>65	35	27	23	22	14	13	136	(49.63)
ICU General Deaths	14	19	19	12	3	8	75	**(27.37)**
HAI Deaths	0	4	0	0	0	0	4	**(1.46)**

Notes: June (Jun), July (Jul), August (Aug), September (Sep), October (Oct), November (Nov).
Source: Author, 2022.

In terms of the final outcome, 27.37% of patients admitted to the general ICU passed away within the study period. In July (6.93%) and August (6.93%), the highest numbers of ICU deaths were observed, with July being the month when all HAI-related deaths (1.46%) associated with COVID-19 were recorded during the study period.

Table 2 presents the types of invasive devices in the ICU, their utilization, and the diagnosis of HAIs through microbiological culture. It's observed that out of a total of 274 patients, 91 (33.21%) utilized invasive devices, amounting to a total of 180 devices used during the study period. In June, there was a usage of 53 (29.44%) devices, with 54.71% of them being Indwelling Urinary Catheters (IUC). In the subsequent months, the numbers of admissions and usage of invasive devices decreased. Among those admitted while using invasive devices, 89 (97.80%) out of a total of 91 patients used IUC, 53.84% used Central Venous Catheters (CVC), and 46.15% used Mechanical Ventilation (MV).

Table 2. Types of invasive devices used and laboratory diagnosis of HAIs in COVID-19 patients admitted to the ICU of a Hospital in Southern Maranhão, between June 2020 and November 2020. (n=274)

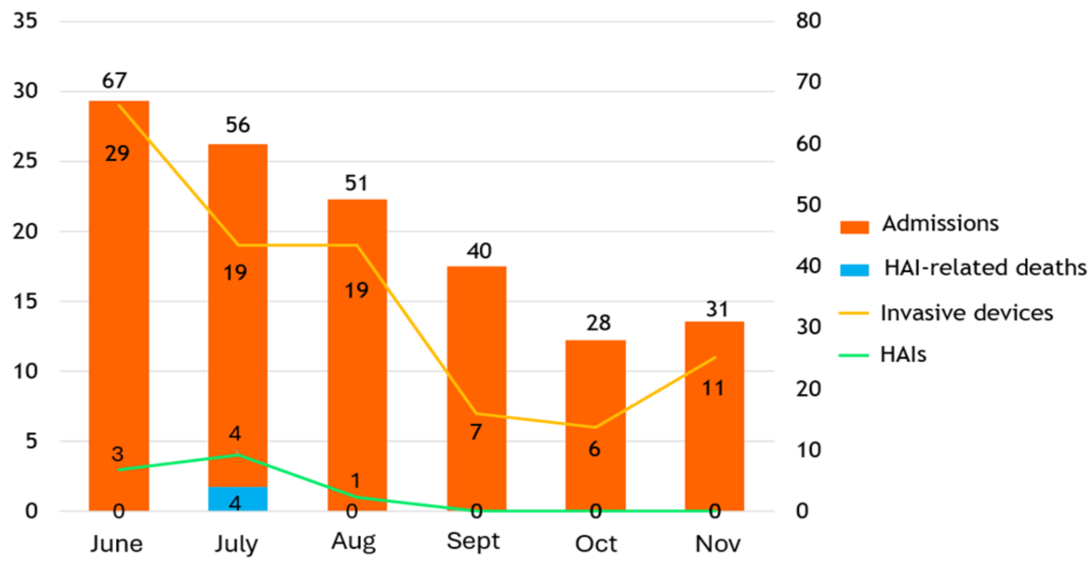
Month	Jun	Jul	Aug	Sep	Oct	Nov	N (%)
Patients using invasive devices	29	19	19	7	6	11	**91 (33.21)**
Devices	53	33	43	17	16	18	180
VM	11	7	13	5	4	2	42
IUC	29	18	18	7	6	11	89
CVC	13	8	12	5	6	5	49
HAIs	3	4	1	0	0	0	**8 (2.91)**
Positive cultures meeting HAI criteria							
Blood culture	0	1	0	0	0	0	1
Urine culture	3	3	1	0	0	0	7

Notes: June (Jun), July (Jul), August (Aug), September (Sep), October (Oct), November (Nov), Mechanical Ventilation (VM), Indwelling Urinary Catheter (CVD), Central Venous Catheter (CVC).
Source: Author, 2022.

