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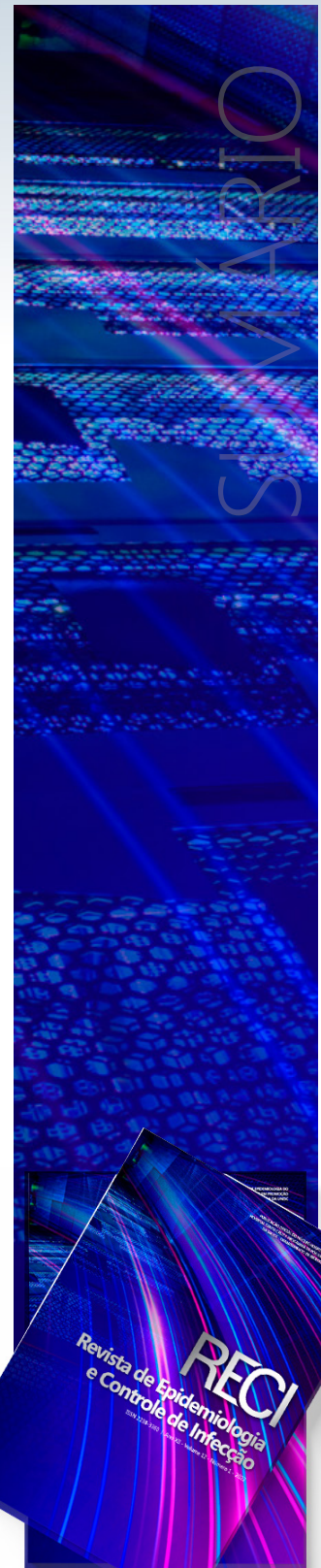
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Historical geographic overlap of human rickettsiosis with animal reservoirs in Juiz de Fora, Minas Gerais, Brazil

Sobreposição geográfica histórica da riquetsiose humana com reservatórios animais em Juiz de Fora, Minas Gerais, Brasil

Historical geographic overlap of human rickettsiosis with animal reservoirs in Juiz de Fora, Minas Gerais, Brazil

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Corresponding Author:

Rafael Veríssimo Monteiro
monteiro.rafael@ufff.br

Departamento de Medicina Veterinária. R.
Espírito Santo, 993. Centro – Juiz de Fora, MG.

Rafael Veríssimo Monteiro¹ 

José Geraldo de Castro Jr.² 

Ralph Maturano¹ 

Marcia Chame³ 

¹ Universidade Federal de Juiz de Fora, Juiz de Fora, MG, Brazil.

² Prefeitura da Cidade de Juiz de Fora, Juiz de Fora, MG, Brazil.

³ Fiocruz, Rio de Janeiro, RJ, Brazil.

ABSTRACT

Background and objectives: we investigated the existence of a historical geographic overlap between the location of spotted fever group rickettsiosis human cases, a disease caused by the gram-negative bacterium *Rickettsia* sp., and that of mammalian reservoirs, specifically domestic horses and capybaras, in the urban perimeter of the city of Juiz de Fora, Minas Gerais, Brazil. **Methods:** cases of human rickettsiosis that occurred during a period of 17 years (2003-2020) were geolocated and the distribution of cases in time and geographic space was assessed using 1st and 2nd order geospatial association indicators. We also analyzed the overlap between the locations of human rickettsiosis cases and the area of occurrence of domestic horses and capybaras. **Results:** men were diagnosed more often than women, but a large proportion of affected women died. The results indicate an aggregation of human rickettsiosis cases in time (cases tend to occur close to each other at each epidemic event) and in geographic space (cases are concentrated in a specific geographic region of the urban perimeter). Human cases seem to be more associated with city regions with: i) higher local frequency of domestic horses and not capybaras; ii) lower rates of family development. **Conclusion:** it is suggested that, in the local epidemiological scenario, domestic horses appear to be the main sources of the rickettsia infecting humans, not capybaras.

Keywords: Spatio Temporal Analysis. Geographical Localization of Risk. *Rickettsia rickettsii*. Spotted Fever Group Rickettsiosis.

RESUMO

Justificativa e objetivos: foi investigada a existência de uma sobreposição geográfica histórica entre a localização dos casos de riquetsiose humana do grupo da febre maculosa, um grupo de doenças causadas pela bactéria

Gram-negativa *Rickettsia* sp., e dos reservatórios mamíferos, especificamente cavalos domésticos e capivaras, no perímetro urbano do município de Juiz de Fora, Minas Gerais, Brasil. **Métodos:** foram geolocalizados os casos de riquetsiose humana ocorridos durante um período de 17 anos (2003-2020), sendo avaliada a distribuição dos casos no tempo e espaço geográfico através de indicadores de associação geoespacial de 1ª e 2ª ordem. Também analisamos a superposição dos locais dos casos de riquetsiose humana com a área de ocorrência de cavalos domésticos e capivaras. **Resultados:** homens foram diagnosticados mais frequentemente que as mulheres, mas grande proporção das mulheres acometidas faleceu. Os resultados indicam uma agregação dos casos de riquetsiose humana no tempo (os casos tendem a ocorrer próximos entre si a cada evento epidêmico) e no espaço geográfico (os casos se concentram em uma região geográfica específica do perímetro urbano). Os casos humanos aparentam ser mais associados às regiões da cidade com: i) maior frequência local de cavalos domésticos e não das capivaras; ii) menores índices de desenvolvimento familiar. **Conclusão:** sugere-se que, no cenário epidemiológico local, são os cavalos domésticos que aparentam ser as principais fontes da riquetsia infectando os humanos, não as capivaras.

Descritores: Análise Espaço-Temporal. Localização Geográfica de Risco. *Rickettsia* sp. Riquetsiose do Grupo da Febre Maculosa.

RESUMEN

Justificación y objetivos: investigamos la existencia de una superposición geográfica histórica entre la localización de casos de rickettsiosis exantemáticas humana, enfermedad causada por la bacteria gramnegativa *Rickettsia* sp., y la de mamíferos reservorios, específicamente caballos domésticos y capivaras, en el perímetro urbano de la ciudad de Juiz de Fora, Minas Gerais, Brasil. **Métodos:** se geolocalizaron los casos de rickettsiosis humana ocurridos durante un período de 17 años (2003-2020), y se evaluó la distribución de casos en el tiempo y espacio geográfico utilizando indicadores de asociación geoespacial de 1er y 2do orden. También analizamos la superposición entre las ubicaciones de los casos de rickettsiosis humana y el área de ocurrencia de los caballos domésticos y capivaras. **Resultados:** los hombres fueron diagnosticados con más frecuencia que las mujeres, pero una gran proporción de mujeres afectadas fallecieron. Los resultados indican una agregación de casos de rickettsiosis humana en el tiempo (los casos tienden a ocurrir cerca uno del otro en cada evento epidémico) y en el espacio geográfico (los casos se concentran en una región geográfica específica del perímetro urbano). Los casos humanos parecen estar más asociados con regiones urbanas con: i) mayor frecuencia local de caballos domésticos y no de capivaras; ii) menores tasas de desarrollo familiar. **Conclusión:** se sugiere que, en el escenario epidemiológico local, los caballos domésticos parecen ser las principales fuentes de la rickettsia que infecta a los humanos, no los capivaras.

Palabras clave: Análisis Espacio-Temporal. Localización Geográfica de Riesgo. *Rickettsia rickettii*. Rickettsiosis Exantemáticas.

INTRODUCTION

Spotted fever group (SFG) rickettsiosis is an infectious, systemic disease caused mainly by the Gram-negative bacterium *Rickettsia rickettsii* (Wolbach 1919) Brumpt 1922, although other species of the same genus may cause a milder disease. These bacteria are mainly transmitted by ticks *Amblyomma sculptum* (Berlese, 1888) and *Amblyomma aureolatum* (Pallas, 1772), which acquire them from an infected host during hematophagy, especially during the rickettsia's bloodstream phase, amplifying transmission to new hosts in subsequent blood repast. In addition to the human species, a wide range of domestic and wild mammals, including carnivores, rodents and herbivores, can be infected, and each of these taxa participates with different competences in transmission cycle and in the local maintenance of rickettsiae. Regardless of hematophagy, transovarian and transstadial transmission allows the spread of rickettsia to its progeny, but in the case of *R. rickettsii* infecting *A. sculptum*, the levels of vertical transmission do not ensure bacterium maintenance without the participation of amplifying vertebrate hosts.^{2,3} In endemic areas for such

rickettsiae, where capybaras (*Hydrochoerus hydrochaeris*, Linnaeus, 1766) occur, the tick population is predominantly *A. sculptum*, while in non-endemic areas, there is a population balance of this species with *Amblyomma dubitatum* (Neumann, 1899). These invertebrates tend to have larger populations in degraded areas covered by grasses.¹

Domestic horses and free-ranging capybaras have been described as preponderant for the local persistence of rickettsia in urban and peri-urban environments. Horses appear to be less competent as reservoirs than capybaras, but both are capable of sustaining the local transmission cycle for tick vectors and, consequently, for humans. Regarding capybaras, an ecological phenomenon has added to their competence as a reservoir: the growing urbanization in Brazil since the end of the last century. The largest rodent in the world has become accustomed to human presence, gradually expanding its presence in urban centers with hydrology favorable to its presence, as it prefers riparian forest associated with freshwater courses and collections, where they find shelter and feed on riverine vegetation.^{4,5,6}

These SFG have been sparsely diagnosed in Minas Gerais municipalities since 1945. In Juiz de Fora, speci-

fically, the first confirmed case was described in 1995. Since then, intermittent outbreaks of Brazilian spotted fever (BSF) in humans have been diagnosed by health agencies in the municipality, as well as horses, dogs and ticks infected with *R. rickettsii* in several regions.^{7,8}

As the participation of horses, dogs and their ticks in transmission cycle was already well characterized at the time, after successive episodes of SFG in Juiz de Fora since 1995, the City Hall carried out a program to fumigate horses in the municipality from 2007 to 2011, notably in the so-called "carrier" horses. These are informal workers who use horses for animal traction, performing small cargo transport services where other forms of transport are unfeasible, costly or non-existent. Usually, these workers live in poor regions and, commonly, horses "live" together with people in a complex equine stall room, intensely facilitating horse-tick-human transmission, being such an interaction a risk factor for the disease occurrence in humans, as well as the proximity to capybaras.⁸

The hydrological situation of the city of Juiz de Fora favors the presence of capybaras in the urban environment. The city is cut in its lower part by the Paraibuna river valley, which receives several streams and streams tributaries of all the hills and mountains surrounding the city. Thus, capybaras perennially occupy the Paraibuna valley and can be seen in other water bodies in the city. Occupation by capybaras is considered a risk for rickettsia transmission to humans, due to its central ecological role in the bacterium transmission cycle. Government agencies are considering the culling of capybaras in the urban perimeter as a way of controlling SFG in humans (Rafael Veríssimo Monteiro, personal communication), following examples from other situations.⁹

In this way, the conditions that describe the favorable scenario for SFG transmission to humans can be summarized as: i) proximity to transitional vegetation areas, with greater presence of grasses and low shrubs; ii) proximity to capybaras and horses; iii) presence of transmitting ticks, *Amblyomma sculptum*. All these conditions are present in Juiz de Fora.^{9,10}

Considering the conditions described above, this research aimed to investigate the possibility of a geospatial overlap between the location of human cases of spotted fever group rickettsiosis and mammalian reservoirs in the urban perimeter of Juiz de Fora. To achieve these objectives, we: i) georeferenced the human cases registered in the urban perimeter of Juiz de Fora, from 2003 to 2020; ii) we verified the geographic overlap of SFG cases with the areas of occurrence of horses and capybaras in the urban perimeter of the city, to estimate which of these hosts offers the greatest risk of transmission to humans; iii) we verified, through spatial analysis tools, the potential existence of aggregations of human cases in time and geographic space that could reveal areas in the city with greater risk of occurrence of SFG.

METHODS

Human cases

SFG human cases in the urban perimeter of Juiz de Fora were georeferenced, using public information and/or registered in the Information System of Notifiable Diseases (SINAN - *Sistema de Informação de Agravos de Notificação*) of the Ministry of Health, from 2003 to 2020. According to Resolution 510/2016 of the Brazilian National Health Council (CNS), this type of study is exempt from an ethical license. One of us (JGCJ) was primarily responsible for epidemiological surveillance and epidemiological screening of 80% of cases, in addition to collecting data from SINAN. From these sources, in addition to the geographical coordinate relating to the affected person's place of residence, information was collected on whether the probable infection site of the case was autochthonous or not in the municipality, gender, whether there was hospitalization, the type of diagnosis used and the final result (death/cure). For georeferencing, the WGS 84 datum, and the QGIS[®] 3.16 software and the Rstudio 1.1[®] platform running R[®] version 3.5.3 were used for map generation and statistical analysis. Fisher's exact test was used to compare the rates of death from SFG between the sexes, with a significance level at $p < 0.05$.

Capybara location

To map the geographic occurrence of capybaras, observations from two different sources were included, obtained from September 2016 to December 2017:

Information on the collection of capybaras in the urban perimeter made by the fire department teams, IBAMA (Brazilian Institute for the Environment and Renewable Natural Resources) and IEF (State Institute of Forestry, Minas Gerais), georeferenced from the collection address (5 locations).

Information obtained from the Information System for Wild Health (SISS-GEO) application, managed by the Biodiversity and Wild Health Institutional Platform/Fiocruz, for monitoring wild animals and generating epizootic alerts. The application captures the geographic coordinates by GPS of the animal's photographic record in real time, in addition to other observations.¹¹

Domestic horse location

The locations of sightings of domestic horses found in the city were mapped, georeferenced from Google Earth[®] satellite image. Cart horses, although they circulate throughout the city, occupy fixed points of waiting for work, often on the banks of the Paraibuna river. Four of the known points have been geolocated. The places defined as tick fumigation points for domestic horses were also mapped, chosen by the city hall precisely because they are places of concentration of cart horses for grazing, walking and/or waiting for requisition for work. Tick fumigation took place from 2007 to 2011, from June to November, with intervals of approximately 21 days between each tick fumigation, at nine different points, also including the horses eventually parked on the banks of the Paraibuna river.

Epidemiological and geospatial analyzes

Two epidemiological and geospatial analyzes were

performed concerning human cases. First, the density of observations in the study area was assessed, a 1st order property of the case distribution pattern, capable of revealing local clusters of cases. For this analysis, a heatmap or Kernel density map was generated, with a parabolic density probability function, based on geographic occurrence of human cases of BSF in the urban perimeter of Juiz de Fora, from 2003 to 2020 (Heatmap plugin QGIS 3.10). A distance of 2,000 m was used as the influence radius of each point in the model, based on the fact that the average daily walking distance of a normal person is around 4,000 m. This heatmap (Kernel) intends to reveal an eventual overlap of the area of daily displacement of human cases of SFG that occurred in the analyzed period. Areas of great overlap would be areas of greater risk of exposure to rickettsia contamination. The property of the 2nd order of distribution pattern of cases was also assessed, i.e., whether each case can interfere with the occurrence of others. To this end, we calculated the Average Nearest Neighbor (ANN) of observed cases and compared it with a Monte Carlo simulation (600 iterations), based on the random generation of cases in the geographic occurrence window delimited by the cases that have already occurred. We compare the observed ANN with the average obtained in the 600 iterations, generating the probability that the observed cases present a certain pattern of geographic aggregation (random, uniform or aggregated).¹²⁻¹⁴

RESULTS

A total of 34 cases of human SFG were identified in the urban perimeter of Juiz de Fora in the period from 2003 to 2020, i.e., an average frequency of two cases of SFG per year. The fatality rate was 47% among those infected (16 deaths), and there was a statistical difference in lethality between the sexes (Fisher's exact test, $p=0.03$),

with women presenting a lethality rate of 85.7% (6 deaths in 7 cases). All cases underwent hospitalization. Thirty of the cases had laboratory confirmation by indirect fluorescent antibody test (IFAT), while the rest underwent clinical diagnosis; however, two of these cases occurred almost simultaneously with cases of relatives who had laboratory confirmation by IFAT.

Human case geospatial distribution (2003-2020)

The temporal distribution of BSF cases in Juiz de Fora can be seen in Figure 1. It is noted that there are annual gaps in disease occurrence, while some years bring together several cases. Apparently, there is a 6-year cycle between epidemic peaks. Although cases can happen in almost any month of the year, there is a concentration of cases in the period from August to November, months that concentrated 56% of cases in the analyzed period.

Geographic occurrence of human cases in the considered period can be seen in Figure 2. The concentration of disease cases can be observed in the northwest to east quadrants, mainly in peripheral places to the Krambeck Forest. Another cluster of cases to the south can also be characterized.

Host geospatial distribution

Figure 2 shows the distribution of capybaras and domestic horses that were located in the urban perimeter of the city. Capybaras are stably distributed along the course of the Paraibuna river, but can occasionally be seen in other watercourses that cross the entire municipality. They are mostly seen in family groups, but solitary individuals can be found. Cart horses occupy several points on the edge of the Paraibuna, usually individually. The nine tick fumigation points, marked on the map in Figure 2, are distributed throughout the urban perimeter. It was not possible to map carters' horses that are housed inside the families' homes.

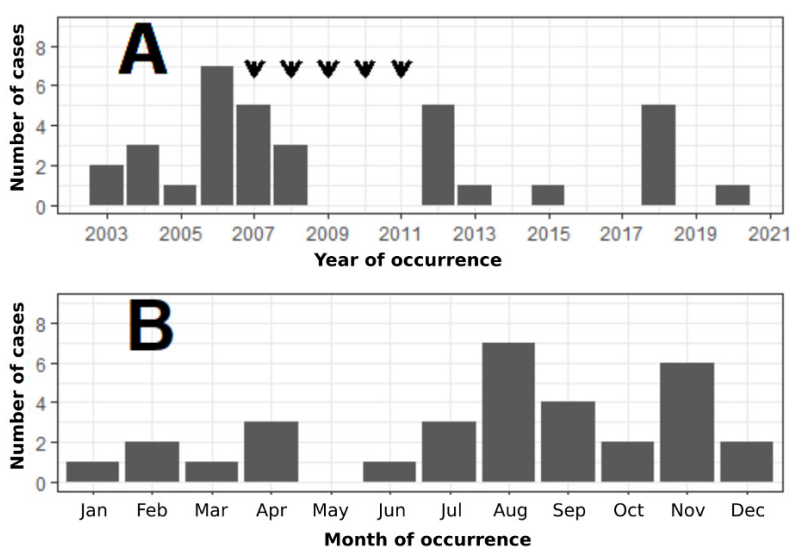


Figure 1. Distribution of frequency of human cases of Brazilian spotted fever in the urban perimeter of Juiz de Fora, Minas Gerais, from 2003 to 2020. **Caption:** A) clustered by year of occurrence. B) clustered by month of occurrence. The arrows on panel A indicate the years in which there was an equine tick fumigation program carried out by the city.

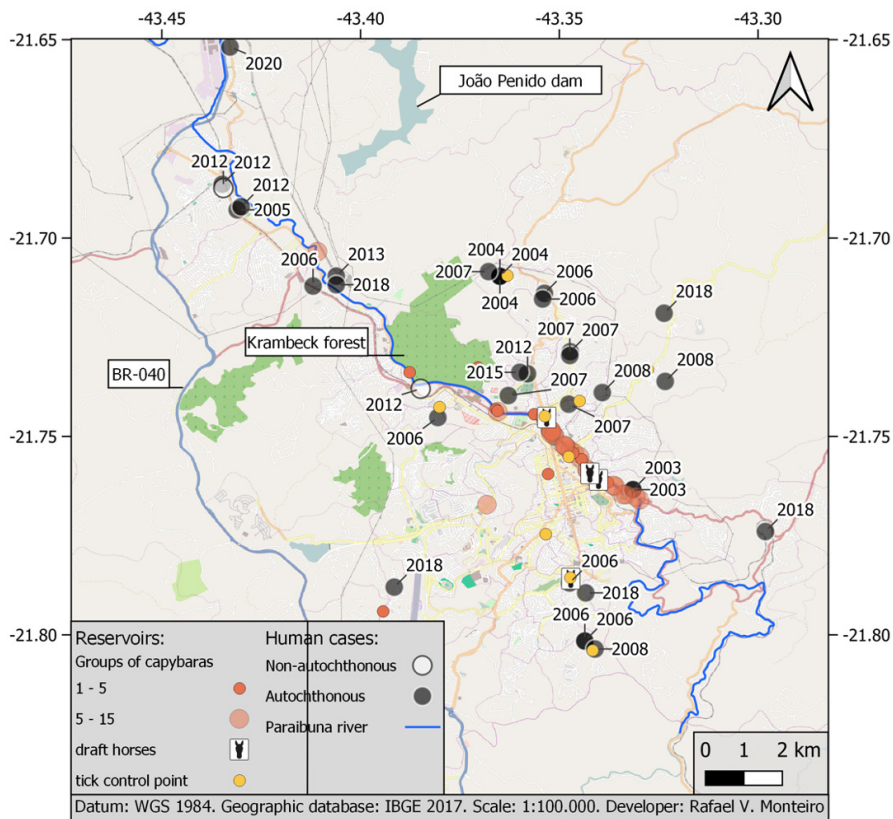


Figure 2. Geolocation of human cases of Brazilian spotted fever that occurred in the urban perimeter of Juiz de Fora, Minas Gerais, Brazil, from 2003 to 2020.
Note: geolocation of capybara sightings, the waiting points for carters and tick fumigation points used by the city hall from 2007 to 2011 is also indicated.

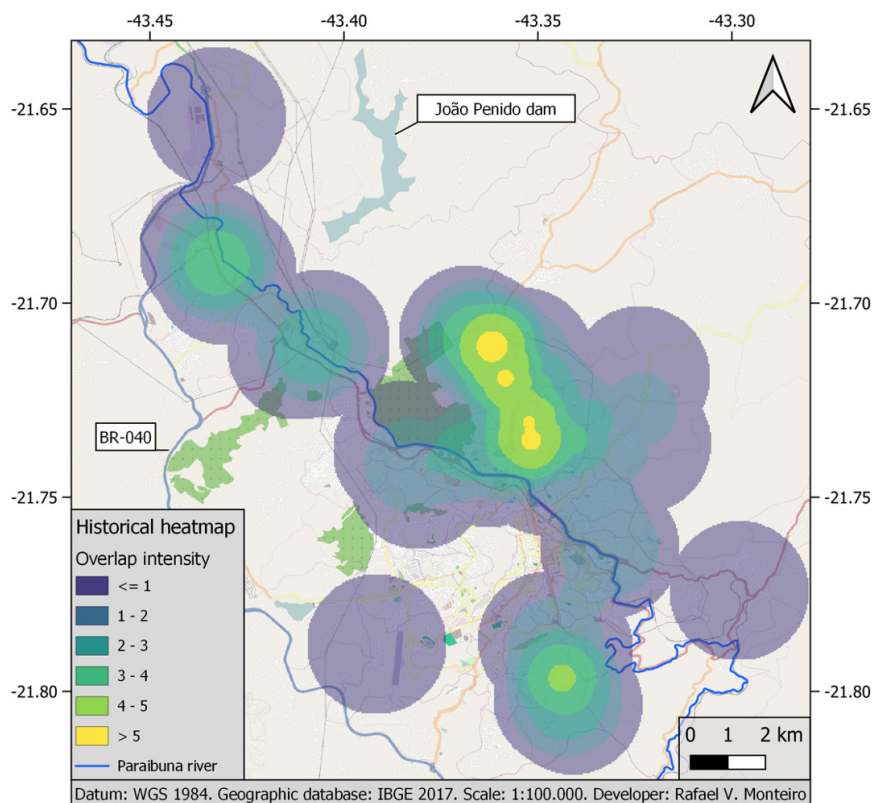


Figure 3. Heatmap, prepared with a parabolic function, on geolocation of human cases of Brazilian spotted fever in the urban perimeter of Juiz de Fora, Minas Gerais, Brazil
Note: higher overlap intensities would indicate overlap of daily circulation site of more cases. Used radius: 2,000 m.

Epidemiological and geospatial analyzes

Figure 3 shows a heatmap of occurrence of human cases of BSF in the municipality of Juiz de Fora, resulting from the first-order geospatial analysis. It can be seen that, under the conditions of comparison established here, there seems to be an area that concentrates the probability of acquiring the infection in the municipality in the years analyzed. On the other hand, the second-order analysis indicated a geospatial pattern of distribution of cases of aggregate character, since the average distance to the nearest neighbor observed (712.1 m) was statistically smaller than the average obtained in the Monte Carlo simulation (1,422.7 m; $p=0.002$). This aggregate character indicates that, in each outbreak, the cases tend to happen close together. The neighborhoods in the urban perimeter of Juiz de Fora that are included in the hottest spot in Figure 3, relative to overlap intensities greater than 5 (Bairu, Bandeirantes, Granjas Bethânia, Manoel Honório, Progresso and Santa Terezinha), had an average Family Development Index (FDI) of 0.733 (ranging from 0.665 to 0.779), an index equivalent to category D3, low-income families.¹⁵

DISCUSSION

The occurrence of SFG in Juiz de Fora follows a pattern equivalent to an endemic area with disease outbreaks. In the historical sequence analyzed here, it can be noted that there are years with a higher occurrence (7 cases in the highest frequency), while in other years, there are no cases (up to 3 years without cases). It is noteworthy that the 3-year gap in occurrence of human cases coincided with the execution of the city hall's tick fumigation program from 2007 to 2011 (Graph 1, panel A). Regarding lethality, the local rate is within the disease historical rates, although the lethal involvement in women has been statistically pointed out.¹⁶ The higher number of cases in men than in women is also in line with the traditional disease epidemiological characteristics, as men have greater exposure to transmitting ticks during their daily work. Another common aspect of SFG is the concentration of human cases from August to November of each year, when larvae and nymphs predominate in the local population of ticks. These immature forms are considered to be at greater risk for transmission, as they are of small size, which makes it difficult to identify the presence of a tick and does not alert the infected person to infestation, increasing the probability that the tick remains on individuals and the time required for rickettsiae transmission.¹⁷

The geographic distribution of cases seems to follow an aggregate pattern in time and geographic space. Over the years, the cases were concentrated in a preferred geographic region (Figures 2 and 3), and the cases tended to occur in regions close to each other or even within the same family/residential group (Average Nearest Neighbor). This could be due to: i) higher concentration of infected ticks in the region where such cases occur; ii) increased likelihood of adequate contact between ticks and people in such locations.

Two factors should be associated to justify the higher concentration of locally infected ticks: i) having vertebrate animals that support a large population of ticks; ii) that rickettsia is circulating in the region. Thus, these two factors would allow that, with proximity between people and the population of infected ticks, transmission cycle can be completed with human infection, that is, there is an increase in the probability of adequate contact between ticks and people. Other factors may be associated with this higher probability of contact between a tick and a human host, such as residents' occupation, whether they work with horses or frequent pastures for leisure or work, risk factors already characterized for SFG. The presence of this set of factors is complete in the common scene in the countryside cities of Brazil: people living in situations of vulnerability, living together or very close to their horses' stalls, often in peri-urban places.^{9,10}

In the situation described above, the participation of capybaras in occurrence of local human cases can be considered small, with the exception of places where rickettsia is introduced from these rodents. This situation does not seem to be the case in Juiz de Fora, where rickettsia has already been identified in *A. sculptum* in a neighboring municipality and in *R. sanguineus* in the municipal kennel.^{7,18} However, recent research on ticks collected on the banks of the Paraibuna river revealed the presence only of *Rickettsia amblyommii*, a bacterium whose pathogenicity is unknown.¹⁹ This condition of lesser relevance of capybaras in the local epidemiological chain is strengthened by the decrease in human cases during the period in which the city carried out tick fumigation of cart horses, indicating that transmission from ticks parasitizing horses is the most common epidemiological situation (Figure 1, panel A). Additionally, the municipal legislation of Juiz de Fora started to prohibit the circulation of cart horses in the urban perimeter as of December 2019. Although it is premature to assess the effect of such legislation for the future, we hope that, if horses really are the main carriers of ticks transmitting BSF rickettsiae in Juiz de Fora, the annual average of cases drops to levels below the current 2 cases per year.

The spatial distribution of capybaras also does not show a spatial overlap in agreement with human cases (Figures 2 and 3). Capybaras are distributed throughout the city following the waterways, and reside permanently on the banks of the Paraibuna river. However, most human cases did not occur near this watercourse, weakening the possibility that ticks of the capybaras of this river are the main sources of transmission to humans, although these rodents possibly contribute to the maintenance and potential infection by *R. rickettsii* in local populations of *A. sculptum*, a tick species proven to be resident in endemic areas for the disease.^{1,20} The presence of established immunity against rickettsia in these family groups of capybaras permanently residing in the riverbed of the Paraibuna cannot be ruled out, which would reduce rickettsia transmissibility to the tick population on the edge of the Paraibuna.²¹ Thus, the presence of these fixed groups of capybaras occupying the Paraibuna river could

be attenuating the infection of *R. rickettsii* on the local populations of *A. sculptum*. The finding of *R. amblyommii* adds another species of rickettsia to the local population of capybaras and ticks, and this may be involved in the local immunity of these hosts against *R. rickettsii*, a phenomenon already characterized.^{19,22}

Culling of wild animals is often proposed as a way to control human and farm animal diseases, in which these animals are considered relevant in transmission cycle.⁹ This approach may not always be the most appropriate, as ecological studies and mathematical simulations show that, in certain situations, the disturbance caused in the wild population subjected to such a procedure can increase disease prevalence in them, increasing the risk for human and animal populations for which disease control was desired.²³⁻²⁵ Bearing this in mind, the culling of capybaras is not suggested as a strategy to control BSF in the urban perimeter of Juiz de Fora without a greater ecoepidemiological knowledge of the place, since such action may be inappropriate and/or counterproductive.

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AUTHORS' CONTRIBUTIONS:

José Geraldo Castro Jr contributed with article field data collection, design and writing. **Ralph Maturano** contributed to article conception, experimental design and writing. **Rafael Veríssimo Monteiro and Márcia Chame** contributed to the planning, experimental design, data collection, data analysis, writing and final approval of the article.

Relation between anemia and hospitalized older adults' nutritional status

Relação entre anemia e estado nutricional de idosos hospitalizados

Relación entre anemia y estado nutricional de los adultos mayores hospitalizados

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Corresponding Author:

Leucinéia Schmidt

leucineia@hotmail.com

Address: BR 285, São José, Universitário, Passo Fundo, RS, Brazil.

Leucinéia Schmidt¹ 

Daiana Argenta Kümpel¹ 

Ana Luisa Sant'Anna Alves¹ 

Marilene Rodrigues Portella¹ 

¹ Universidade de Passo Fundo, Passo Fundo, RS, Brasil.

ABSTRACT

Background and Objectives: Malnutrition is frequent in hospitalized older adults, favoring nutritional deficiencies, such as anemia. Several studies have associated anemia with reduced performance in daily activities, which may increase morbidity and mortality. This study aimed to assess the relation between anemia and older adults' nutritional status. **Methods:** This is a cross-sectional study with hospitalized older adults. Anemia was investigated via hemoglobin. The chosen outcome variables were anemia and hemoglobin and the exposure variables gender, age group, skin color, marital status, education, and nutritional status. Variables were described in absolute and relative frequencies. For statistical analysis, the Chi-square and ANOVA tests were used. **Results:** Overall, we evaluated 272 hospitalized older adults and found a 65.1% prevalence of anemia. We associated anemia with age group, malnutrition, and decreased muscle mass. Hemoglobin levels decreased as participants' nutritional status worsened, with malnutrition showing the lowest average. **Conclusion:** Anemia was associated with nutritional status by the evaluated instruments and we observed a reduction in hemoglobin levels as volunteers' nutritional status worsened. Therefore, research must understand the factors associated with anemia, and healthcare providers should investigate anemic older adults' clinical history anemic to search for its basic cause.

Keywords: Health of the Elderly. Anemia. Hematology. Nutritional Status. Malnutrition.

RESUMO

Justificativa e Objetivos: A desnutrição é frequente em idosos hospitalizados, favorecendo deficiências nutricionais, como a anemia. Diversos estudos associaram a anemia com a redução do desempenho nas atividades diárias, podendo aumentar a morbidade e mortalidade. Este estudo objetivou avaliar a relação entre anemia e estado nutricional de idosos hospitalizados. **Métodos:** Estudo transversal com idosos hospitalizados. A anemia foi investigada através da hemoglobina. As variáveis desfecho foram a anemia e a hemoglobina; e as variáveis de exposição foram:

gênero, faixa etária, cor da pele, situação conjugal, escolaridade e estado nutricional. As variáveis foram descritas em frequência absoluta e relativa. Para análise estatística, utilizou-se os Testes Qui-quadrado e Anova. **Resultados:** Foram avaliados 272 idosos hospitalizados, nos quais a prevalência de anemia foi de 65,1%. Verificou-se associação dessa condição com a faixa etária, desnutrição e massa muscular diminuída. Os níveis de hemoglobina diminuíram conforme a piora do estado nutricional, sendo que os desnutridos tiveram a menor média. **Conclusão:** A anemia foi associada com o estado nutricional pelos instrumentos avaliados, também se observou a redução dos níveis de hemoglobina conforme a piora do estado nutricional. Portanto, a compreensão dos fatores associados à anemia é necessária, sendo fundamental que os profissionais de saúde investiguem a história clínica do idoso anêmico em busca de sua causa básica.

Descritores: Saúde do Idoso. Anemia. Hematologia. Estado Nutricional. Desnutrição.

RESUMEN

Justificación y Objetivos: La desnutrición es frecuente en los adultos mayores hospitalizados, favoreciendo deficiencias nutricionales como la anemia. Varios estudios han asociado la anemia a un rendimiento reducido en las actividades diarias, lo que predispone a un aumento de la morbilidad y la mortalidad. Este estudio tuvo como objetivo evaluar la relación entre anemia y estado nutricional de los adultos mayores hospitalizados. **Métodos:** Estudio transversal con adultos mayores hospitalizados. La anemia se investigó a través de la hemoglobina. Las variables de resultado fueron la anemia y la hemoglobina; y las variables de exposición fueron sexo, grupo de edad, color de piel, estado civil, educación y estado nutricional. Las variables se describieron en frecuencias absolutas y relativas. Para el análisis estadístico se utilizaron las pruebas de Chi-cuadrado y ANOVA. **Resultados:** Se evaluaron a 272 adultos mayores hospitalizados, en los cuales la prevalencia de anemia fue del 65,1%. Se encontró que la anemia estaba asociada al grupo de edad, la desnutrición y la disminución de la masa muscular. Los niveles de hemoglobina disminuyeron a medida que empeoraba el estado nutricional, con un promedio más bajo en los desnutridos. **Conclusión:** La anemia se asoció al estado nutricional en los instrumentos evaluados, se observó también una reducción en los niveles de hemoglobina a medida que empeoraba el estado nutricional. Por tanto, es necesario conocer los factores asociados a la anemia, y los profesionales de la salud necesitan investigar la historia clínica del adulto mayor anémico en busca de su causa básica.

Palabras clave: Salud del Anciano. Anemia. Hematología. Estado Nutricional. Desnutrición.

INTRODUCTION

Increasing longevity is one of humanity's greatest achievements. People live longer due to advances in health conditions, medicine, nutrition, health care, and education and economic well-being. Estimates suggest that, by 2050, 64 countries will join Japan, with an older population of more than 30% of its total.¹ In Brazil, in 2000, older adults totaled 14.2 million, reaching 19.6 million in 2010. This population is expected to reach 41.5 million in 2030 and 73.5 million in 2060.² This has brought challenges to healthcare providers and services and the need to develop new ways of caring and monitoring this population. Thus, specific protection and care actions have gained relevance in the public agenda.

Malnutrition is one of the important geriatric syndromes among older adults, and is often associated with anemia, as this study shows. Anemia prevalence was 82.4% and 66.7% in malnourished patients and those at risk of malnutrition. Thus, risk of anemia was 4.2 times higher in malnourished patients and 1.9 times higher in those at risk of malnutrition.³

A recent study showed that hospitalized older adults show a 48.9% and 48.6% prevalence of malnutrition and risk of it, respectively.⁴ Thus, such syndrome in hospitalized patients is a public health problem and

its impact on the course of diseases is considered significant, making it essential to screen and monitor older adults' nutritional status.

To evaluate hospitalized geriatric patients and adequately track malnutrition and its risk,⁵ the Mini Nutritional Assessment (MNA; established for nutritional screening and evaluation) can be used, as can calf circumference (CC), an anthropometric parameter closely related to muscle mass and a valid measure to predict nutritional risk.⁶ Moreover, body mass indices (BMI) can indicate older adults' nutritional status, provided that assessments use age-specific cutoff points and consider changes in body composition with aging.^{7,8}

In addition to assessing patients' nutritional status, we stress the importance of monitoring laboratory tests since anemia most often affect hospitalized older adults (54.2%).⁹ This condition is often associated with negative clinical outcomes in geriatric patients, such as functional impairment, falls, multiple comorbidities, longer hospitalization, and mortality.¹⁰

Based on the assumption that malnutrition is a factor which may be associated with anemia, we find the need to assess older adults' nutritional status. This study aimed to evaluate the relation between anemia and hospitalized older adults' nutritional status.

METHODS

This cross-sectional study was conducted in a high-complexity hospital in the municipality of Passo Fundo, in northern Rio Grande do Sul, Brazil.

Older adults (aged 60 years or above), hospitalized in clinical units, were evaluated from May to August 2019. Data was collected by an able and trained researcher.

To calculate our sample, a 95% confidence interval, 80% statistical power, 1:3 ratio between unexposed and exposed patients, 40% prevalence of anemia,¹¹ and a 2-prevalence ratio was considered, totaling 248 individuals. A further 10% was added to this number for possible losses and refusals (N=272).

Our inclusion criteria were older patients of all genders who could understand this research and walk for a short distance and who had undergone hemoglobin testing on their first hospitalization day. Exclusion criteria were composed of hospitalization for more than 72 hours, severely compromised health status, amputation, confinement to bed, inability to answer questions or absence of a companion at the time of evaluation.

Anemia was chosen as our outcome – diagnosed if blood hemoglobin parameters were lower than 12.0 g/dL in women and 13.0 g/dL in men, according to the cutoff points proposed by the World Health Organization.¹²

Our chosen exposure variables were gender (male/female), age group (in years), skin color (white and non-white), marital status (with and without a partner), schooling (in complete years of study), and nutritional status (by MNA, BMI, and CC).

To assess volunteers' nutritional status, three different methods (MNA, BMI, and CC) were used due to their particular importance. MNA is recommended by the European Society for Clinical Nutrition and Metabolism to assess older adults' nutritional status since it is sufficiently sensitive and specific to identify malnutrition. BMI is one of the most common components of nutritional screening tools, threatening normal physiological processes and increasing the risk of adverse clinical outcomes if below normal.¹³ CC is important for assessing muscle mass since values below recommended levels may correlate with reduced muscle mass and greater nutritional risk for patients.⁶

MNA comprises 18 questions, grouped into four categories: anthropometric evaluation; general lifestyle, medication use and mobility; dietary evaluation; and self-assessment (perception of health). Total score, obtained by summing points, were categorized into equal or above 23.5 as good nutritional status; from 17 to 23.5, as risk of malnutrition; and below 17, as malnutrition.¹⁴

To evaluate BMI, the Lipschitz's proposal was used, classified as low weight - BMI<22kg/m²; eutrophic - BMI between 22 and 27kg/m²; and overweight - BMI>27kg/m².⁸ CC was measured on the left leg, bent at 90° to the knee, with an inelastic measuring tape in its most protuberant part. Muscle mass thus estimated was considered normal if equal to or greater than 33 and 34 cm for women and men, respectively.¹⁵

Variables were described in absolute (n) and relative

(%) frequencies. For statistical analysis, the Chi-square test was used for the association between the outcome variable and exposure ones. The statistical test ANOVA (variance analysis) was also applied to assess the difference between hemoglobin means in the three nutritional status levels evaluated by MNA. A 0.05% significance level (p<0.05) and a 95% confidence interval were adopted.