It is also observed that the diagnoses of HAIs are concentrated in the first three months of the study. The ratio of HAIs per patient using invasive devices is 8/91 (8.79%), which were diagnosed through blood culture or urine culture. The rate of HAIs among all COVID-19 patients admitted to the ICU was 2.91%.

Graph 1 summarizes the absolute quantity of invasive device usage and HAI diagnoses, as well as admissions and HAI-related deaths of patients admitted to the ICU for COVID-19. There was a decrease in the usage of devices and diagnoses of HAIs during the study period.

Graph 1. Relationship between the use of invasive devices, admissions, HAIs, and HAI-related deaths in COVID-19 patients admitted to the ICU of a Hospital in Southern Maranhão, between June 2020 and November 2020. (n=274)



Notes: June (Jun), July (Jul), August (Aug), September (Sep), October (Oct), November (Nov).
Source: Author, 2022.

Table 3 presents the etiological profile of the causative agents of HAIs in the ICU of this study, with the genus Candida (50%) being the most frequent agent, followed by K. *pneumoniae* (25%).

Table 3. Etiological profile of the pathogens causing HAIs in the COVID ICU of a Hospital in Southern Maranhão, between June 2020 and November 2020

Quantity	Agent	Culture
2	*Candida albicans*	Urine culture
1	*Candida krusei*	Urine culture
1	*Candida glabrata*	Urine culture
2	*Klebsiella pneumoniae*	Urine culture
1	*Staphylococcus haemolyticus*	Blood culture
1	*Enterococcus faecium*	Urine culture

Source: Authors.

DISCUSSION

In our retrospective study of 274 patients, the average age was 63 years, similar to the main references in the literature.[24-25] Regarding the sex of patients admitted to the ICU, we did not find a significant difference; however, some studies describe a male predominance.[26,25]

In this study, we observed a low rate of HAIs in COVID-19 patients in the ICU (2.91%) and a predominance of *Candida spp*. and *Klebsiella Pneumoniae* pathogens during June and November 2020. Furthermore, in an English meta-analysis, the rate of bacterial infection acquired in ICU patients with COVID-19 was 14%, with the pathogens identified as *M. pneumoniae*, followed by *P. aeruginosa*, *H. influenzae*, *and K. pneumoniae*.[27]

In other studies, the rate of acquired infection in the ICU in patients with COVID-19 varies from 70.6% to 4.7%.[28-32] Overall, it is important to note that rates of acquired infection in the ICU vary greatly depending on the country, and some data refer to the initial months of the pandemic in 2020, which may not provide a reliable comparison.

A US study evaluates the increase in HAIs when comparing the respective quarters of 2019 and 2020. In the third quarter of 2020, CBSIs by CVCs (46.4%) showed the highest increase, followed by VAP (29.0%) and UTIs by IUCs (12.7%); in the fourth quarter, there was an increase of 47%, 44.8%, and 18.8%, respectively.[33] Studies from the US and Italy also confirm this increase in HAIs from invasive devices in 2020 compared to 2019,[34] with an increase in VAP (46.9%) and UTIs by IUCs (21.9%).[26]

This data reflects a challenging scenario in the treatment and control of secondary infections acquired in the ICU during this period. Although these are robust studies, such data differ from ours, as in this study, the results showed a reduction in diagnosed cases of HAIs from June to November 2020. It is suggested that there may be difficulty in comparing between countries during the months of the first wave of the COVID-19 pandemic, as diagnostic criteria and pandemic guidelines for each country may have been divergent.

The proportion of HAIs among ICU admissions (2.91%) is lower or similar to the main references in the literature. [27-32] This may have been contributed to by the fact that the Hospital included in the study has a Hospital Infection Control Committee (HICC) with daily visits to ICU beds, following Bundles and main national protocols proposed by ANVISA[18] for the prevention and management of HAIs, in addition to periodic training of the multidisciplinary team in the face of the pandemic situation.

In this study, eight cases of HAIs were found, of which 50% were caused by fungi of the *Candida genus*. In a multicenter study, this pathogen is rarely identified among the causes of HAIs in patients with COVID-19, as fungal microbiological confirmation was a limitation during the first wave of the pandemic. [27] A study conducted in Taiwan shows that *Candida sp*. (43.2%) was the most frequent pathogen in the COVID-19 ICU, followed by gram-negative bacteria. [35]

A study, including 1179 patients with COVID-19 in the ICU, observes the growth of *Candida spp*. in half of the positive urocultures for HAIs.[31] The description of fungal infection associated with COVID-19 has recently been increasing in the literature, including *Candida spp.*, *Cryptococcus, Mucorales*, and *Aspergillus spp.*, however, among them, only the *Candida genus* was found in this study.[35-36]

Candida spp. pathogens are colonizers of invasive devices such as catheters[25] and all microorganisms of this genus were found in invasive devices of the CVD type in our study, although it is more commonly reported in intravascular catheters.[36-37] This fact may be justified due to poor handling of the CVD during device application and maintenance in the hospital environment in the context of the pandemic, as well as insufficient adherence to infection control measures in the ICU and possibly inadequate diagnostic criteria. This reality may have favored the occurrence of HAIs in COVID-19 hospitalized patients.[38]

Furthermore, hospitalized patients with COVID-19, especially if severely ill, are almost invariably treated with antibiotics.[38-39] The rate of patients with COVID-19 receiving empirical antibiotic treatment was reported at 68% and 72% before hospital admission.[25,39] Several studies indicate an increase in antimicrobial consumption during the COVID-19[25,38-39] case outbreak, suggesting bacterial resistance to broad-spectrum antibiotics. The inappropriate use of these antibiotics favors the selection of pathogens such as *C. difficile* and *Candida spp.*[36]

A Brazilian study suggests that high doses of corticosteroids for an undetermined period increase the risk of candidemia in COVID-19 patients admitted to the ICU, with 8 deaths out of 11 patients and a mortality rate of 72.7%.[40] Therefore, it is presumed that immunosuppressive drugs, therapy for severe COVID-19 patients, combined with excessive use of antibiotics, may increase susceptibility to HAIs by fungal pathogens, as observed in our study.

The mortality rate for ICU-acquired infections in COVID-19 patients varies depending on the pandemic period studied in the main literature references. In a study including 375 hospitalized COVID-19 patients, a 15% rate of ICU-acquired secondary infection was found, with 45% of these cases progressing to death due to HAIs.[31] Conversely, a larger study with 1565 patients observed that 3.7% of COVID-19 patients acquired HAIs in the ICU, and 40.7% progressed to death.[24] In this study, there was a 2.91% rate of diagnosed HAIs in patients with the disease, with 50% of them progressing to death.

Some limitations of the current study are highlighted: a short evaluation period; no stratification of disease severity, with all COVID-19-positive patients requiring intensive care admitted to the Field Hospital ICU; patient comorbidities were not assessed; viral tests for etiology other than SARS-CoV-2 were not performed; microbiological culture was not conducted on all hospitalized patients, only on those using invasive devices and clinically and/or laboratory suspected infections, hence bacterial and fungal infections may be underdiagnosed.

CONCLUSION

In this study, conducted on COVID-19 ICU patients after 72 hours of hospitalization, a high mortality rate was observed among ICU patients diagnosed with COVID-19 (27.37%) without associated HAIs (25.91%). In contrast, a low mortality rate was observed in COVID-19 patients with associated HAIs (1.46%). Despite the limited hospital infrastructure and low access to specialized healthcare in the southern region of Maranhão, HAI rates were lower than those reported in major national and international hospital centers.