The Guidelines and Norms Regulating Research Involving Human Beings were met, according to the recommendations of Resolution No. 466/2012. Confidentiality and anonymity were preserved via consent forms for the use and processing of personal data and informed consent forms. This study was approved by the Ethics Committee of Universidade de Passo Fundo (RS) under opinion no. 3.281.211 and CAEE no. 09235719.9.0000.5342.

RESULTS

This study included 272 older adults, with a mean age of 73.19 (8.53) years. Men's age averaged 71.89 (± 8.12) years and women's, 75.01 (± 8.78). Most participants were self-reported white (86.0%) men (58.5%), aged from 60 to 69 years (40.1%), with partners (59.9%) and schooling between one and four years of complete studies (50.4%) (Table 1).

Table 1. Hospitalized older adults' sociodemographic characteristics, Passo Fundo/RS, 2019.

Variables	n (%)
Gender	
Male	159 (58.5)
Female	113 (41.5)
Age group	
60 – 69 years	109 (40.1)
70 – 79 years	92 (33.8)
80 years or above	71 (26.1)
Skin color	
White	234 (86.0)
Non-white	38 (14.0)
Marital status	
With partner	163 (59.9)
Without partner	109 (40.1)
Schooling	
Illiterate	14 (5.1)
1 – 4 years	137 (50.4)
5 – 8 years	66 (24.2)
9 – 12 years	29 (10.7)
13 years or more	26 (9.6)

Table 2 shows that most older adults showed anemia (65.1%), malnourishment (via MNA; 39.7%), eutrophic BMI (43.3%), and normal muscle mass (54.4%).

Table 2. Hospitalized older adults' clinical and nutritional variables, Passo Fundo/RS, 2019.

Variables	n (%)
Anemia*	
Yes	177 (65.1)
No	95 (34.9)
Nutritional status (MNA)	
Malnutrition	108 (39.7)
Risk of malnutrition	88 (32.4)
Normal	76 (27.9)
Body mass index (BMI)	
Underweight	57 (21.0)
Eutrophic	118 (43.3)
Overweight	97 (35.7)
Muscle mass (CC)	
Normal	148 (54.4)
Diminished	124 (45.6)

*Anemia: Hemoglobin concentrations <12.0 g/dL for women and <13.0 g/dL for men.¹²

Our bivariate analysis associated anemia with age (a 91.5% prevalence in those aged 80 years or above), malnutrition (MNA; 99.1%), low weight (BMI; 78.9%), and decreased muscle mass (80.6%) (Table 3).

Table 3. Nutritional variables associated with anemia in hospitalized older adults, Passo Fundo/RS, 2019.

Variables	Anemic n (%)	Non-anemic n (%)	p-value*
Total	177 (65.1)	95 (34.9)	
Gender			
Female	79 (69.9)	34 (30.1)	0.158
Male	98 (61.6)	61 (38.4)	
Age group			
60 – 69 years	54 (49.5)	55 (50.5)	
70 – 79 years	58 (63.0)	34 (37.0)	0.001**
80 years or above	65 (91.5)	6 (8.5)	
Nutritional status (MNA)			
Malnutrition	107 (99.1)	1 (0.9)	
Risk of malnutrition	67 (76.1)	21 (23.9)	0.001**
Normal	3 (3.9)	73 (96.1)	
Body mass index (BMI)			
Underweight	45 (78.9)	12 (21.1)	
Eutrophic	81 (68.6)	37 (31.4)	0.002**
Overweight	51 (52.6)	46 (47.4)	
Muscle mass (CC)			
Diminished	100 (80.6)	24 (19.4)	0.001**
Normal	77 (52.0)	71 (48.0)	

*Chi-square; ** 0.05 significance level (p<0.05).

Table 4. Comparison of mean hemoglobin according to hospitalized older adults' nutritional status (MNA), Passo Fundo/RS, 2019.

	Mean	Standard deviation	95% CI for the mean		p-value*
			Lower Limit	Upper Limit	
Malnourished ^a	9.71	1.68	9.39	10.03	<0.001 ^{bc**}
Risk of malnutrition ^b	11.49	1.38	11.20	11.79	<0.001 ^{ac**}
Normal ^c	13.53	0.91	13.32	13.74	<0.001 ^{ab**}

*Anova; ** 0.05 significance level (p<0.05).

By comparing hemoglobin means and the three MNA classifications, we found a significant difference between means; the lowest in malnourished patients and the highest in individuals with normal nutritional status (Table 4).

DISCUSSION

Our analysis found a 65.1% anemia prevalence among participants, a value similar to other studies, showing a prevalence of anemia between 54.9% and 60% in older adults.^{16,17}

We observed that the greater the age, the greater the anemia prevalence, corroborating other studies.^{16,18} Several mechanisms may be associated with increased anemia prevalence in older adults. Factors contributing to this health problem include lower erythropoietin levels, greater pro-inflammatory cytokines and hepcidin levels (secondary to inflammation), and cytokine suppression for erythrocyte production.¹⁹

This study significantly associated anemia with participants' malnutrition (MNA; 99.1%), low weight (BMI; 78.9%), and decreased muscle mass (80.6%). These data show that patients at malnutrition risk should have their hemoglobin levels monitored for the early diagnosis and appropriate treatment of this syndrome.

Our data showing an association of anemia with malnutrition and risk of it (by MNA) corroborate an analysis which showed a 2.12 times higher risk of anemia in patients at risk of malnutrition and 5.05 times higher in malnourished ones.¹⁶ Another study found that 57.7% of anemic patients were malnourished or at risk of it (according to MNA). Thus, the literature attests a significant association between nutritional status and anemia.²⁰

Our BMI results also showed that underweight older adults, i.e., malnourished, showed a significant association with anemia. Thus, lower BMI increases the risk of adverse clinical outcomes, highlighting the importance of monitoring hemoglobin levels in older adults with BMI<22kg/m².¹³

Malnutrition is common in hospitals and is significantly associated with lower muscle mass. CC, then, is highly sensitive and specific to identify this factor and may serve as an isolated parameter to nutritionally assess hospitalized older adults since it proved effective to detect nutritional risk.²¹

In this study, 80.6% of older adults who showed decreased muscle mass (by CC) were also anemic. Muscle depletion (by CC) is associated with the severity of anemia in hospitalized patients. Thus, those without it or who with

mild cases showed no calf depletion. However, patients who had moderate or severe anemia had muscle depletion.²²

Thus, we observed that mean hemoglobin decreased as nutritional status (by MNA) worsened. We found the lowest mean (9.7g/dl) among malnourished older adults and the highest, among individuals with normal nutritional status (13.5g/dl), corroborating a study in which malnourished patients had statistically lower hemoglobin levels (9.5 g/dl) than those without malnutrition (11 g/dl).²³ Another analysis showed (by MNA) that hospitalized malnourished older adults showed lower hemoglobin parameters (10.1±1.6) than those with normal nutritional status (11.4 ± 2.0).²⁴

Thus, anemia in older individuals requires greater attention in public health not only because of its prevalence but also for its potential health consequences. Thus, due to its association with increased morbidity and mortality in older adults and its higher prevalence and more severe forms in more vulnerable populations, interventions to treat and prevent anemia to reduce inequities are necessary.²⁵

This study found the association of anemia with nutritional status by using the evaluated instruments since mean hemoglobin decreased as participants' condition worsened. Understanding the factors associated with anemia is necessary and healthcare providers must further investigate the clinical history of anemic older adults to seek its underlying cause. Effectively structuring programs aimed at promoting health for older adults may avoid (or even postpone) the onset of anemia and diseases linked to aging.

We suggest longitudinal studies which evaluate the association of anemia with other health conditions in older adults and reduce the occurrence of adverse outcomes in them.

Regarding the limitations of this study, we stress that our results are peculiar to the studied population, so generalizations should be viewed with caution to avoid misunderstandings. Moreover, since this is a cross-sectional study, it is unable to determine the causality of anemia and its associated factors.

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AUTHORS' CONTRIBUTION

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All authors approved the final version of this manuscript and declare themselves responsible for all its aspects, guaranteeing their accuracy and integrity.

Incidence and lethality by COVID-19 in the population of the Federal District: an ecological study

Incidência e letalidade por COVID-19 na população do Distrito Federal: um estudo ecológico

Incidencia y letalidad por COVID-19 en la población del Distrito Federal: un estudio ecológico

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Corresponding Author:

Jackson Gois Teixeira

jacksonudf1@gmail.com

Address: Mc 01 Lote 43 Apartamento 101
- Condomínio Império dos Nobres, Distrito Federal, FD, Brasil.

Jackson Gois Teixeira¹ 

Antonio Carlos dos Santos² 

¹ Centro Universitário do Distrito Federal, Brasília, FD, Brazil.

² Universidade de Brasília, Brasília, FD, Brazil.

ABSTRACT

Background and objectives: understanding the social situation of COVID-19 in poor and less developed countries is still doubtful. Thus, this study aimed to estimate the incidence and lethality by COVID-19, according to the per capita income of the administrative regions of the Federal District (FD). **Methods:** this is a descriptive ecological study, based on secondary data. Thirty-one administrative regions of the FD were included, and the population consisted of 382,488 individuals. The variables considered were sex, incidence, mortality, lethality, age group, population estimate and education. **Results:** despite the greater contamination by women, in terms of total mortality, more men died, representing 57.3% of the total deaths in the period. Regarding the influence of the level of education and income on the incidence, it appears that the highest rates of confirmed cases occurred in groups with higher levels of education and income. Despite this higher incidence, it is the group that exhibits the lowest lethality and the third lowest mortality per 100,000 inhabitants. **Conclusion:** the highest incidence rates were observed in regions with higher per capita income. On the other hand, lethality occurred more incisively in regions with lower purchasing power. In view of this, it is necessary to apply long-term preventive measures in unequal regions.

Keywords: COVID-19. Incidence. Lethality. Per Capita Income.

RESUMO

Justificativa e objetivos: o entendimento da situação social da COVID-19 em países pobres e menos desenvolvidos ainda é dubitável. Desse modo, o objetivo deste estudo é estimar a incidência e letalidade por COVID-19, de acordo com a renda *per capita* das regiões administrativas do Distrito Federal (DF). **Métodos:** trata-se de um estudo ecológico descritivo, baseado em dados secundários. Foram incluídas 31 regiões administrativas do DF, e a população foi composta por 382.488 indivíduos. Consideraram-se como variáveis sexo, incidência, mortalidade, letalidade, faixa etária, estimativa populacional e escolaridade. **Resultados:** apesar da contaminação maior por parte das mulheres,

em termos de mortalidade total, mais homens foram a óbito, representando 57,3% do total de mortos no período. A respeito da influência do grau de escolaridade e da renda na incidência, verifica-se que os maiores índices de casos confirmados aconteceram em grupos com maior nível de escolaridade e de renda. Apesar dessa maior incidência, é o grupo que exibe a menor letalidade e a terceira menor mortalidade por 100.000 habitantes. **Conclusão:** as mais altas taxas de incidência foram observadas nas regiões com maior renda *per capita*. Por outro lado, a letalidade ocorreu, de forma mais incisiva, nas regiões de menor poder aquisitivo. Diante disso, é necessário aplicar medidas preventivas de longo prazo em regiões desiguais.

Descritores: COVID-19. Incidência. Letalidade. Renda Per Capita.

RESUMEN

Justificación y objetivos: la comprensión de la situación social del COVID-19 en los países pobres y menos desarrollados aún es dudosa. Así, el objetivo de este estudio es estimar la incidencia y letalidad por COVID-19, según el ingreso per cápita de las regiones administrativas del Distrito Federal (DF). **Métodos:** se trata de un estudio ecológico descriptivo, basado en datos secundarios. Se incluyeron 31 regiones administrativas del DF, la población estuvo conformada por 382,488 individuos. Se consideraron como variables el sexo, la incidencia, la mortalidad, la letalidad, el grupo de edad, la población estimada y la escolaridad. **Resultados:** a pesar de la mayor contaminación por mujeres, en términos de mortalidad total, fallecieron más hombres, representando el 57,3% del total de defunciones en el período. En cuanto a la influencia del nivel de educación e ingresos en la incidencia, parece que las tasas más altas de casos confirmados ocurrieron en grupos con mayores niveles de educación e ingresos. A pesar de esta mayor incidencia, es el grupo que presenta la menor letalidad y la tercera mortalidad más baja por 100.000 habitantes. **Conclusión:** las tasas de incidencia más altas se observaron en las regiones con mayor ingreso per cápita. Por otro lado, la letalidad se produjo de forma más incisiva en las regiones de menor poder adquisitivo. Ante esto, es necesario aplicar medidas preventivas a largo plazo en regiones desiguales.

Palabras clave: COVID-19. Incidencia. Letalidad. Renta Per Capita.

INTRODUCTION

The COVID-19 pandemic called SARS-CoV-2 severe respiratory syndrome was identified in China at the end of 2019, taking on greater proportions that spread across the globe, being considered the greatest health challenge of this century. Due to the magnitude and dispersion of the virus, on March 11, 2020, the World Health Organization (WHO) declared a pandemic.¹ In view of this, social isolation has been applied as a way to reduce the spread of the virus.²

Therefore, there was an increase in research on coping strategies focused on discerning the disease in vulnerable groups. However, the understanding of the social situation of the disease in poor and less developed countries is still doubtful. Some studies have indicated a possible relationship between per capita income and disease incidence³, because in low-income countries, population groups have difficulty in adopting preventive measures, such as social isolation, and are more exposed in the context of vulnerability, which increases the risk of contamination and, if infection occurs, people have limited access to health services.¹

In addition to affecting populations' health around the world, health crises involving viral agents tend to have even more harmful effects and their impact on population subgroups is uneven. Thus, regions in an unequal context the burden of morbidities tends to be higher.² Thus, this study aimed to estimate the incidence and lethality of COVID-19 according to the per capita income of the administrative regions (AR) of the Federal District (FD), Brazil.

METHODS

This is a descriptive ecological study, based on secondary data obtained by the website "Painel COVID-19", from the epidemiological reports of the FD Department of Health. The study population consisted of 382,488 individuals, men and women, who tested positive for COVID-19 between March 2020 and August 2021.

The study included notified data of residents of the FD and who lived in some registered AR. This study was carried out in July 2021 in Brasília, FD, Brazil, with 31 AR as units of analysis.

In the data collection process, information was tabulated, organized and filtered in spreadsheets using Microsoft Excel® of cases of contamination and death by COVID-19 by sex and age group, per capita income, education by AR. All these data were obtained from the District Household Sample Survey (PDAD - *Pesquisa Distrital por Amostra de Domicílios*), which was carried out by the Federal District Planning Company (Codeplan - *Companhia de Planejamento do Distrito Federal*), whose latest version is from 2018.

The variables contained in this study are sex (female or male), notifications of people who tested positive for COVID-19, deaths, age group (≤ 19 years old; 20-29 years old; 30-39 years old; 40-49 years old; 50-59 years old; ≥ 60 years old), population estimate, education (no education; complete elementary school; incomplete elementary school; incomplete high school; complete high school; incomplete higher education; complete higher education) and AR made up of 31 regions. Águas Claras/Arniqueira, Ceilândia/Pôr do Sul were grouped

in the analyses, because when the Codeplan research took place there were only Águas Claras and Ceilândia, totaling 31 regions. Subsequently, there was a subdivision creating the Arniqueira and Pôr do Sol region, which today comprises 33 AR.

To analyze the number of infected people and deaths by sex, the percentage by age group was calculated. The analysis of the population affected by COVID-19 was carried out as follows: incidence of contamination (number of cases/population estimate) and mortality rate (number of deaths/population estimate *100,000).

With regard to income, the calculation was made taking into account the per capita income range by AR in relation to the number of infected people and deaths. Education by group was also analyzed in relation to the incidence of contaminated and mortality by percentage. Analysis was presented by groups of regions, as the education data presented by Codeplan were grouped. Finally, the case fatality rate was calculated: the number of deaths in relation to the number of confirmed cases per AR (death/confirmed cases).

The research used secondary data in the public domain, and no approval from the Research Ethics Committee was required.

RESULTS

The total number of confirmed cases of COVID-19, in all AR in the FD, in the period defined for the present research, was 382,488 individuals. A total of 169,961 (44.4%) people were male and 212,527 (55.6%) were female. Despite the greater contamination by women, in terms of total mortality, more men died, representing 57.3% of the total deaths in the period (Figure 1).

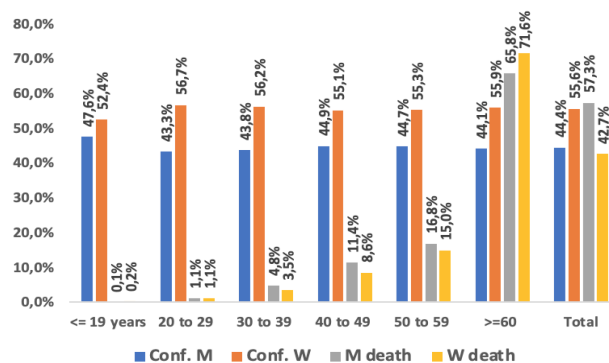


Figure 1. Cases and deaths confirmed by sex and age group in the Federal District. **Note:** Conf. M: confirmed men; M - man; Conf. W - confirmed women; W - woman.

Table 1. Population, confirmed cases, deaths, incidence and mortality of COVID-19 in the administrative regions of the Federal District. Brazil, 2021.

Administrative region	Populational estimate	Confirmed cases	Deaths	Incidence	Mortality per 100.000 Inhabitants
SIA	1.549	96	0	6,2%	0,0
Fercal	8.583	519	6	6,0%	69,9
Itapoã	62.208	3.411	60	5,5%	96,5
Sobradinho II	85.574	3.163	92	3,7%	107,5
Riacho Fundo II	85.658	4.555	108	5,3%	126,1
SCIA	35.520	2.272	48	6,4%	135,1
São Sebastião	115.256	11.243	206	9,8%	178,7
Sudoeste/Octogonal	53.770	10.006	97	18,6%	180,4
Águas Claras/ Amiqueiras	161.184	25.277	308	15,7%	191,1
Jardim Botânico	26.449	4.540	58	17,2%	219,3
Recanto Das Emas	130.043	11.337	337	8,7%	259,1
Varião	8.802	963	25	10,9%	284,0
Cruzeiro	31.079	5.189	90	16,7%	289,6
Lago Norte	33.103	6.051	96	18,3%	290,0
Planaltina	177.492	16.988	518	9,6%	291,8
Paranoá	65.533	7.290	193	11,1%	294,5
Plano Piloto	221.326	44.905	658	20,3%	297,3
Lago Sul	29.754	7.307	93	24,6%	312,6
Samambaia	232.893	25.327	734	10,9%	315,2
Santa Maria	128.882	13.379	414	10,4%	321,2
Park Way	20.511	3.517	67	17,1%	326,7
Vicente Pires	66.491	8.694	222	13,1%	333,9
Guará	134.002	22.210	449	16,6%	335,1
Ceilândia/ Pôr do sol	432.927	50.216	1520	11,6%	351,1
Candangolândia	16.489	2.415	62	14,6%	376,0
Brazlândia	53.534	6.910	204	12,9%	381,1
Riacho Fundo	41.410	6.636	170	16,0%	410,5
Núcleo Bandeirante	23.619	3.877	100	16,4%	423,4
Gama	132.466	20.193	573	15,2%	432,6
Taguatinga	205.670	36.018	949	17,5%	461,4
Sobradinho	60.077	17.984	462	29,9%	769,0

Regarding the age group, contamination was predominant in individuals aged ≤ 19 years (47.6%) among men and 20 to 29 years (56.7%) among women. On the other hand, mortality increased with aging, becoming the majority in the age group ≥ 60 years, 65.8% male and 71.6% female.

The largest number of confirmed cases and deaths was from Ceilândia/Pôr do Sol, with 50,166 cases and 1,520 deaths, followed by Plano Piloto, with 44,905 cases and 658 deaths, and Taguatinga, with 36,018 cases and 949 deaths. The region with the lowest number of cases of the disease was SIA, with 96 cases and no reported deaths, followed by Fercal, with 519 cases and 6 deaths, and Varjão, with 963 cases and 25 deaths (Table 1).

Regarding incidence, the highest rate occurred in Sobradinho (29.9%), followed by Taguatinga (17.5%) and Gama (15.2%). The lowest occurred in Sobradinho II (3.7%), Itapoã (5.5%) and Fercal (6.0%), respectively. Regarding mortality per 100,000 inhabitants, the highest rates were also in Sobradinho (769.0), Taguatinga (461.4) and Gama (432.6). The smallest, with the exception of SIA, with no record of deaths, are repeated in Fercal (69.9) and Itapoã (96.4).

To analyze the possible relationship between purchasing power and COVID-19 in the FD, AR were segre-

gated by per capita income and by lethality in relation to the number of confirmed cases, as can be seen in Table 2. With this approach, it appears that the lethality of confirmed cases was higher in those AR with lower purchasing power.

The mortality rate in the FD was 2.3% and, of the 31 AR, 17 had a result higher than this rate. Of these, only one, Vicente Pires, had a per capita income above the FD average. On the other hand, of the 14 regions that had a lethality rate lower than the average for the federal capital, ten have the highest per capita incomes in the FD. The four that are not part of this group are São Fercal, Itapoã, São Sebastião and SCIA.

Regarding the influence of the level of education and income on the incidence, it appears that the highest incidence rates occurred in those groups with the highest level of education and income (Table 3). Group 1 had an incidence of 19.8%, the highest among the four groups, and a higher level of education, with 76.6% of individuals having completed higher education and with an average per capita income of R\$ 6,739.00 (about US\$1,225.27), i.e., also the highest income of the FD. Despite this higher incidence, it is the group with the lowest lethality and the third lowest mortality per 100,000 inhabitants.

Table 2. Population, confirmed cases, deaths from COVID-19, per capita income and lethality in the administrative regions of the Federal District. Brazil, 2021.

Administrative region	Populational estimate	Confirmed cases	Deaths	Per capita income	Lethality
SIA	1.549	96	0	3.800	0,00%
Sudoeste/Octogonal	53.770	10.006	97	7.131	0,97%
Fercal	8.583	519	6	816	1,16%
Águas Claras/ Ariqueiras	161.184	25.277	308	6.505	1,22%
Lago Sul	29.754	7.307	93	8.323	1,27%
Jardim Botânico	26.449	4.540	58	5.846	1,28%
Plano Piloto	221.326	44.905	658	6.750	1,47%
Lago Norte	33.103	6.051	96	6.440	1,59%
Cruzeiro	31.079	5.189	90	3.749	1,73%
Itapoã	62.208	3.411	60	932	1,76%
São Sebastião	115.256	11.243	206	1.375	1,83%
Park Way	20.511	3.517	67	5.946	1,91%
Guará	134.002	22.210	449	3.689	2,02%
SCIA	35.520	2.272	48	573	2,11%
FEDERAL DISTRICT	2.881.854	382.488	8.919	2.827	2,33%
Riacho Fundo II	85.658	4.555	108	803	2,37%
Vicente Pires	66.491	8.694	222	2.979	2,55%
Riacho Fundo	41.410	6.636	170	1.321	2,56%
Candangolândia	16.489	2.415	62	1.435	2,57%
Sobradinho	60.077	17.984	462	2.128	2,57%
Núcleo Bandeirante	23.619	3.877	100	2.377	2,58%
Varjão	8.802	963	25	841	2,60%
Taguatinga	205.670	36.018	949	2.212	2,63%
Paranoá	65.533	7.290	193	830	2,65%
Gama	132.466	20.193	573	1.604	2,84%
Samambaia	232.893	25.327	734	997	2,90%
Sobradinho II	85.574	3.163	92	2.354	2,91%
Brazlândia	53.534	6.910	204	1.129	2,95%
Recanto Das Emas	130.043	11.337	337	860	2,97%
Ceilândia/ Pôr do sol	432.927	50.216	1520	1.767	3,03%
Planaltina	177.492	16.988	518	1.139	3,05%
Santa Maria	128.882	13.379	414	991	3,09%

Table 3. Education, income, incidence, mortality, and case fatality of proven COVID-19 cases by Federal District administrative region groups.

Cathergorization	Group 1	Group 2	Group 3	Group 4	Federal District
Education					
Up to incomplete high school	6,0%	20,3%	41,6%	53,4%	29,9%
Complete high school and incomplete higher education	17,3%	36,8%	42,4%	36,9%	36,0%
Complete higher education	76,6%	42,8%	16,0%	9,7%	33,9%
Mean per capita income	6.739	2.903	1.480	809	2.827
Incidence	19,8%	15,8%	10,7%	8,3%	13,3%
Mortality per 100,000 inhabitants	277,7	360,8	305,1	215,3	309,5
Lethality of confirmed cases	1,4%	2,3%	2,9%	2,6%	2,3%

Source: PDAD 2018/Codeplan - Own elaboration.

Note: Group 1 - Plano Piloto, Jardim Botânico, Lago Norte, Lago Sul, Park Way and Sudoeste/Octogonal; Group 2 - Águas Claras, Candangolândia, Cruzeiro, Gama, Guarã, Núcleo Bandeirante, Sobradinho, Sobradinho II, Taguatinga, Vicente Pires; Group 3 - Brazlândia, Ceilândia, Planaltina, Riacho Fundo, Riacho Fundo II, SIA, Samambaia, Santa Maria and São Sebastião; Group 4 - Fercal, Itapoã, Paranoá, Recanto das Emas, SCIA/Estrutural and Varjão.

In contrast, Group 4 exhibits the lowest incidence (8.3%), the lowest per capita income (R\$809.00 or US\$147.09), the lowest mortality per 100,000 inhabitants and the lowest education, with 53.4% of individuals with education to incomplete high school. On the other hand, despite the low incidence and mortality per 100,000 inhabitants, this group has the second highest fatality rate among confirmed cases, second only to Group 3, which has the second worst income and education.

DISCUSSION

The results of this study indicate greater contamination by women and in the age groups formed by young adults ≤ 19 years, for men, and 20 to 29 years, for women. Nevertheless, the highest mortality rate occurred in males, with 57.3% of all deaths. With advancing age, the mortality rate increased for both sexes, with the most affected age group being ≥ 60 years, for both men (65.8%) and women (71.6%).

Supporting these findings, a cross-sectional study carried out with the population of Rondônia showed that contamination of women by COVID-19 was also higher.⁴ In another observational study, females again had a higher percentage of contamination.⁵ This evidence suggest that this is because women are more at risk, as they are health professionals and are on the front lines of COVID-19 mitigation efforts in communities. Moreover, many women are part of the labor market, even if informally, and need to move because they are responsible for family income.⁴

About women representing the majority of those infected and still having lower mortality rates than men, the literature indicates that they are more resistant than men in extreme situations such as epidemics, hunger and slavery. This may be due to the relevance of X chromosome and female hormones, which induce them to have a stronger immune response to viral infections. Despite this, there are also cases in which men were more infected than women.¹⁶ However, what really became evident, through a series of cases, was that 75% of deaths were among men.¹⁷ These results were revalidated in a cohort

study, which showed a significant association between male sex and mortality from COVID-19.¹⁸

In addition to this, in the male context, other factors can influence higher mortality, such as excessive consumption of alcoholic beverages, violence, abuse of toxic substances, pre-existing diseases, such as hypertension, diabetes, cardiovascular and chronic lung diseases.¹⁹ Moreover, men comply less with hand hygiene practices, delay in seeking health care²⁰ and wear less face mask.²¹ In other words, science shows a disadvantage for men, whether for genetic, immunological or lifestyle reasons.²²

In general, the sex issue is still little discussed and there is a neutral positioning regarding public policies, as if men and women were equally infected and affected⁷ and, therefore, more robust studies are necessary to assess the differences pointed out.

The finding of the predominance of mortality in patients aged ≥ 60 years is also attested by similar studies in countries such as China, Mexico and Peru, which also had a higher number of deaths in people ≥ 60 years.^{8,9} In the United States, Similar data indicated that 80% of COVID-19 deaths also corresponded to older ages.¹⁰ Mortality among older adults tends to be nine times higher than in other age groups, as at this stage of life they are more likely to have comorbidities and structural health determinants that increase morbidity and mortality.^{9,11} In addition, factors related to health and care systems, public policies and programs that integrate older adults into society are still few, making them even more vulnerable to epidemics.⁴

However, although older adults were the most affected by COVID-19,^{12,9} young adults are also dying from the disease¹² as well as a large percentage of younger people are being hospitalized.¹³ In other words, this is not just an older adult disease, since individuals of any age can be infected with COVID-19.¹⁴ Despite this, the disease affected more older adults, males and who had some type of comorbidity.¹⁵

The present study also demonstrates that the highest incidence rates were observed in regions with higher education and per capita income. On the other hand, lethality occurred more incisively in regions with lower purchasing power and lower education. Education

has been exposed as a risk factor in the dissipation of the disease and evolution to death in previous pandemics. The seriousness of the disease and schooling may be associated with social class, income, lifestyle, understanding of the disease and seeking medical care.^{23,24}

There are studies that show that people from lower social classes complied less with COVID-19 restrictions.^{19,25} Furthermore, individuals with low education are more likely to contract the disease, as they use public transport, live in overcrowded places, have less purchasing power, which reduces preventive measures such as the purchase of gel alcohol, predisposing the individual to death from the disease.^{19,23}

In Brazil, more specifically, a higher incidence rate was observed in municipalities with greater social vulnerability. Additionally, mortality caused by the disease mainly affected the family provider, increasing poverty.¹ Otherwise, when relating the economic inequality in different Brazilian regions and the impacts of COVID-19, it is not possible to assert that the most economically vulnerable are the most affected, but in areas of greater inequality, the pandemic is more likely to cause more severe impacts to the population.²

The occurrence of higher incidence in higher income regions¹ evidenced in another study carried out in the Metropolitan Region of the city of Rio de Janeiro,³ initially, because, due to the higher population density in peripheral and poor areas, the most obvious assumption would be that there would be a higher incidence in these places, in the same way that it occurs with other infectious diseases of a respiratory nature.

However, there may be greater underreporting in these regions, as the testing of the population has not been homogeneous and those with greater purchasing power are more likely to carry out tests in specialized laboratories, clinics and hospitals. Moreover, the proportion of asymptomatic infections and people with mild and even moderate disease are unlikely to go to health units to undergo tests.^{1,3}

The greater lethality in less favored regions is related to worse public health, safety, sanitation and urbanism structures, aspects that deteriorate everyone's quality of life, but that have a more serious impact on the less economically well off. In these locations, the greater the number of people with impaired health, including chronic diseases currently recognized as risk conditions for COVID-19. Another aggravating factor is the scarcity of beds in Intensive Care Units (ICU) for patients in the Unified Health System (SUS - *Sistema Único de Saúde*), which is up to five times smaller than those available in the private network. As a result, it is assumed that the risk of death from COVID-19 is up to 10 times higher among the most vulnerable.²

It is important to highlight the limitations arising from the study design, whose generalization, as it is an ecological study, applies to the population and not to the individual. Additionally, by using data collected from the state, given that Brazil does not carry out mass testing, underreporting for confirmation of cases and deaths by

COVID-19 may have influenced the results. However, the findings of this research can help governments in the creation of public policies and long-term measures in regions with greater social vulnerability aimed at reducing economic inequality.

In conclusion, the present study observed that the highest incidence rates were observed in the regions with the highest per capita income. On the other hand, lethality occurred more incisively in regions with lower purchasing power. Therefore, studies with other metrics are necessary to assess the influence of income associated with infection and death from COVID-19. It is also necessary to apply long-term preventive measures in unequal regions. In addition, well-structured public policies need to be created to reduce economic vulnerability to combat future health crises in Brazil.

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AUTHORS' CONTRIBUTIONS:

Jackson Gois Teixeira contributed to article conception, design, analysis and writing;

Antonio Carlos dos Santos contributed to the analysis, review and final approval of the article;

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Profile of patients hospitalized by COVID-19: the importance of hospital epidemiological surveillance

Perfil dos pacientes internados por COVID-19: a importância da vigilância epidemiológica hospitalar

Perfil de pacientes hospitalizados por COVID-19: la importancia de la vigilancia epidemiológica hospitalaria

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Corresponding Author:

Catia Cristina Martins de Oliveira
catiac.oliveira@fiocruz.br

Address: Av. Brasil, 4365. Manguinhos, Rio de Janeiro, RJ, 21.040-360

Catia Cristina Martins de Oliveira¹ 

Fabiane Canellas de Paula² 

Nadja Raquel Lustosa Lopes² 

Renata Vasconcelos² 

¹ Fundação Oswaldo Cruz, Rio de Janeiro, RJ, Brasil.

² Secretaria Municipal de Saúde do Rio de Janeiro, Rio de Janeiro, RJ, Brasil.

ABSTRACT

Rationale: Since December 2019, the novel coronavirus SARS-Cov-2, also called COVID-19, has spread rapidly across countries, making it one of the biggest health challenges of this century. In Brazil, it was declared a public health emergency in March 2020. The aim of this study was to describe the profile of patients hospitalized by COVID-19 in an emergency hospital in the city of Rio de Janeiro, as well as the factors associated with in-hospital death. **Methods:** Retrospective observational study, which included patients hospitalized between March and December 2020 with a confirmed diagnosis of COVID-19. The epidemiological, clinical, and laboratory aspects were extracted from the epidemiological investigation files and the hospital chart. **Results:** 582 suspected cases of COVID-19 were hospitalized and 317 were confirmed, of which 182 (57.5%) were male, and most were residents in the north of Rio de Janeiro (42.5%). Main tomographic or radiological findings: ground glass (34.7%) and pulmonary infiltrate (15.4%), and more than half of those hospitalized (64.0%) had at least one comorbidity. Among hospitalized patients, the overall lethality was 53.6%, and among those admitted to the ICU, this percentage was 84.5%. Age and use of ventilatory support and ICU were the variables that showed a statistically significant association with in-hospital mortality. **Conclusion:** This study reinforces the importance of epidemiological surveillance, in a hospital setting, especially for diseases in which the passive surveillance system may not be able to adequately report, as in the case of COVID-19.

Keywords: Epidemiology. Severe Acute Respiratory Syndrome. COVID-19. Epidemiological surveillance.

RESUMO

Justificativa: Desde dezembro de 2019, o novo coronavírus SARS-Cov-2, também chamado COVID-19, tem se espalhado rapidamente pelos países, tornando-se um dos maiores desafios sanitários deste século. No Brasil, ele foi declarado como uma emergência de saúde pública em março de 2020. O objetivo deste estudo foi descrever o perfil

dos pacientes hospitalizados por COVID-19 em um hospital de emergência no município de Rio de Janeiro, bem como os fatores associados ao óbito hospitalar. **Métodos:** Estudo observacional retrospectivo, que incluiu pacientes internados entre março e dezembro de 2020 com um diagnóstico confirmado de COVID-19. Os aspectos epidemiológicos, clínicos, e laboratoriais foram extraídos das fichas de investigação epidemiológica e do prontuário hospitalar. **Resultados:** Foram internados 582 casos suspeitos de COVID-19 e 317 foram confirmados, dos quais 182 (57,5%) eram do sexo masculino, e a maioria era residente na zona norte do Rio de Janeiro (42,5%). Principais achados 'tomográficos ou radiológicos': vidro fosco (34,7%) e infiltrado pulmonar (15,4%), e mais da metade dos hospitalizados (64,0%) apresentava pelo menos uma comorbidade. Entre os pacientes hospitalizados, a letalidade geral foi de 53,6% sendo que entre os internados na UTI esse percentual foi de 84,5%. Idade e uso de suporte ventilatório e UTI foram as variáveis que mostraram associação estatisticamente significativa com mortalidade intra-hospitalar. **Conclusão:** Este estudo reforça a importância da vigilância epidemiológica, em âmbito hospitalar, principalmente para as doenças em que o sistema de vigilância passivo pode não ser capaz de reportar adequadamente, como no caso da COVID-19.

Palavras chave: Epidemiologia. Síndrome Respiratória Aguda Grave. COVID-19. Vigilância Epidemiológica.

RESUMEN

Justificación: Desde diciembre de 2019, el coronavirus SARS-Cov-2, también llamado COVID-19, se ha extendido rápidamente por los países, convirtiéndose en uno de los mayores retos sanitarios de este siglo. En Brasil, se declaró una emergencia de salud pública en febrero de 2020. El objetivo de este estudio es describir el perfil de los casos hospitalizados por COVID-19 en un hospital de urgencias de la ciudad de Río de Janeiro, así como los factores asociados a la muerte hospitalaria. **Métodos:** Estudio observacional, retrospectivo, que incluyó pacientes hospitalizados entre marzo y diciembre de 2020 con diagnóstico confirmado de COVID-19. Los aspectos epidemiológicos, clínicos y de laboratorio fueron extraídos del formulario de investigación epidemiológica y de los registros hospitalarios. **Resultados:** Se hospitalizaron 582 casos sospechosos de COVID-19 y se confirmaron 317, de los cuales 203 (57,5%) eran hombres, la mayoría residentes en el norte de Río de Janeiro (42,5%). Los principales hallazgos tomográficos o radiológicos: vidrio deslustrado (34,7%) e infiltrado pulmonar (15,4%) y más de la mitad de los hospitalizados (64%) tenían al menos 1 comorbilidad. La letalidad global entre los hospitalizados fue del 53,6% y entre los ingresados en la UCI, este porcentaje fue del 84,5%. Las variables que mostraron una asociación estadísticamente significativa con la mortalidad intrahospitalaria fueron la edad, el uso de soporte ventilatorio y el uso de la UCI. **Conclusiones:** El estudio refuerza la importancia de la vigilancia epidemiológica en el ámbito hospitalario, especialmente para aquellas enfermedades en las que el sistema de vigilancia pasiva puede no informar adecuadamente, como es el caso de la COVID-19.

Palabras clave: Epidemiología. Síndrome Respiratorio Agudo Severo. COVID-19. Vigilancia Epidemiológica.