Therefore, it cannot be affirmed that the quantity of deaths in the COVID-19 ICU from June to November 2020 was influenced by HAIs, as the pathological process of COVID-19 itself and potential comorbidities associated with hospitalized patients are determining factors for the final outcome. This study reaffirms the need to promote complete

COVID-19 vaccination. Further studies are needed to evaluate the progression of HAIs in COVID-19 patients throughout the pandemic.

RESUMO

Introdução: A pandemia de COVID-19, causada pelo vírus SARS-CoV-2, causou uma crise na saúde global. Isso possivelmente elevou as infecções relacionadas à assistência à saúde (IRAS). **Objetivo:** Observar a influência das IRAS em pacientes com COVID-19 internados na UTI de um Hospital no Sul do Maranhão. **Delineamento**: Trata-se de um estudo descritivo, retrospectivo, de abordagem quantitativa, feito com dados primários de prontuários hospitalares durante o período de junho a novembro de 2020. **Resultados:** O estudo foi realizado com 274 pacientes, com média de idade de 63 anos (18-97 anos). Foi encontrada uma baixa taxa de IRAS em pacientes com COVID-19 na UTI (2,91%) durante o período estudado. A taxa de utilização de dispositivos invasivos é 33,21%, sendo o CVD (97,8%) o tipo de dispositivo mais utilizado. A ITU por CVD do gênero *Candida sp.* foi responsável por 50% das IRAS diagnosticadas. A taxa de óbitos por IRAS em pacientes com COVID-19 na UTI é de 1,46%, já a taxa sem IRAS é de 25,91%. **Implicações:** O estudo mostra uma baixa influência das IRAS no desfecho clínico do paciente com COVID-19 internado na UTI, sendo interessante incentivar o esquema vacinal completo para o COVID-19.

DESCRITORES

COVID-19; Infecção hospitalar; Unidade de Terapia Intensiva.

RESUMEN

Introducción: La pandemia de COVID-19, causada por el virus SARS-CoV-2, ha precipitado una crisis de salud global, potencialmente amplificando las infecciones asociadas a la atención de la salud (IAAS). **Objetivo**: Observar el impacto de las IAAS en pacientes con COVID-19 ingresados en la UCI de un hospital en el sur de Maranhão. **Delineación**: Este estudio es descriptivo, retrospectivo y cuantitativo, basado en datos primarios de registros hospitalarios que abarcan desde junio hasta noviembre de 2020. **Resultados**: El estudio incluyó a 274 pacientes, con una edad promedio de 63 años (rango: 18-97 años). Se observó una baja incidencia de IAAS en pacientes con COVID-19 en la UCI (2,91%) durante el período de estudio. La tasa de utilización de dispositivos invasivos fue del 33,21%, siendo el CVD (97,8%) el tipo predominante. La infección del tracto urinario (ITU) asociada al CVD causada por Candida sp. representó el 50% de las IAAS diagnosticadas. La tasa de mortalidad atribuible a las IAAS en pacientes con COVID-19 en la UCI es del 1,46%, mientras que la tasa entre aquellos sin IAAS es del 25,91%. **Implicaciones**: El estudio revela un impacto limitado de las IAAS en los resultados clínicos de los pacientes con COVID-19 ingresados en la UCI, lo que sugiere la necesidad de promover la vacunación completa contra COVID-19.

DESCRIPTORES

COVID-19; Infección Hospitalaria; Unidades de Cuidados Intensivos.

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COLLABORATIONS

All authors contributed to the design of the project, collection, analysis and interpretation of data. There was active participation in discussing the results and writing the article, as well as in the review and final approval of the version to be published. All authors agree to the veracity and integrity of the information in the manuscript. **All authors agree and are responsible for the content of this version of the manuscript to be published.**

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AVAILABILITY OF DATA

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Not applicable.

CONFLICTS OF INTEREST

There are no conflicts of interest to declare.