INTRODUCTION

Emerging and reemerging diseases have been a public health challenge. Since December 2019, the SARS-Cov-2 coronavirus, also called COVID-19, has spread rapidly across countries, infecting thousands of people despite global efforts to prevent its spread. In March 2020, it was declared an international public health emergency by the World Health Organization.^{1,2}

The clinical spectrum of the disease, which has high transmissibility, with an enormous impact in terms of morbidity and mortality for the population, ranges from asymptomatic infections and mild flu-like syndromes to more severe respiratory conditions, such as severe acute respiratory syndrome (SARS), depending on the organism and the comorbidities it presents.^{3,4}

As hospitals serve a large volume of patients and are considered the gateway to various unusual and emerging diseases, they assume a strategic position in the fight against diseases, mainly by helping in the timely detection and diagnosis of cases. In this context, the hospital surveillance centers (HSC) were established by the Ministry of Health (MH) in 2004, aiming to improve

the coverage and effectiveness of the epidemiological surveillance system. MH's assumption was to invest in improving the identification, registration, and monitoring of the clinical and epidemiological characteristics of compulsory notification diseases, especially communicable diseases. The active search conducted by the HSC occurred mainly in places considered strategic, such as outpatient clinics, inpatient units, and laboratories.^{5,6}

Since the active hospital surveillance modality was implemented, it has been an important advance in the national health surveillance network; it comprehensively captures hospitalized cases, therefore, those of greater severity, helping to better understand the pathogenesis and its risks in the short and long term.⁶

In 2009, with the premise of identifying and monitoring the occurrence of respiratory viruses in hospitalized patients, especially those with a severe clinical condition or in a situation of a suspicious death, the SARS surveillance was implemented by the MH. This guideline was formulated after the influenza A (H1N1) pandemic; from then on, the cases of patients hospitalized started to be registered in the Information System of Epidemiological Surveillance of Influenza, centralizing the notifications to the MH.⁷

Concerning cases of COVID-19, hospital surveillance assumed a relevant role, given the limited knowledge of the disease, with unpredictable impacts on public health. Furthermore, as it was a disease that absorbs health system resources, an additional concern arose about the pressure it exerts on hospitals to care for people affected by severe forms of the disease.^{8,9} In a study conducted by Guan *et al.* (2020), 1099 laboratory-confirmed patients with COVID-19 were investigated in 552 hospitals in China. The authors highlighted the importance of hospital surveillance in producing fast and effective responses, as being crucial to support the adoption of control measures that can interrupt the disease transmission chain in the population.¹⁰ Therefore, the objective of this study was to describe the profile of cases hospitalized by COVID-19, as well as the factors associated with in-hospital death, in an emergency hospital in the city of Rio de Janeiro.

METHODS

Study design

This is a sectional observational study that included patients with a confirmed diagnosis of COVID-19 admitted between March and December 2020 at an emergency hospital in Rio de Janeiro. This hospital has an installed capacity of 400 inpatient beds; given its strategic location and technological complexity in the municipality, it receives patients from other regions, attending to various specialties and with various diagnostic support services. Currently, it is considered one of the sentinel hospitals for surveillance of COVID-19, being part of the Municipal Contingency Plan for Public Health Emergency.

Hospital Surveillance Center (HSC)

The HSC was implemented at the hospital in 2001 with the premise of timely detecting and investigating cases of compulsory notification, monitoring risk factors through epidemiological investigations, providing permanent technical guidance to health professionals, and supporting decision-making on measures of disease prevention and control. To monitor COVID-19, the HSC has developed a database for recording individual SARS cases, standardized as per the recommendation of the MH, in addition to conducting notification and investigation of patients. To track the flu syndrome, clinical and epidemiological information was collected and, then, patients were classified as suggestive or not of COVID-19. In confirmed cases, patients were followed up until the hospital outcome (discharge, transfer, or death).

Information source

To describe the clinical features and the baseline predictors of mortality, the information base of the present study was extracted from the HSC database. As an eligibility criterion, all hospitalized cases were considered, laboratory-confirmed by RT-PCR (reverse transcriptase polymerase chain reaction) for SARS-CoV-2, regardless of signs and symptoms and/or the presence of a clinical-epidemiological finding, according to the

criteria defined by the MH.¹¹ The analysis variables were as follows: demographic data (age, sex, and region of residence, categorized into areas: North, Central, West, and South Zones), presence of comorbidities (diabetes mellitus, DM; cardiovascular disease, CVD; neoplasia; obesity; respiratory disease, etc.), admission to the Intensive Care Unit (ICU), use of (invasive and non-invasive) ventilatory support, tomographic or radiological examinations (normal; interstitial infiltrate; consolidation; mixed; other; not performed), and case evolution (cure; death; transfer). In-hospital (yes or no) death was the outcome variable up to the study completion date.

Data analysis

Data were organized in a Microsoft Excel (2016) spreadsheet, and analyzes were conducted in the Stata (Stata Corporation; College Station, USA) software (v. 14.0).

Descriptive statistics were calculated, including mean, median, standard deviation (SD), frequency, and ratio. Pearson's or Fisher's chi-square tests were used for categorical variables and $p < 0.05$ was considered statistically significant. The multivariate logistic regression model was applied to study factors associated with the dependent variable (hospital death), and the Odds Ratio (OR), its 95% confidence intervals (_{95%}CI), and p -value were estimated, and variables with a significance level of up to 10% were included in the model.

The present study is part of the project "Epidemiological Surveillance of COVID-19 and Sequelae in patients hospitalized by SARS-COV-2", which was approved by the Research Ethics Committee (CEP/REC) of the Municipal Health Department (Rio de Janeiro; 16/07/2021; detailed opinion: 4,862,998).

RESULTS

Clinical and epidemiological profiles of patients hospitalized by COVID-19

During the period of analysis, 582 suspected cases of COVID-19 were hospitalized and 317 (54.5%) were confirmed. Table 1 presents the demographic, clinical, and epidemiological characteristics of patients confirmed for COVID-19; 182 (57.5%) of these patients were male, and most of them resided in the north (42.5%) and west (14.1%) and downtown (14.1%) zones of Rio de Janeiro. Other municipalities contributed with 18.3% of patients. The 40-59 age group concentrated on the highest percentage of hospitalized patients (minimum age: 7 years; maximum age: 102 years; mean: 62.9 years; median: 55 years).

Among confirmed COVID-19 patients, 251 (79.2%) did not require an ICU, 101 (31.9%) received non-invasive mechanical ventilation, and 59 (18.6%) used invasive mechanical ventilation.

Based on the clinical history of the patients, the main tomographic or radiological findings of the hospitalized patients were the following: ground-glass pattern (110; 34.7%), pulmonary infiltrate (49; 15.4%), and at least one comorbidity (more than half of those hospitalized; 64.0%). Chronic cardiovascular disease (CHD; 118 patients;

38.0%), followed by diabetes mellitus (DM; 77 patients; 24.4%), chronic kidney disease (CKD; 26 patients; 8.2%), and obesity (11 patients, 3.4%) were among the most prevalent comorbidities (Table 2). Among hospitalized patients, the overall lethality was 53.6% (mean age: 61.6 years; SD=15.4).

Table 1. Demographic, clinical, and epidemiological characteristics of patients confirmed for SARS-CoV-2 in an emergency hospital (Rio de Janeiro, RJ, Mar-Dec 2020).

Patient characteristics (n= 317)	n	%
Sex		
Male	182	57.5
Female	135	42.5
Age range (years)		
0-9	3	0.9
10-19	3	0.9
20-39	18	5.6
40-59	101	31.8
60-69	81	25.5
70-79	61	19.2
≥ 80	50	16.1
Areas of residence		
North Zone	135	42.5
South Zone	7	2.2
Central Zone	46	14.1
West Zone	46	14.1
Other municipalities	58	18.3
Ignored	25	8.8
Comorbidities		
Chronic cardiovascular disease	118	38
Diabetes Mellitus	77	24.4
Chronic kidney disease	26	8.2
Obesity	11	3.4
Others	33	10.4
No comorbidity	52	15.6
Tomographic findings		
Frosted glass pattern	110	34.7
Pulmonary infiltrate	49	15.4
Consolidation	20	6.1
Mixed	9	2.8
Others	129	41
Ventilatory Support		
Invasive ventilatory support	59	18.6
Non-invasive ventilatory support	101	31.9
No ventilatory support	157	49.5
Use of ICU*		
Yes	66	20.8
No	251	79.2
Hospital outcomes		
Discharge	140	44.1
Death	170	53.6
Transference	7	2.3

*Intensive Care Unit.

Among the patients admitted to the ICU, the highest percentages were male (57.5%) and elderly (72.8%), showing that older age groups were more hospitalized in this sector (Table 2). About 95.5% used mechanical ventilation; in this group, 98.4% had at least one comorbidity. The main comorbidities were as follows: cardiovascular diseases (34.8%), diabetes mellitus (30.3%), and chronic kidney disease (16.6%). Among patients admitted to the ICU, lethality increased to 84.5% (mean age: 65 years; SD=16.5).

Table 2. Characteristics of patients confirmed for COVID-19 admitted to the ICU of an emergency hospital according to the selected variables (Rio de Janeiro, RJ, Mar-Dec 2020).

Patient characteristics (n= 317)	n	%
Sex		
Male	38	57.5
Female	28	42.5
Age range (years)		
0-9	00	00
10-19	02	3.0
20-39	03	4.5
40-59	13	19.7
60-69	19	28.7
70-79	16	24.4
≥ 80	13	19.7
Comorbidities		
Chronic cardiovascular disease	23	34.8
Diabetes Mellitus	20	30.3
Chronic kidney disease	11	16.6
Obesity	04	6.1
Others	08	12.2
Use of ventilatory Support		
Yes	63	95.5
No	03	4.5
Outcomes		
Discharge	10	15.1
Death	56	84.5

Table 3 shows the outcome of the investigated cases (death; not death) according to the variables analyzed. For males, OR=1.24 was considered statistically non-significant (p -value=0.887; 95%CI=0.930; 1,670). The presence of at least one comorbidity increased the chance of death by 1.37 among hospitalized patients. However, this association was also not statistically significant (p -value=0.3226; 95%CI=1.041; 1.820).

The variables that showed the greatest association with the study outcome (chance of death) were the older age groups, with an increasing effect with advancing age, reaching OR=3.54 for age ≥80 years (p -value=0.000; 95%CI=1.815; 6.922), taking the age group 0-9 years, use of invasive ventilatory support (OR=10.80; p -value=0.003; 95%CI=4.327; 26.997), and ICU admission (OR=5.60; p -value=0.000; 95%CI=2.857; 10.975) as references.

Table 3. Bivariate analysis between hospital outcomes of patients confirmed by COVID-19 and selected variables in an emergency hospital (Rio de Janeiro, RJ; Mar-Dec 2020).

Variables	No Death		Death		P-values	OR (95%CI)
	N	%	N	%		
SEX						
Male	81	44.5	101	55.5	0.887	1.24 (0.930; 1.670)
Female	59	43.7	76	56.3		1.00
AGE RANGE (years)						
0-9	03	100.0	00	0.0	0.000	1.00
10-19	02	66.7	01	33.3		0.50 (0.045; 5.514)
20-39	13	72.2	05	27.8		0.38 (0.137; 1.078)
40-59	58	57.4	43	42.6		0.74 (0.499; 1.099)
60-69	36	44.4	45	55.6		1.25 (0.806; 1.937)
70-79	17	27.9	44	72.1		2.58 (1.478; 4.529)
≥ 80	11	22.0	39	78.0		3.54 (1.815; 6.922)
PRESENCE OF COMORBIDITY (at least 1)						
Yes	85	42.1	117	57.9	0.322	1.37 (1.041; 1.820)
No	55	47.8	60	52.2		1.00
USE OF VENTILATORY SUPPORT						
Yes: invasive	05	8.5	54	91.53	0.003	10.80 (4.327; 26.997)
Yes: no invasive	40	39.6	61	60.40		1.52 (1.023; 2.272)
No use	44	78.6	12	21.43		1.00
HOSPITALIZATION IN THE ICU						
Yes	10	15.2	56	84.9	0.000	5.60 (2.857; 10.975)
No	91	55.2	74	44.9		1.00

DISCUSSION

The demographic profile of patients admitted to this hospital is consistent with that of most studies reviewed, which highlight the greater predominance of male patients in older age groups.^{3,4,12} This situation can be attributed to the fact that men usually seek health services when their clinical condition becomes more serious and elderly people are more vulnerable to the severe form of COVID-19, leading to an increase in hospitalization cases. A recent study with hospitalized patients in the south of Santa Catarina also found a predominance of males.¹² Regarding age, research conducted in several countries has shown an exponential increase in the mortality of patients with COVID-19 from 60 years of age, which was also found in the present study.³⁻⁷

As for the place of residence, the north and west zones were the main areas of origin of the patients, although vulnerable areas are spread throughout the municipal territory. According to the study conducted by Santos (2020) to monitor the spatial distribution of COVID-19 in Rio de Janeiro (RJ), the higher intra-household densities in these areas reflect urban complexity.¹³ The results found in this present study reinforce the urgency of intensifying territorial surveillance strategies considering particular aspects of greater risk for the occurrence of COVID-19.

In the present study the expressive percentage of patients who needed ICU or used ventilatory support (the method used when the infected patient reaches a level of compromise of the lungs that causes severe res-

piratory weakness) shows the severity of the hospitalized cases and the dimension of technological demand in the health system. The literature highlights that in moderate to severe cases of COVID-19, hospitalization and use of ICU are required.¹⁴

In studies conducted in Spain, Italy, and the USA, a significant demand for ICU patients was observed, and ICU complications were also higher, including respiratory and renal failure, when compared to patients admitted to the clinical sectors of these hospitals.¹⁵ In a survey conducted in Australia (June 2020), 15% of reported cases were admitted to the hospital; of these cases, 19% were admitted to the ICU and 28% of these admissions required ventilatory support.⁹

In a study conducted by Escosteguy *et al.* (Brazil, 2020), it was observed that the use of ICU and ventilatory support, in addition to findings on radiological images with a ground-glass pattern, contributed to a worse prognosis among hospitalized patients.¹⁶

The radiological and tomographic findings of the present study are consistent with studies conducted in other hospitals in Brazil, where more common patterns in chest tomography were found, such as ground-glass opacity (84.6%) and irregular bilateral consolidations (79.5%), with ground glass being the earliest finding (0-4 days after the onset of symptoms).^{17,18}

The presence of at least one comorbidity was not shown to be associated with death with statistical significance. In a study conducted in the metropolitan area of Detroit (USA), Suleyman (2020) found that the

majority of hospitalized patients (94.0%) had at least one comorbidity, mainly hypertension (63.7%), chronic kidney disease (39.3%), and diabetes (38.4%).¹⁸ A study conducted in Spain showed that cardiovascular factors such as arterial hypertension (44.6%), dyslipidemia (33.5%), *diabetes mellitus* (18.8%), and obesity (14.3%) were the most prevalent comorbidities, followed by respiratory diseases (17.3%) and cancer (9.7%).¹⁵ Escosteguy *et al.* (2020) identified that patients with a higher chance of death had neoplasia (OR=2.58; 95%CI=1.48; 4.52) and chronic liver disease (OR=4.02; 95%CI=1.32; 12.26).¹⁶

Although some comorbidities and risk factors have already been identified as facilitators of disease worsening and death, few studies have described such aspects in Brazil. Cohort studies conducted in Europe and USA showed a clinical interaction between SARS and chronic diseases, especially cardiovascular disease and diabetes, which seem to facilitate the activity of the virus in the body of patients, triggering more serious clinical conditions.¹⁵

In this study, factors such as advanced age, use of ventilatory support, and having been admitted to the ICU were shown to be more associated with worse prognosis among hospitalized patients. Galvão and Rocalli (2021) observed a higher risk of death by COVID-19 among older individuals (>80 years) with comorbidity, male gender, and non-white skin color.²⁰

CONCLUSIONS

Patients with COVID-19 who went to the ICU and received ventilatory support are important aspects of their prognosis. Critical patients demanding more intensive care tend to have a longer hospital stay, contributing to overloading the health system. This study made it possible to highlight that epidemiological surveillance in the hospital environment helps in the production of evidence, collaborating as a guideline, both to implement more effective preventive and therapeutic measures at distinct levels of health management and to face the current context of the SARS-CoV-2 pandemic, and strengthen expertise for future global events.

Furthermore, deepening the analysis of the average length of stay, historical series of the number of patient-days, and monthly hospital occupancy rate would be interesting, as these indicators are fundamental to prospect scenarios, assist decision-making, and improve the care provided to patients.

INTEREST CONFLICTS

There is no conflict of interest or financial support for the study.

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AUTHORS' CONTRIBUTIONS

Catia Cristina Martins de Oliveira contributed to the conception, design of the analysis, and writing of the manuscript;

Fabiane Canellas de Paula, Renata Vasconcelos and **Nadja Raquel Lustosa Lopes** contributed to the planning, design, and review of the manuscript.

All authors approved the final version to be submitted, being responsible for all aspects of the study, including its accuracy and integrity.

Sensitivity profile of blood culture isolates in a clinical analysis laboratory, Fortaleza, CE

Perfil de sensibilidade de isolados de hemocultura em um laboratório de análises clínicas, Fortaleza, CE

Perfil de sensibilidad de hemocultivos aislados en un laboratorio de análisis clínicos, Fortaleza, CE

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Corresponding Author:

Cecília Leite Costa
cecilialcosta@hotmail.com

Address: R. João Adolfo Gurgel, 133 - Cocó,
Fortaleza, CE, Brazil.

André Luis Almeida Alves Filho¹ 
Alexandre Amaral Medeiros² 
Francisco Wallyson Calixto Marques³ 
Cecília Leite Costa^{1,4} 

¹ Centro Universitário Christus (Unichristus), Fortaleza, CE, Brazil.

² Universidade Estadual do Ceará (UECE), Fortaleza, CE, Brazil.

³ UniFanor, Fortaleza, CE, Brazil.

⁴ Universidade Federal do Ceará (UFC), Fortaleza, CE, Brazil.

ABSTRACT

Background and objectives: bacteremia is defined from the presence of bacteria in the bloodstream. Its clinical importance is associated with the high morbidity and mortality rate in the world. In severe cases, it can culminate in sepsis, with a constant increase in cases in Brazil. Therefore, this study aims to assess the main bacterial isolates in blood cultures and a possible change in their sensitivity profiles in a clinical analysis laboratory in Fortaleza, Ceará. **Methods:** an epidemiological, descriptive, retrospective study was carried out, with a quantitative approach of positive blood cultures, seeking to assess the main isolated microorganisms and their sensitivity profiles. The data used were obtained from the laboratory system through the EpiCenter→ software, from January 2019 to December 2020. Statistical analysis was performed using the Graphpad 7.0 software. **Results:** 840 microorganisms were identified from blood cultures, and the main ones were *E. coli*, *K. pneumoniae*, *P. aeruginosa*, *S. epidermidis*, *S. aureus* and *S. haemolyticus*. Some isolates show a change in the sensitivity profile, such as *K. pneumoniae* and *P. aeruginosa*, showing an increase in sensitivity to carbapenems and cephalosporins, while *S. epidermidis* showed a decrease in sensitivity to minocycline in the comparison between years 2019 and 2020. **Conclusion:** clinical isolates from blood cultures showed a change in the sensitivity profile between 2019 and 2020, taking into account that, for *K. pneumoniae*, *P. aeruginosa*, this change resulted in an increase in sensitivity, with an increase in resistance in *S. epidermidis* isolates.

Keywords: Bacteremia. Blood Culture. Bacterial Resistance. Sensitivity Profile.

RESUMO

Justificativa e objetivos: bacteremia é definida a partir da presença de bactérias na corrente sanguínea. Sua importância clínica está associada à alta taxa de morbidade e mortalidade no mundo. Nos casos graves, pode culminar em sepse, com constante aumento dos casos no Brasil. Portanto, o presente estudo tem como objetivo avaliar

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os principais isolados bacterianos em hemoculturas e uma possível alteração nos seus perfis de sensibilidade em um laboratório de análises clínicas de Fortaleza, Ceará. **Métodos:** foi realizado um estudo epidemiológico, descritivo, retrospectivo, com abordagem quantitativa de hemoculturas positivas, buscando avaliar os principais microrganismos isolados e seus perfis de sensibilidades. Os dados utilizados foram obtidos a partir do sistema laboratorial através do *software* EpiCenter→, referente ao período de janeiro de 2019 a dezembro de 2020. A análise estatística foi realizada pelo *software* Graphpad 7.0. **Resultados:** foram identificados 840 microrganismos a partir das hemoculturas, sendo os principais *E. coli*, *K. pneumoniae*, *P. aeruginosa*, *S. epidermidis*, *S. aureus* e *S. haemolyticus*. Alguns isolados apresentam uma alteração no perfil de sensibilidade, como *K. pneumoniae* e *P. aeruginosa*, apresentando um aumento na sensibilidade frente aos carbapenêmicos e as cefalosporinas, enquanto o *S. epidermidis* apresentou uma diminuição na sensibilidade frente à minociclina na comparação entre os anos de 2019 e 2020. **Conclusão:** os isolados clínicos de hemocultura apresentaram uma alteração no perfil de sensibilidade entre 2019 e 2020, levando em consideração que, para *K. pneumoniae* e *P. aeruginosa*, essa alteração resultou no aumento na sensibilidade, com aumento na resistência nos isolados de *S. epidermidis*.

Descritores: Bacteremia. Hemocultura. Resistência Bacteriana. Perfil de Sensibilidade.

RESUMEN

Justificación y objetivos: la bacteriemia se define por la presencia de bacterias en el torrente sanguíneo. Su importancia clínica está asociada con la alta tasa de morbimortalidad en el mundo. En casos severos, puede culminar en sepsis, con un aumento constante de casos en Brasil. Por tanto, este estudio tiene como objetivo evaluar los principales aislados bacterianos en hemocultivos y un posible cambio en sus perfiles de sensibilidad en un laboratorio de análisis clínicos en Fortaleza, Ceará. Métodos: se realizó un estudio epidemiológico, descriptivo, retrospectivo, con abordaje cuantitativo de hemocultivos positivos, buscando evaluar los principales microorganismos aislados y sus perfiles de sensibilidad. Los datos utilizados se obtuvieron del sistema de laboratorio a través del *software* EpiCenter→, para el período de enero de 2019 a diciembre de 2020. El análisis estadístico se realizó mediante el *software* Graphpad 7.0. **Resultados:** se identificaron 840 microorganismos a partir de hemocultivos, siendo los principales *E. coli*, *K. pneumoniae*, *P. aeruginosa*, *S. epidermidis*, *S. aureus* y *S. haemolyticus*. Algunos aislados muestran un cambio en el perfil de sensibilidad, como *K. pneumoniae* y *P. aeruginosa*, mostrando un aumento en la sensibilidad a los carbapenémicos y cefalosporinas, mientras que *S. epidermidis* mostró una disminución en la sensibilidad a la minociclina, en la comparación entre los años de 2019 y 2020. **Conclusiones:** los aislados clínicos de hemocultivos mostraron un cambio en el perfil de sensibilidad entre 2019 y 2020, teniendo en cuenta que para *K. pneumoniae*, *P. aeruginosa*, este cambio resultó en un aumento de la sensibilidad, con un aumento de la resistencia en los aislados de *S. epidermidis*.

Palabras clave: Bacteriemia. Cultura de Sangre. Resistencia Bacteriana. Perfil de Sensibilidad.

INTRODUCTION

Bacteremia is associated with the presence of bacteria in the bloodstream, which may have a primary (direct entry into the bloodstream via needles, contaminated infusions, catheter, etc.) or secondary origin (from a primary focus of infection, with possible hematogenous or lymphatic spread), having great clinical importance due to the high morbidity and mortality when associated with sepsis,¹ considering the increase in sepsis cases in Brazil.² According to the Global Sepsis Alliance (GSA), sepsis can be caused by blood infections, urinary tract infections, lung infections, intestinal infections, and skin infections, being characterized by an inflammatory reaction that affects organs and systems from infections caused by viruses, bacteria, fungi and parasites.³

Given the increase in cases of bacteremia and sepsis, blood culture has emerged as the main laboratory methodology for identifying microorganisms, enabling the assessment of the sensitivity profile of clinical isolates.^{4,5} The main microorganisms present in bacteremia differ in terms of age. In children, the most reported cases are caused by *Streptococcus pneumoniae*, *Neisse-*

ria meningitidis and *Haemophilus influenzae*⁵. In adult patients, the most frequent isolates are *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Enterococcus* spp., *S. pneumoniae*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Klebsiella* spp.⁶ and *Acinetobacter baumannii*.⁷

The main blood culture isolates show considerable resistance to antibiotics of clinical importance⁷. Thus, it is possible to observe that antimicrobial resistance patterns have been altered and multidrug-resistant bacteria have increased alarmingly, resulting in serious infections with complicated treatments.⁸ Antimicrobial resistance is a characteristic that can be intrinsic or acquired horizontally, through the acquisition of resistance genes, or through spontaneous mutations.⁹ This resistance is an inevitable evolutionary process,¹⁰ whose species with the highest frequency of antimicrobial resistance are *S. aureus*, *Enterococcus faecium*, *E. faecalis*, *S. pneumoniae*, *E. coli*, *K. pneumoniae*, *P. aeruginosa* and *A. baumannii*.¹¹ Duval et al (2019) highlight the main multidrug-resistant microorganisms of global importance, such as carbapenem-resistant *A. baumannii*, carbapenem-resistant *P. aeruginosa*, and 3rd generation carbapenem- cephalosporin-resistant *Enterobacterales* (*K. pneumoniae*, *E. coli*,

Enterobacter spp., *Serratia spp.* and *Proteus spp.*).¹²

Identifying the pattern of antimicrobial resistance makes it possible to support empirical treatments,⁴ since the release of blood cultures is a slow process, often unable to provide support and rapid therapeutic interventions. As a result, empirical treatment ends up being the only immediate solution, but empirical treatments end up being performed with broad-spectrum antibiotics, harming the patient due to drug toxicity and aiding in the selection of multidrug-resistant microorganisms.⁶

In Brazil, the main bacteria of clinical importance are non-fermenting bacteria, Extended Spectrum Beta-lactamase (ESBL) producing enterobacteria and methicillin-resistant *S. aureus*. Those related to cases of bacteremia are *S. aureus*, coagulase-negative *Staphylococcus*, *Enterococcus spp.*, *E. coli* and *Klebsiella spp.*⁷ Therefore, the present study aims to assess the main bacterial isolates in blood cultures and a possible change in their sensitivity profiles in a clinical analysis laboratory in Fortaleza, Ceará.

METHODS

This is an epidemiological, descriptive, retrospective study with a quantitative approach of outsourced blood cultures from patients admitted to a tertiary hospital, a reference in Fortaleza, featuring 23 specialties, with 296 beds and eight operating rooms equipped with laminar flow.

This research was carried out taking into account the guarantee of the ethical and legal principles that govern research on human beings, recommended in Resolution 466/2012 of the Brazilian National Health Council (CNS), approved by the Research Ethics Committee, with CAAE (Certificado de Apresentação para Apreciação Ética - Certificate of Presentation for Ethical Consideration) 42401920.0.0000.5049.

Samples were collected from January 2019 to December 2020, and analyzed in a clinical analysis laboratory in Fortaleza, Ceará. Patients of both sexes without age restriction who were admitted to the hospital were included.

Patient data was collected in EpiCenter→ system from the laboratory's database, along with software linked to BD Phoenix™, MicroScan and AutoSCAN-4. The results were based on plotting performed in EpiCenter→ software, dividing Gram-positive cocci (GPC) and Gram-negative bacilli (GNB) into groups, selecting the seven main microorganisms isolated from each group and performing the comparison through the elaboration of tables and graphs, demonstrating the total number of microorganisms isolated and analyzing the sensitivity profiles of the three main microorganisms of each group by drug tested. In addition to the aforementioned analyses, the analysis of the amounts of positive blood cultures and contaminants from 2019 and 2020 was carried out. The drugs used to compare the sensitivity profile of GNB and GPC were pre-established according to BrCast, version 9.0 of 2019, valid from 02/04/2019, assessing the minimum inhibitory concentration (MIC) of each drug to the respective identified microorganism.¹³

In the study, all samples of positive blood cultures and confirmed by the responsible laboratory were included. Through microbiological analysis, antimicrobial susceptibility tests were performed, following the standardization institution BrCast, classifying sensitive only the values referring to the usual doses.

The analysis of the sensitivity profile of the classes of antibiotics was performed through the arithmetic mean of the individual percentages of each drug against the species analyzed using Graphpad 7.0. The assessment of the change in antibiotic sensitivity profiles in 2019 and 2020 was compared using the chi-square test with Yates' correction ($\alpha = 5\%$), using Graphpad 7.0, considering an increase or decrease in sensitivity if p-value is above 0.05.

RESULTS

During the research period, 840 microorganisms isolated from blood cultures of patients admitted to a tertiary hospital from January 2019 to December 2020 were identified.

In 2019, 64% (254/397) GNB and 36% (143/397) GPC were isolated from blood cultures. In 2020, 43.3% (192/443) GNB and 56.6% (251/443) GPC were isolated. The main isolates from the GNB group in 2019 were *E. coli*, 34.6% (88/254) *K. pneumoniae*, 29.1% (74/254), and *P. aeruginosa*, 18.5% (47/254). The main GPC isolates in 2019 were *S. epidermidis*, 39.8% (57/143), *S. aureus*, 24.4% (35/143), and *S. haemolyticus*, 12.6% (18/143).

In 2020, the main GNB isolates were *E. coli*, 31.2% (60/192), *K. pneumoniae*, 26.5% (51/192) and *P. aeruginosa*, 23% (44/192), while those of GPC were *S. epidermidis*, 51.4% (129/251), *S. haemolyticus*, 19.5% (49/251), and *S. hominis*, 13.5% (34/251), showing a change in prevalence between 2019 and 2020.

In 2019, the main GNB isolates showed the following sensitivity profiles: *E. coli* showed lower sensitivity to sulfonamides (53.85%), monobactams (58.82%) and penicillin (62.01%); *K. pneumoniae* showed lower sensitivity to phosphomycin (0%), to monobactams (58.82%) and to penicillin (34.09%); *P. aeruginosa* was less sensitive to phosphomycin (0%), glycylicline (0%) and sulfonamides (0%). While GPC isolates showed the following sensitivity profile: *S. epidermidis* showed lower sensitivity to cephalosporins (7.78%), penicillin (15.05%) and quinolones (39.09%); *S. aureus* showed lower sensitivity to penicillin (41.03%), cephalosporins (72.92%) and quinolones (92.68%); and *S. haemolyticus* showed lower sensitivity to penicillin (16.67%), cephalosporins (33.33%) and aminoglycosides (37.50%) (Table 1).

In 2020, the main GNB isolates showed the following sensitivity profiles: *E. coli* showed lower sensitivity to monobactams (57.14%), penicillin (57.97%) and sulfonamides (59.38%); *K. pneumoniae* showed lower sensitivity to penicillin (46.43%), to monobactams (62.50%) and to sulfonamides (62.96%); *P. aeruginosa* showed lower sensitivity to phosphomycin (0%), sulfonamides (0%) and glycylicline (6.25%). In GPC isolates, *S. epidermidis* showed a lower sensitivity to penicillin (17.70%), quinolones

(38.07%) and sulfonamides (38.61%); *S. aureus* showed a lower sensitivity to penicillin (75.76%); and *S. haemolyticus* showed lower sensitivity to penicillin (8.14%), quinolones (25.74%) and aminoglycosides (32.43%). (Table 1).

Comparative assessment of the change in sensitivity profile was observed for the main GNB and GPC isolates from blood cultures, from January 2019 to December 2020. As for GNB, *E. coli* isolates showed a decrease in their percentage of sensitivity to amikacin, amoxicillin-clavulanate, aztreonam, cefuroxime, ciprofloxacin, phosphomycin with G6P, gentamicin levofloxacin and tigecycline. However, no statistical difference was observed in susceptibility in the other antibiotics tested. *K. pneumoniae* isolates showed a percentage increase in the susceptibility of their isolates, comparing the two years, as 2019 isolates are less susceptible to the antibiotics tested. A change was observed in the susceptibility of *K. pneumoniae* to cefazolin (p=1.14), cefepime (p=0.39), ceftazidime (p=0.20), ceftriaxone (p=0.56), ertapenem (p=0.10), gentamicin (p=3.36), imipenem (p=2.34), meropenem (p=1.91), tigecycline (p=0.09), all representing an increase in sensitivity when compared to the years 2019 and 2020. *P. aeruginosa* isolates showed a decrease in the percentage of their sensitivity to amikacin and aztreonam (Table 2). A change in the susceptibility of *P. aeruginosa* to imipenem (P=3.54) was observed,

representing an increase in sensitivity when compared to the years 2019 and 2020.

GPC isolates such as *S. epidermidis* demonstrated a percentage decrease in sensitivity to ciprofloxacin, clindamycin, erythromycin, levofloxacin, minocycline, oxacillin, rifampicin and trimethopim-sulfamethoxazole. A change in the susceptibility of *S. epidermidis* to minocycline was observed (p=0.01), representing a decrease in sensitivity when compared to the years 2019 and 2020. *S. aureus* isolates showed a decrease in sensitivity to clindamycin and erythromycin. An alteration was observed in the susceptibility of *S. aureus* to penicillin G (p=3.41), representing an increase in sensitivity when compared to the years 2019 and 2020. *S. haemolyticus* isolates showed a decrease in the percentage sensitivity to amoxicillin-clavulanate, ampicillin-sulbactam, ceftriaxone, ciprofloxacin, clindamycin, chloramphenicol, levofloxacin, rifampicin and trimethoprim-sulfamethoxazole. However, no statistical difference was observed in susceptibility in other antibiotics tested (Table 3).

The rate of positivity and contaminants in blood cultures is variable when comparing 2019 and 2020. In 2019, 4% (10/233) of the isolates were contaminants and 95% (223/233) were blood cultures confirmed as positive. In 2020, 16% (49/309) of the isolates were contaminants and 84% (260/309) were blood cultures confirmed as positive.

Table 1. Sensitivity rate to the classes of antibiotics used for Gram-negative and Gram-positive bacilli, compared to the main isolates from blood cultures in 2019 and 2020.

Antimicrobial sensitivity rate (%) (2019)										
Microorganisms	Penicillin	Cephalosporins	Carbapenems	Aminoglycosides	Quinolones	Sulphonamides	Glycycycline	Monobactam	Phosphomycin	Glycopeptide
Gram-negative	39.13%	44.47%	65.38%	67.69%	62.84%	32.11%	53.31%	52.54%	33.33%	-
<i>E. coli</i>	62.01%	72.3%	98.29%	82.35%	69.23%	53.85%	100%	58.82%	100%	-
<i>K. pneumoniae</i>	34.09%	34.74%	62.39%	52.28%	52.06%	42.47%	56.94%	23.81%	0%	-
<i>P. aeruginosa</i>	21.28%	26.38%	35.46%	68.44%	67.22%	0%	0%	75.00%	0%	-
Gram-positive	24.25%	38.01%	100%	67.55%	59.13%	67.02%	-	-	-	98.17%
<i>S. epidermidis</i>	15.05%	7.78%	100%	68.00%	39.09%	44.00%	-	-	-	95.94%
<i>S. aureus</i>	41.03%	72.92%	100%	97.14%	92.68%	97.06%	-	-	-	98.57%
<i>S. haemolyticus</i>	16.67%	33.33%	100%	37.50%	45.63%	60.00%	-	-	-	100%
Antimicrobial sensitivity rate (%) (2020)										
Microorganisms	Penicillin	Cephalosporins	Carbapenems	Aminoglycosides	Quinolones	Sulphonamides	Glycycycline	Monobactam	Phosphomycin	Glycopeptide
Gram-negative	44.12%	56.85%	79.94%	81.17%	71.82%	40.78%	65.44%	61.31%	55.30%	-
<i>E. coli</i>	57.97%	73.25%	100%	87.12%	62.13%	59.38%	96.00%	57.14%	90.91%	-
<i>K. pneumoniae</i>	46.43%	67.15%	89.29%	69.64%	67.86%	62.96%	93.75%	62.50%	75.00%	-
<i>P. aeruginosa</i>	27.96%	30.15%	50.54%	86.76%	85.49%	0%	6.25%	64.29%	0%	-
Gram-positive	33.87%	72.18%	100%	68.42%	54.60%	61.44%	-	-	-	99.38%
<i>S. epidermidis</i>	17.70%	62.00%	100%	72.82%	38.07%	38.61%	-	-	-	99.48%
<i>S. aureus</i>	75.76%	100%	100%	100%	100%	100%	-	-	-	100%
<i>S. haemolyticus</i>	8.14%	54.55%	100%	32.43%	25.74%	45.71%	-	-	-	98.65%

Table 2. Comparison of antimicrobial susceptibility profiles of the main Gram-negative bacilli (GNB) isolated from blood cultures, between 2019 and 2020.

Antibiotics	% <i>S. E. Coli</i>		% <i>S. K. Pneumoniae</i>		% <i>S. P. Aeruginosa</i>	
	2019	2020	2019	2020	2019	2020
Amicacin	98.72%(77/78)	96.97%(32/33)	76.71%(56/73)	89.29%(25/28)	85.11%(40/47)	83.87%(26/31)
Amoxicillin-clavulanate	64.71%(11/17)	42.86%(3/7)	35.00%(7/20)	50.00%(4/8)	0.00%(0/1)	
Ampicillin	35.90%(28/78)	37.50%(12/32)	0.00%(0/72)	0.00%(0/27)	0.00%(0/35)	0.00%(0/16)
Ampicillin-sulbactam	48.72%(38/78)	54.55%(18/33)	24.66%(18/73)	46.43%(13/28)	0.00%(0/35)	0.00%(0/16)
Aztreonam	58.82%(10/17)	57.14%(4/7)	23.81%(5/21)	62.50%(5/8)	75.00%(9/12)	64.29%(9/14)
Cefazolin	72.13%(44/61)	76.92%(20/26)	31.91%(15/47)	73.33%(11/15)	0.00%(0/35)	0.00%(0/15)
Cefepime	75.32%(58/77)	72.73%(24/33)	36.99%(27/73)	71.43%(20/28)	61.70%(29/47)	77.42%(24/31)
Cefotaxime	68.75%(11/16)	71.43%(5/7)	31.82%(7/22)	50.00%(4/8)		
Cefoxitin	79.22%(61/77)	81.82%(9/11)	45.83%(33/72)	70.00%(7/10)	0.00%(0/35)	0.00%(0/16)
Ceftazidime	71.43%(55/77)	75.76%(25/33)	33.33%(24/72)	70.37%(19/27)	70.21%(33/47)	73.33%(22/30)
Ceftriaxone	70.49%(43/61)	76.92%(20/26)	36.00%(18/50)	77.78%(14/18)	0.00%(0/35)	0.00%(0/15)
Cefuroxime	68.75%(11/16)	57.14%(4/7)	27.27%(6/22)	57.14%(4/7)		
Ciprofloxacin	69.23%(54/78)	57.58%(19/33)	47.95%(35/73)	67.86%(19/28)	72.74%(34/47)	87.10%(27/31)
Ertapenem	97.44%(76/78)	100.00%(33/33)	60.27%(44/73)	89.29%(25/28)	0.00%(0/35)	0.00%(0/16)
Phosphomycin with G6P	100.00%(2/2)	90.91%(20/22)	0.00%(0/3)	75.00%(15/20)	0.00%(0/7)	
Gentamicin	91.03%(71/78)	90.91%(30/33)	56.94%(41/72)	82.14%(23/28)	70.21%(33/47)	80.65%(25/31)
Imipenem	98.72%(77/78)	100.00%(33/33)	63.89%(46/72)	89.29%(25/28)	51.06%(24/47)	77.42%(24/31)
Levofloxacin	69.23%(54/78)	66.67%(22/33)	56.16%(41/73)	67.86%(19/28)	61.70%(29/47)	83.87%(26/31)
Meropenem	98.70%(76/77)	100.00%(33/33)	63.01%(46/73)	89.29%(25/28)	55.32%(26/47)	74.19%(23/31)
Piperacillin-tazobactam	96.15%(75/78)	100.00%(33/33)	52.05%(38/73)	71.43%(20/28)	68.09%(32/47)	80.00%(24/30)
Tigecycline	100.00%(78/78)	96.00%(24/25)	56.94%(41/72)	93.75%(15/16)	0.00%(0/35)	6.25%(1/16)
Tobramycin	82.35%(14/17)	83.33%(5/6)	47.62%(10/21)	57.14%(4/7)	66.67%(8/12)	92.86%(13/14)
Trimethoprim-sulfamethazole	53.85%(42/78)	59.38%(19/32)	42.47%(31/73)	62.96%(17/27)	0.00%(0/35)	0.00%(0/2)

Note: The main results of the minimum inhibitory concentration were cefazolin (≤ 4), cefepime (≤ 0.125), ceftazidime (≤ 0.5), gentamicin (≤ 2), imipenem (≤ 1), meropenem (≤ 0.125) and tigecycline (≤ 2), for *K. pneumoniae*, and imipenem (≤ 4), for *P. aeruginosa*.

Table 3. Comparison of antimicrobial susceptibility profiles of the main Gram-positive cocci (GPC) isolated from blood cultures, between 2019 and 2020.

Antibiotics	% <i>S. S. Epidermidis</i>		% <i>S. S. Aureus</i>		% <i>S. S. Haemolyticus</i>	
	2019	2020	2019	2020	2019	2020
Amoxicillin-clavulanate	22.58% (7/31)	24.00% (12/50)	61.54% (8/13)	100.00% (7/7)	25.00% (1/4)	9.09% (2/22)
Ampicillin	0.00% (0/44)	5.10% (5/98)	0.00% (0/26)	27.27% (3/11)	0.00% (0/14)	6.25% (2/32)
Ampicillin-sulbactam	22.58% (7/31)	24.00% (12/50)	61.54% (8/13)	100.00% (7/7)	25.00% (1/4)	9.09% (2/22)
Ceftaroline	23.33% (7/30)	100.00% (9/9)	87.50% (14/16)	100.00% (4/4)		100.00% (5/5)
Ceftriaxone		24.00% (12/50)	58.33% (7/12)	100.00% (7/7)	33.33% (1/3)	9.09% (2/22)
Ciprofloxacin	42.00% (21/50)	34.95% (36/103)	90.91% (30/33)	100.00% (11/11)	31.25% (5/16)	29.73% (11/37)
Clindamycin	38.64% (17/44)	33.33% (32/96)	50.00% (16/32)	27.27% (3/11)	31.25% (5/15)	30.56% (11/36)
Chloramphenicol	88.89% (16/18)	95.83% (46/48)	100.00% (16/16)	100.00% (4/4)	90.91% (10/11)	84.62% (11/13)
Daptomycin	100.00% (48/48)	100.00% (101/101)	100.00% (33/33)	100.00% (11/11)	100.00% (16/16)	100.00% (36/36)
Erythromycin	30.00% (15/50)	17.48% (18/103)	33.33% (11/33)	27.27% (3/11)	0.00% (0/16)	21.62% (8/37)
Gentamicin	68.00% (34/50)	72.82% (75/103)	97.14% (34/35)	100.00% (11/11)	37.50% (6/16)	32.43% (12/37)
Levofloxacin	41.94% (13/31)	41.18% (21/51)	94.44% (17/18)	100.00% (7/7)	60.00% (3/5)	21.74% (5/23)
Linezolid	98.00% (49/50)	100.00% (102/102)	97.06% (33/34)	100.00% (11/11)	100.00% (16/16)	100.00% (37/37)
Minocycline	100.00% (19/19)	45.83% (22/48)	100.00% (16/16)	100.00% (3/3)	100.00% (11/11)	100.00% (9/9)
Oxacillin	24.00% (12/50)	20.39% (21/103)	77.14% (27/35)	81.82% (9/11)	18.75% (3/16)	21.62% (8/37)
Penicillin G	2.22% (1/45)	3.06% (3/98)	0.00% (0/26)	27.27% (3/11)	0.00% (0/14)	3.13% (1/32)
Rifampicin	98.00% (49/50)	93.75% (90/96)	91.43% (32/35)	100.00% (11/11)	62.25% (10/16)	51.52% (17/33)
Teicoplanin	93.88% (46/49)	98.96% (95/96)	100.00% (33/33)	100.00% (11/11)	100.00% (16/16)	97.30% (37/37)
Tetracycline	93.55% (29/31)	96.08% (49/51)	82.35% (14/17)	100.00% (7/7)	40.00% (2/5)	95.65% (22/23)
Tigecycline	44.00% (22/50)	100.00% (52/52)	100.00% (16/16)	100.00% (4/4)		100.00% (13/13)
Trimethoprim-sulfamethoxazole		38.61% (39/101)	97.06% (33/34)	100.00% (11/11)	60.00% (9/15)	45.71% (16/35)
Vancomycin	98.00% (49/50)	100.00% (103/103)	97.14% (34/35)	100.00% (11/11)	100.00% (16/16)	100.00% (37/37)

Note: the main results of the minimum inhibitory concentration were minocycline (≤ 0.25), for *S. epidermidis*, and penicillin G (≤ 0.125), for *S. aureus*.

DISCUSSION

In a study carried out with six hospitals in Cascavel, Paraná, it was observed that the main microorganisms isolated in blood cultures were *S. aureus* (17.94%), *S. epidermidis* (16.26%), *K. pneumoniae* (14.52%), *E. coli* (8.97%), *A. baumannii* (8.81%) and *P. aeruginosa* (8.32%).¹⁴

In another study carried out at the *Hospital das Clínicas* of the *Universidade Federal de Pernambuco* (UFPE), Recife, it was identified that 57.64% of the blood culture isolates were Gram-positive bacteria, while 42.36% were Gram-negative bacteria. The main isolates were *S. aureus* (21.62%), coagulase negative *Staphylococcus* (20.54%), *K. pneumoniae* (9.72%), *E. coli* (7.56%) and *A. baumannii* (6.48%).¹⁵

In a study carried out in a tertiary hospital in Minas Gerais, it was shown that 40.6% of those isolated were *S. epidermidis*, 17.2%, *S. aureus*, 7.8%, *Enterobacter spp.* and 6.3% of *Pseudomonas spp.*¹⁶ These studies are similar to what was found in the present study, in 2020, in which the main isolates were *S. epidermidis* (29.12%), *E. coli* (13.54%), *K. pneumoniae* (11, 51%), *S. haemolyticus* (11.06%), *P. aeruginosa* (9.93%) and *S. hominis* (7.67%).

It is possible to observe, considering the analyzed studies, that Gram-negative isolates showed resistance against ampicillin-sulbactam, ceftazidime, ciprofloxacin and levofloxacin. *K. pneumoniae* isolates are less sensitive to aztreonam, cefepime, ceftriaxone, ceftazidime, ciprofloxacin; *E. coli* showed a lower percentage of sensitivity to ceftazidime and cefepime; and *P. aeruginosa* had a lower percentage of sensitivity to polymyxin b, ceftazidime and aztreonam.¹⁵ Another study shows that the isolates belonging to the GPC group showed the following sensitivity pattern: 15.4% of *S. epidermidis* are sensitive to oxacillin; 92.3% are sensitive to vancomycin; 92.3 and 27.3% of *S. aureus* are sensitive to oxacillin; and 100% are sensitive to vancomycin.¹⁶

There is a divergence of data when we compare the assessment of this sensitivity profile of the main isolates, with only the data observed for the GPC group and, individually, for *S. epidermidis* and *S. aureus* agreeing. This divergence regarding the sensitivity profile may occur due to the difference in date between the works and due to the state of study of each work.

Some of the data cited may represent an analytical error in the laboratory or an error in sending the results to the software, as in the case of vancomycin-resistant *S. aureus*, isolated in 2019, and tigecycline-sensitive *P. aeruginosa*.

Clinical isolates from blood cultures showed a change in the sensitivity profile between 2019 and 2020. The sensitivity percentage assessment is changed according to the microorganism in question.

In GNB, when analyzing *E. coli*, it is possible to infer an increase in resistance against penicillin, monobactams, quinolones and phosphomycin, while *P. aeruginosa* shows an increase in resistance against monobactams, and *K. pneumoniae* showed a decrease in the resistance of their isolates, considering that all 2019 isolates are more resistant than those of 2020. While in GPC, *S. epidermidis* isolates show a considerable increase in their resistance

against quinolones, macrolides, lincosamines and against a tetracycline (minocycline). *S. aureus* isolates showed an increase in sensitivity, given that the 2019 isolates were more resistant. In contrast, *S. haemolyticus* isolates showed increased resistance against penicillin, quinolones, lincosamines, amphenicols and macrolides.

The change in the sensitivity profile of the main clinical isolates from blood cultures is broad, taking into account that, for some species, this change resulted in an increase in the sensitivity of these isolates. In contrast, the species, with an increase in resistance observed, were against antibiotics of extreme clinical importance, resulting in the use of more potent broad-spectrum antibiotics.

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AUTHORS' CONTRIBUTIONS

André Luis Almeida Alves Filho contributed to article conception, design, analysis and writing; **Alexandre Amaral Medeiros** contributed to data statistical analysis through the GraphPad Software. **Francisco Wallyson Calixto Marques** contributed to the analysis of blood cultures assessed at the Clinical Analysis Laboratory in Fortaleza, Ceará. **Cecília Leite Costa** contributed to article planning, design, review and final approval.

All authors have approved the final version to be published and are responsible for all aspects of the work, including ensuring its accuracy and integrity.

Mortality from chronic kidney disease secondary to hypertension in Brazil: a study of the "Global Burden of Disease"

Mortalidade por doença renal crônica secundária à hipertensão no Brasil: um estudo do "Global Burden of Disease"

Mortalidad por enfermedad renal crónica secundaria a hipertensión en Brasil: un estudio de la "Global Burden of Disease"

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Corresponding Author:

Matheus Vinicius Barbosa da Silva
matheus.viniciusbarbosa@ufpe.br

address: R. Alto do Reservatório - Alto José Leal,
Vitória de Santo Antão - PE, Brazil.

Matheus Vinicius Barbosa da Silva¹ 

Carlos Antonio de Lima Filho¹ 

Amanda de Oliveira Bernardino² 

Viviane de Araújo Gouveia¹ 

¹ Universidade Federal de Pernambuco, Centro Acadêmico de Vitória, Vitória, PE, Brasil.

² Universidade de Pernambuco, Recife, PE, Brasil.

ABSTRACT

Background and Objectives: Chronic kidney disease (CKD) is one of the main complications resulting from arterial hypertension, and a recent increase in the incidence and prevalence of the disease has been reported, which can lead to an increase in mortality and complications resulting from the disease. Thus, the objective of study is to describe the variations in mortality from CKD secondary to arterial hypertension, in Brazil, between the years 1990 to 2019. **Methods:** Epidemiological study, with a quantitative approach and descriptive character, which analyzed data from the "Global Burden of Disease Study" (GBD) tool. **Results:** In all of Brazil's federative units, the estimate of deaths from CKD secondary to hypertension increased, with the Southeast region having the highest estimates. The States of Rio de Janeiro, Rio Grande do Sul, and Paraíba lead with the highest mortality rates. Regarding sex, in all years, higher rates were observed in males, however, over the years, this difference has been reduced. The age group of ≥ 70 years was the most affected, standing out with the highest death rates. **Conclusion:** the burden of CKD in Brazil has increased in the last 30 years; among the regions of the country, the Southeast recorded the highest estimates of deaths in all the years analyzed, being mainly higher among men.

Keywords: Mortality, Chronic Kidney Disease, Arterial Hypertension, Epidemiology.

RESUMO

Justificativa e objetivos: A doença renal crônica (DRC) é uma das principais complicações decorrentes da hipertensão arterial. Nos últimos anos, tem sido relatado um aumento na incidência e prevalência da doença, o que pode levar ao aumento da mortalidade e das complicações decorrentes da doença. Assim, o objetivo deste estudo

foi descrever as variações da mortalidade por DRC secundária à hipertensão arterial no Brasil entre 1990 e 2019. **Métodos:** Trata-se de um estudo epidemiológico, de abordagem quantitativa e caráter descritivo, que analisou dados da ferramenta *Global Burden of Disease Study* (GBD). **Resultados:** Em todas as unidades da federação, a estimativa de mortes por DRC secundária à hipertensão apresentou aumento, a região Sudeste apresentando as maiores estimativas. Os estados do Rio de Janeiro, Rio Grande do Sul e Paraíba lideram as pesquisas com as maiores taxas de mortalidade. No que diz respeito ao sexo, em todos os anos foram observadas maiores taxas de DRC em indivíduos do sexo masculino; contudo, nota-se que tem ocorrido uma redução dessa diferença. A faixa etária de ≥ 70 anos foi a mais acometida, destacando-se com as maiores taxas de mortes. **Conclusão:** a carga de DRC no Brasil aumentou nos últimos 30 anos. Entre as regiões do país, o Sudeste registrou as maiores estimativas de mortes em todos os anos analisados, principalmente de homens.

Descritores: Mortalidade, Doença renal crônica, Hipertensão Arterial, Epidemiologia.

RESUMEN

Justificación y objetivos: La enfermedad renal crónica (ERC) es una de las principales complicaciones derivadas de la hipertensión arterial, y en los últimos años se ha reportado un aumento en la incidencia y prevalencia de la enfermedad, lo que puede conducir a un aumento de la mortalidad y de las complicaciones derivadas de esta, por lo tanto, el objetivo del estudio es describir las variaciones en la mortalidad por ERC secundaria a la hipertensión arterial en Brasil entre los años 1990 a 2019. **Métodos:** Estudio epidemiológico, con enfoque cuantitativo y carácter descriptivo, que analizó datos de la herramienta *Global Burden of Disease Study* (GBD). **Resultados:** En todas las unidades de la federación, aumentó la estimación de muertes por ERC secundaria a la hipertensión arterial, con la región Sudeste presentando las estimaciones más altas. Los estados de Rio de Janeiro, Rio Grande do Sul y Paraíba lideran con las tasas de mortalidad más altas. Con respecto al sexo, en todos los años se observaron mayores tasas en los varones, sin embargo, con el paso de los años, esta diferencia se ha ido reduciendo. El grupo de edad de ≥ 70 años fue el más afectado, destacándose con las tasas de mortalidad más altas. **Conclusión:** la carga de ERC en Brasil ha aumentado en los últimos 30 años; de las regiones del país, el Sudeste registró las mayores estimaciones de muertes en todos los años registrados entre los analizados, siendo principalmente mayor entre los hombres.

Palabras-clave: Mortalidad, Enfermedad renal crónica, Hipertensión arterial, Epidemiología.

INTRODUCTION

Systemic Arterial Hypertension (SAH) is a multifactorial and complex disease, characterized as an important risk factor for the development of cardiovascular and kidney diseases.¹ Several impacts can be generated by the high global burden of hypertension: from individual impacts, evidenced by the reduction of the quality of life of hypertensive patients,² to economic and administrative impacts on society and health systems.^{3,4}

Among the diseases that can be developed due to ineffective control of SAH, one that stands out is chronic renal failure, also known as chronic kidney disease (CKD). This disease is characterized by the occurrence of kidney damage of at least three months that can cause changes and the progressive decline in renal function.⁵ CKD and SAH are important public health problems worldwide, being highly prevalent in low- and middle-income countries, and there is a direct relationship among them: CKD can be the result of uncontrolled SAH, as well as be responsible for the progression and resistance of SAH. Furthermore, the correlation between these two conditions increases the risk of cardiovascular and cerebrovascular outcomes.^{5,6}

Recent estimates have shown that the prevalence and incidence of patients undergoing dialysis treatment in Brazil has been increasing significantly. This event is

possibly related to the aging process of the population and to the demands for improvements in care and access to dialysis services. As the underlying cause, uncontrolled chronic hypertension stands out for continuing to be the main event related to the development of CKD. Additionally, the overall mortality rate due to CKD also showed an significant increase.^{7,8}

Due to the global increase in the number of patients with CKD who are developing end-stage renal disease and require kidney replacement therapy, the implementation of measures aimed at improving awareness and early diagnosis is urgent in order to establish early management and treatment, thus preventing the evolution to terminal stages.³

Studies on the global burden of diseases allow identifying and comparing changes in disease patterns worldwide, as well as understanding variations, neglected conditions, risk factors, and the possible impacts generated by the high burden of diseases in different countries, thus serving as an effective tool to assist in the formulation of health policies, in the decision-making of health professionals and researchers, and in assisting the development of prevention strategies.⁹

In this context, our study aims to describe the variations of mortality rate for CKD secondary to hypertension, in Brazil, between 1990 and 2019.

METHODS

This is an epidemiological study, with a quantitative approach and descriptive character, that analyzed data from the *Global Burden of Disease Study* (GBD), a software that stores global, national, and regional data on diseases, including prevalence, incidence, deaths, and disability-adjusted life years. The GBD is led and administered by the Institute for Health Metrics and Evaluation at the University of Washington, which enables timely, relevant, and scientifically valid evidence to improve health policies and practices.¹⁰

The information used was collected from January 3 to 8, 2022, and was obtained through the latest available version of GBD, version 2019, its online version is available on the Institute's website (<https://vizhub.healthdata.org/gbd-compare/>). The tool adopts an uncertainty interval of 95% (UI 95%) considering uncertainties arising from the following components: sample size used, adjustments to data sources for the estimation of all-cause mortality, regression model specifications for Gaussian space-time processes, model life table systems, and specifications and estimations of the specific cause model.¹¹

The data presented in this study refer to mortality from chronic kidney disease secondary to hypertension, in Brazil, from 1990 to 2019. The analysis lists the mortality rate per 100,000 inhabitants, adjusted by federative units; the comparison of mortality in Brazil in 1990 and 2019; and the proportional distribution of the number of deaths per region, according to gender and age group.

Additionally, the data were analyzed and expressed

by descriptive statistics, with absolute and relative frequency distribution. This study uses secondary data from GBD – a tool that stores health information from around the world – and is free from identification and rights of use. Thus, it was not necessary to submit the study to the Research Ethics Committee (CEP) involving human beings, as mentioned in Resolution No. 510/2016 of the National Health Council.

RESULTS

The mortality rate for CKD secondary to hypertension showed an increase over the years and in a heterogeneous manner among all units of the Brazilian federation (Figure 1). Among the States, in 1990, Paraíba led with a rate of 3.2 deaths per 100,000 inhabitants, followed by Rio de Janeiro and Minas Gerais, with 2.91 and 2.88, respectively. From 1996, Rio de Janeiro surpassed Paraíba and came to occupy first place, with the mortality rate estimated at 3.79 in the following years. The most recent data available – 2019 – shows the State of Rio de Janeiro with the highest mortality rates. In 2019, the states of Rio de Janeiro, Rio Grande do Sul, and Paraíba recorded the highest mortality rates: 7.44, 6.65, and 5.97, respectively.

Table 1 shows the comparison of the mortality rate of CKD due to hypertension in Brazil, between 1990 and 2019. For all age groups and both sexes, it is possible to observe the increase in the mortality rate in the country. In 1990, the mortality rate per 100,000 inhabitants was 2.41 deaths; whereas in 2019, the estimate was 5.38.

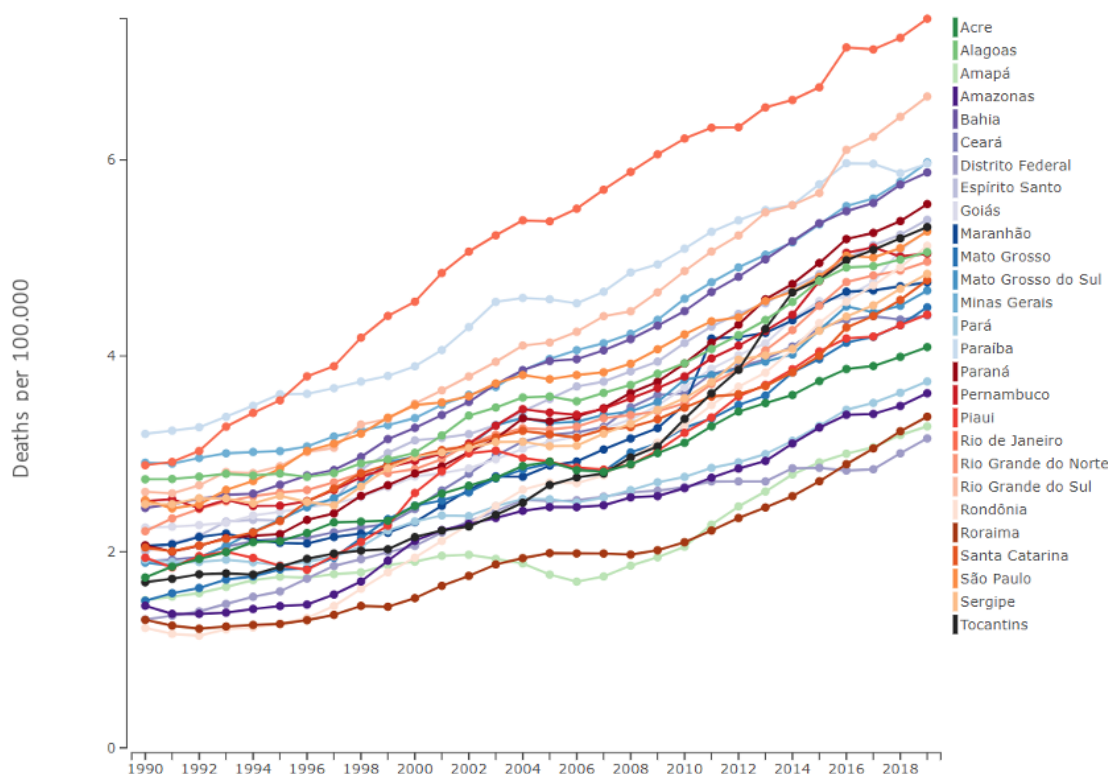


Figure 1. Mortality rate due to chronic kidney disease secondary to hypertension over time (1990-2019), in all ages and both sexes.

Table 1. Comparison of mortality due to chronic kidney disease secondary to hypertension in the 1990.

Country	MR 1990	MR 2019
Brazil	2.41	5.38

Note: MR 1990: Mortality rate per 100,000 inhabitants in 1990; MR 2019: Mortality rate per 100,000 inhabitants in 2019.

Source: Global Burden of Disease Study, 2019. Adapted by the authors

Regarding the average estimate of the number of deaths due to CKD secondary to hypertension in the studied period, we observed that in all units of the federation there was an increase in the number of deaths (Table 2). In the North region, the state of Pará had the highest values for both years: 93, in 1990, and 345, in 2019. In the Northeast, the state of Bahia had the highest number of deaths, with 296, in 1990, and 937, in 2019; followed by the state of Pernambuco: 183 and 511, in 1990 and 2019, respectively. In the Midwest region, the state of Goiás had 93 deaths, in 1990, and 363 deaths, in 2019, making it

the State with the highest number of deaths. In the South and Southeast regions, the highest numbers of deaths were observed in the states of São Paulo and Rio Grande do Sul – São Paulo with 809, in 1990, and 2,486, in 2019; and Rio Grande do Sul with 242, in 1990, and 751, in 2019. We identified an increase in the number of mortality in all regions, with the Southeast region presenting the highest percentage – 1,684 (47.24%), in 1990, and 5,313 (45.55%), in 2019 – followed by the Northeast region, with 1,020 (28.78%), in 1990, and 3,199 (27.43%), in 2019 (Table 3).

Regarding the distribution of mortality by sex, we found that mortality was higher among males for both years, with a proportional distribution of 53.2%, in 1990, and 50.6%, in 2019. Thus, we can observe that there was a reduction in the difference in the number of deaths between the sexes (Table 4).

According to the deaths distributed by age group, the highest number was observed among individuals in the age group of ≥70 years, with 2,045 and 8,123 deaths,

Table 2. Average estimate of deaths and mortality rate due to chronic kidney disease secondary to hypertension, in 1990 and 2019, according to the federative units.

Region/FU	1990	UI 95%	MR	2019	UI 95%	MR
North						
Acre	7	5 - 8	1.74	38	30 - 46	4.09
Amapá	4	3 - 4	1.51	28	22 - 33	3.28
Amazonas	30	24 - 36	1.45	153	122 - 189	3.62
Pará	93	73 - 115	1.92	345	277 - 426	3.74
Rondônia	13	10 - 17	1.22	91	73 - 111	5.12
Roraima	2	2 - 3	1.31	20	16 - 24	3.38
Tocantins	15	12 - 19	1.69	87	70 - 107	5.32
Northeast						
Alagoas	70	56- 86	2.74	185	147 - 227	5.06
Bahia	296	239 - 363	2.45	937	733 - 1178	5.87
Ceará	123	96 - 154	1.9	442	344 - 562	4.41
Maranhão	104	77 - 135	2.06	397	314 - 498	4.75
Paraíba	104	83 - 130	3.2	261	205 - 319	5.96
Pernambuco	183	149 - 222	2.52	511	413 - 623	5.04
Piauí	51	40 - 64	1.94	163	131 - 199	4.42
Rio Grande do Norte	54	43 - 66	2.21	185	144 - 232	4.96
Sergipe	37	29 - 45	2.49	116	91 - 145	4.84
Midwest						
Brasília	21	16 - 26	1.31	95	76 - 119	3.16
Goiás	93	73 - 116	2.25	363	285 - 455	5.29
Mato Grosso	30	23 - 36	1.5	162	129 - 199	4.5
Mato Grosso do Sul	34	27 - 40	1.89	132	105 - 162	4.67
Southeast						
Espírito Santo	52	42 - 63	2.01	214	169 - 263	5.39
Minas Gerais	465	373 - 560	2.91	1296	1047 - 1590	5.97
Rio de Janeiro	377	305 - 448	2.88	1315	1064 - 1593	7.44
São Paulo	809	653 - 972	2.53	2486	1945 - 2953	5.27
South						
Paraná	177	143 - 211	2.07	632	509 - 777	5.55
Rio Grande do Sul	242	196 - 288	2.61	751	601 - 919	6.65
Santa Catarina	93	74 - 111	2.04	342	269 - 423	4.77
TOTAL	3565			11664		

Note: FU: Federative Unit. UI 95%: Uncertainty Interval 95%. MR Mortality rate per 100,000 inhabitants.

Source: Global Burden of Disease Study, 2019. Adapted by the authors

Table 3. Average estimate of deaths and mortality rate due to chronic kidney disease secondary to hypertension, in 1990 and 2019, according to the federative units.

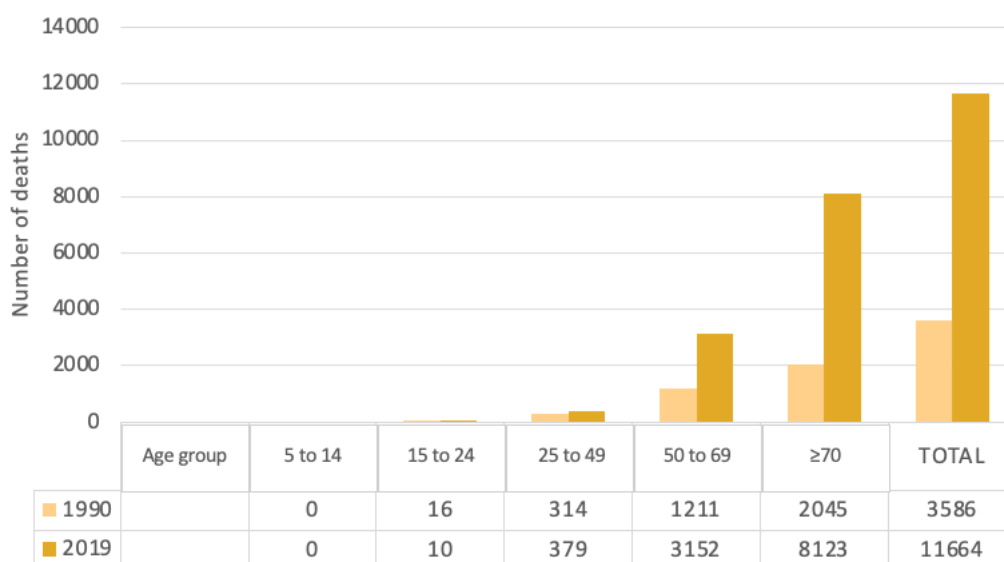
Region	1990 NOD* 1990	PD**(%)	NOD 2019	PD (%)
North	166	4.66	675	5.79
Northeast	1 026	28.78	3199	27.43
Midwest	177	4.96	753	6.46
Southeast	1684	47.24	5313	45.55
South	512	14.36	1724	14.78
Total	3565	100	11664	100

Note:*NOD: Number of deaths per region. **PD: Proportional distribution (NOD*/TOTAL)×100. Source: Global Burden of Disease Study, 2019. Adapted by the authors.

Table 4. Average estimate of deaths and mortality rate due to chronic kidney disease secondary to hypertension, in 1990 and 2019, according to the federative units.

Sex	ND (1990)	PD**(%)	ND 2019	PD (%)
Male	1897	53.2	5902	50.6
Female	1668	46.8	5762	49.4
TOTAL	3565	100	11.664	100

Note:*ND: Number of deaths. **PD: Proportional distribution (ND*/TOTAL)×100. Source: Global Burden of Disease Study, 2019. Adapted by the authors.



Graph 1. Distribution of deaths from chronic kidney disease secondary to hypertension in Brazil, according to age group.

Source: Global Burden of Disease Study, 2019. Adapted by the authors.

in 1990 and 2019, respectively. Followed by the age range of 50 to 69, with 1,211 deaths, in 1990, and 3,152, in 2019. In the range of 5 to 14, for both years, no death was identified by the disease (Graph 1).

DISCUSSION

CKD affects, approximately, 10% of the world's population and every year there has been an increase in the prevalence of CKD, both in Brazil and worldwide. The development of the disease is mainly related to diseases such as diabetes and SAH.^{12,13} Accordingly, this study showed, indirectly, that the prevalence of CKD in Brazil

has been increasing, since the mortality rate showed a significant increase in all federative units, between 1990 and 2019 (Figure 1). This increase can be explained by the high prevalence of nocturnal hypertension, a resistant and uncontrolled asymptomatic hypertension, which causes long-term hypertensive nephroangiosclerosis.¹⁴

Kidney disease, in many cases, is asymptomatic or oligosymptomatic, expressing signs only when progressing to further stages of severity, which makes early diagnosis difficult.¹⁵ A study conducted with hypertensive patients in the state of Santa Catarina pointed out that 45% of these patients surveyed already had stage 2 CKD, which shows the importance of early detection

of the disease for a proper management focused on its control.¹⁵ An important parameter used for the detection, evaluation, treatment, and prognosis of CKD is the glomerular filtration rate (GFR), since it helps to understand the number of functional nephrons.¹⁶

CKD can be defined by the presence of the following factors: sustained reduction of GFR below 60 mL/min/1.73m²; proteinuria, with presence of albumin in urine ≥ 30 mg for 24 hours; abnormalities in urinary sediment; hematuria; or a histology suggestive of injury.^{5,6}

According to the results of this research, the mortality rate and the overall number of deaths due to CKD increased in Brazil. This finding is similar to that seen in another study that revealed a growth in the number of patients of the Unified Health System (SUS) with CKD, undergoing dialysis treatment, along with high numbers of deaths from treatment abandonment.¹³ The results are also in agreement with the increase in prevalence and death from CKD in other parts of the world.¹⁷

Regarding the regions of the country, the Southeast region had the highest mortality rates due to CKD, followed by the Northeast region. A study that analyzed the situation of CKD in Brazil found that the highest prevalence of CKD was in the Southeast and Northeast region of Brazil, which can be explained by the high population density of these regions. Additionally, the high rates of death in the region can also be explained by the process of population aging, the epidemiological and demographic transition, and the increase in diseases such as SAH.^{18,19}

Mortality due to CKD secondary to SAH in males was higher than in females for all the analyzed years. Similarly, a previous study evaluating patients treated in a hemodialysis service showed that men are the most affected by CKD due to hypertension than women, as shown in another study that observed that men had higher blood pressure values, lower GFR, and higher serum creatinine levels in relation to women, suggesting a greater risk.²⁰ Older women, however, presented events contrary to those observed in younger women, a relationship that did not occur in the analysis among men. This shows that differences in gender and age should be considered.²¹⁻²³ Such differences are possibly related to the protective effects of estrogen in women and/or the deleterious effects of testosterone in association with bad life habits in men, which causes a faster decrease in GFR in the male population.²⁴

Regarding age groups, the vast majority of deaths were observed at ages above 50 years, specially in patients over 70 years of age, which corroborates other studies that showed that the highest mortality rate due to CKD was present in the age group above 60 years.²⁵ Moreover, it was observed that individuals aged 45 years are among the most prevalent population in dialysis treatment centers.^{7,8}

In this sense, aging is an important risk factor, since, in this process, events such as arteriosclerosis with concomitant progressive loss of renal function, evidenced by the reduction of GFR with advancing age, may further

compromise renal function in the presence of diseases such as SAH, which presents itself as one of the most prevalent diseases in the elderly, generating direct stress on the renal system.²⁶

In the context of the detection and prevention of CKD and SAH, primary health care stands out as an important measure, which, with programs such as *HiperDia*, can perform follow-up and request tests during consultations, in order to identify and reduce early diseases related to SAH and diabetes, which are the main risk factors for the development of CKD.²⁷

Annually, billions of money is directed to the treatment of CKD patients worldwide, which generates a direct impact on the economy and local development of countries, showing the importance of prevention strategies for the main risk factors for CKD, such as SAH, as well as a timely diagnosis.²⁸

This study has limitations, regarding not only those inherent to the *Global Burden of Disease Study* but also those of the data sources, which depend on the accuracy with which the underlying cause of death is attributed, which can be complicated when multimorbidities are present. Nonetheless, this study showed the importance of describing mortality from CKD secondary to hypertension in Brazil, and may, in the future, support not only new policies but also comparative and intervention studies that monitor the transitions in trends of prevalence, incidence, and mortality of SAH and CKD.

With this study, we observed that the burden of CKD in Brazil increased in the last 30 years along with its mortality, which increased in all regions and federative units of the country; the Southeast being the region with the highest estimates of deaths in all years analyzed. Mortality was mainly higher among males but showed a tendency toward the inversion of this reality. Regarding the age group, deaths were higher in individuals over 70 years of age.

Thus, with SAH being an important risk factor for the development of CKD, we would like to draw attention to strategies and efforts aimed at the early identification and prevention of the disease, in concomitance with the strengthening of strategies for early detection of CKD, so that adequate management and treatment is carried out in a timely manner, in order to mitigate the risk of evolution to the terminal stage of the disease.

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AUTHORS' CONTRIBUTIONS

Matheus Vinicius Barbosa da Silva and **Viviane de Araújo Gouveia** contributed to the conception, design, analysis, and writing of the article. **Matheus Vinicius Barbosa da Silva**, **Carlos Antonio de Lima Filho**, **Amanda de Oliveira Bernardino**, and **Viviane de Araújo Gouveia** contributed to the planning and design of the article and the review and final approval of the article.

All authors approved the final version of the manuscript and declare themselves responsible for all its aspects, guaranteeing their accuracy and integrity.

Use of protective face mask by the population against infection by the SARS-CoV-2: expectations and reality

Uso de máscara de proteção pela população contra infecção pelo SARS-CoV-2: expectativas e realidade

Uso de mascarilla protectora por parte de la población frente a la infección por el SARS-CoV-2: expectativas y realidad

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Corresponding Author:

Ernandes Gonçalves Dias
ernandesgdias@yahoo.com.br

Adress: Avenida José Alves Miranda, 500, Alto São João, Mato Verde, MG, Brasil

Ernandes Gonçalves Dias¹ 

Débora Rejane Santos Veloso Ribeiro² 

Vanessa Augusto Bardaquim³ 

¹ Faculdade Verde Norte (Favenorte), Mato Verde, MG, Brasil.

² Prefeitura Municipal de Monte Azul, Monte Azul, MG, Brasil.

³ Prefeitura Municipal de São Carlos, São Carlos, SP, Brasil.

Dear Editor,

Due to the Coronavirus Disease 19 (COVID-19) pandemic, society has sought for alternatives for prevention and health care. One of the most recommended strategies is physical distancing, hygiene care in general, particularly hand and environmental hygiene and the use of face masks.^{1,2} From this premise, the regular use of protective face masks is essential, as it works as a barrier to prevent infection by SARS-CoV-2 and the spread of viral particles that can be released by those infected, including asymptomatic ones.²

In April 2020, the Brazilian Ministry of Health recommended the use and released a manual with guidelines for making homemade face masks for the entire population as a strategy to deal with the spread of COVID-19 in the country, although they were aware that face masks cannot completely prevent an infection, but are capable of minimizing contamination, with the added benefits of ease of use, low cost, and reutilization.³

Specialists in the area suggested that the efficiency of fabric face masks was conditioned to the type of fabric

used in their manufacture, number of layers, adjustment to the face and care adopted during the use.⁴

In this way, the population was instructed on the time of use and the appropriate procedures for washing and reuse, so that the use would not compromise the effect desired and increase the risk of contamination of the population.⁵

Thus, in the course of the COVID-19 pandemic, the expectation was that everyone would wear face masks, either by government decree or out of awareness. However, reality shows the lack of or incorrect use of homemade face masks. The habit of not covering the nose is common, as well as leaving the chin exposed or even lowering it completely. In addition, touching the face mask improperly and removing it from the face without any care contradicts the recommendations for its use. The moment of packaging for reuse or disposal of the equipment is also very important to ensure that the care taken has not been in vain, as the external face of the mask may be contaminated after some time of use.

A study carried out from 12,588 observations reve-

aled that 45.1% of people used the mask properly, 15.5% did not use it at all and 39.5% used it inappropriately (12.9% with the nose and/or mouth exposed, 12% with the nose exposed, 7.8% touching the mask frequently and 6.8% with the mask poorly fitted to the face).⁶

However, there are still gaps in the scientific literature regarding the effectiveness of masks to reduce the transmission of COVID-19 in the community. There is experimental evidence that masks are able to retain infectious droplets and potentially reduce transmission. there are also reports of decreased transmission due to mask use, however, there is no evidence to demonstrate that such reduction occurs in a community setting.⁵

The behavior adopted by the population with regard to the use of face masks (already reported), suggests that their use has caused a false sense of protection, when in fact it is possible that they are even more susceptible to contamination by SARS-CoV-2, because the effect is the same as not being under any protection.

This perception is reinforced by the literature, which states that the routine use of protective face masks against COVID-19 generates a false sense of security, in a way that can increase viral transmission due to inadequate handling and hygiene of the mask.⁵⁻⁷

Therefore, reality imposes that collective measures to prevent infections and diseases, now and in the future, require to be accompanied by intense campaigns of permanent health education for the communication of risk and to increase the adherence to the recommendations, as well as actions to engage the community and develop in the citizens a sense of responsibility for their own health and the community. In this way, health authorities need to be concerned with educating people about the need and scope of prevention measures more than making them mandatory, so that adherence occurs out of awareness of the importance and need rather than by an imposition.

Descriptors: *Coronavirus Infections. COVID-19. Protective Equipment. Personal Protection. Health Risk Behaviors.*

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AUTHORS' CONTRIBUTION

Ernandes Gonçalves Dias, Débora Rejane Santos Veloso Ribeiro e Vanessa Augusto Bardaquim contributed to the conception, design, analysis and writing of the article.

The authors have approved the final version to be published and are responsible for all aspects of the work, including ensuring its accuracy and integrity.

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