Faculdade de Medicina de Olinda

YEAR 3
EDITION 06

FMO
Anais da Faculdade de Medicina de Olinda
*Annals of Olinda Medical School*

# HEALTH SOCIAL RESPONSIBILITY

NUMBER 6 N 1 2020
www.fmo.edu.br

ISSN: 2595-1734

# ANNALS OF OLINDA MEDICAL SCHOOL

*ANAIS DA FACULDADE DE MEDICINA DE OLINDA*

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# SUMMARY

## Revision articles



## Point of view

### Book review



## Instructions for authors

# Letter to the editor

Carta ao editor

**Dr. Inácio de Barros Melo Neto**[1]

The year 2020 ended as the most challenging for humanity and the most unique for science. Millions of lives were lost due to the COVID-19 pandemic worldwide, and the number reached hundreds of thousands in Brazil. Even the most optimistic people were unable to predict how the epidemic that began in 2019 would unfold; moreover, we thought it would take a long time to reach the West due to its geographical distance, in terms of deaths, economic impact, and extreme levels of exhaustion of healthcare teams globally.

The world agonized, and the economy stopped, but humanity reacted. Medicine was challenged to face an unprecedented and open debate. Due to the disclosure of information via social media with instant opinions, the debate surrounding the COVID-19 pandemic has reached the most distant corners.

With humanity put to the test, the reaction came through science, with the rapid and unprecedented development in the history of vaccines, which were created in traditional and innovative ways, using genetic engineering that was never previously used. It was already announced that besides the challenge of producing an effective vaccine, its access to everyone worldwide needed to be ensured.

In this sense, the Faculdade de Medicina de Olinda, through its students and teachers, deepened its knowledge and practices and disclosed them to society using various initiatives. Some of them are recorded in this issue of the Annals of the Faculdade de Medicina de Olinda, with the work learned during the COVID-19 pandemic period.

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# Letter from the editor

Carta do editor

**Prof. Paulo Sávio Angeiras de Goes - PhD**

We have reached No. 6 of the Annals of the Faculdade de Medicina de Olinda, which highlights, at the institutional level, the needed approach to the challenges of the COVID-19 pandemic proposed by our teachers and students. Despite the challenge of maintaining academic activities, the strengthening of research and extension actions conducted by students and professors throughout 2020 is recorded in these pages of our journal.

Besides the original articles, we included records of the fight against COVID-19 in the social space and several reviews made within the scope of knowledge about the disease. This issue is a historic number for the AFMO, which ends its fourth year not only on an upward curve but also consolidates itself as an important channel for publishing studies conducted in the field of medicine.

The review of the journal's rules must be highlighted, which was updated to further assist authors who submit their manuscripts and raise the standard that AFMO has implemented for its readers. This review contributes to increasing your credibility among your readership, composed by the academic and clinical community not only in the medical field but in the entire health sphere.

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# EPIDEMIOLOGICAL PANORAMA OF HUMAN RABIES IN NORTHEASTERN REGION OF BRAZIL FROM 2013 TO 2017

*Panorama epidemiológico da raiva humana na região Nordeste do Brasil de 2013 a 2017*

**Short title: Rabies in Northeastern from 2013 to 2017**

**Camila Joyce Alves da Silva, Natanael da Silva Bezerra Júnior, Lucas Soares Bezerra, Isvânia Maria Serafim da Silva Lopes**

## ABSTRACT

**Objectives:** This study aimed to report the number of cases of human rabies from 2013 to 2017 in the Northeast region of Brazil and identify factors correlated to the distribution in the epidemiological panorama. **Methodology:** The data were collected from the Notifiable Diseases Information System. **Results:** The Northeast region accounted for over half of confirmed cases of human rabies in Brazil (67%). Most cases affected men (89%) aged from 20 to 39 years (56%), residents of urban areas (56%), and originated from aggressions by unvaccinated animals (80%). **Conclusion:** The incidence of human rabies in the Northeast region seems to be related to low development rates, lack of information regarding infection pathways and disease severity, inadequate post-exposure prophylaxis, and discontinuation of treatment. In addition, underreporting of suspected cases impairs the actions of local health authorities.

**Keywords:** Brazil; Epidemiology; Rabies.

## RESUMO

**Objetivos:** Relatar o número de casos da raiva na região Nordeste no período de 2013 a 2017 e identificar aspectos correlacionados ao panorama epidemiológico de sua distribuição. **Metodologia:** Os dados foram coletados do Sistema de Informação de Agravos de Notificação. **Resultados:** A região Nordeste foi responsável por mais da metade dos casos confirmados de raiva humana no Brasil (67%). A maioria desses casos acometeu homens (89%), entre 20 e 39 anos (56%), residentes de áreas urbanas (56%), e originadas de agressões por animais não vacinados (80%). **Conclusão:** A incidência de raiva humana no Nordeste parece estar atrelada a baixos índices de desenvolvimento humano, falta de informações a respeito das vias de infecção e da gravidade da doença, profilaxia de pós-exposição inadequada e interrupção do tratamento. Além disso, a possível subnotificação de casos suspeitos dificulta as ações das autoridades de saúde locais.

**Palavras-chave:** Brasil; Epidemiologia; Raiva.

## INTRODUCTION

Rabies is an anthropozoonotic viral disease transmitted to humans from saliva and secretions of infected animals through scratches, contact with mucous membranes, open wounds, and especially by bites. The fatality rate is near 100%, becoming a serious public health issue worldwide[1-3].

In Brazil, rabies is an endemic disease with a highly heterogeneous epidemiological distribution associated with socioeconomic and cultural conditions, with cases registered in Southeast and Central-West regions and predominantly in the North and Northeast regions[4, 5].

Rabies is a neurotropic virus of the genus *Lyssavirus*. The virus replication in neurons causes a characteristic clinical presentation of acute encephalomyelitis, with the formation of cytoplasmic inclusion bodies named Negri bodies[1, 2]. Clinical signs are highly variable and depend on the affected region since the virus replicates in any region of the nervous system. The incubation period is 12 days on average, with animal death five days after the onset of clinical signs. As a public health issue or event, rabies has mandatory notification by physicians and healthcare professionals, according to ordinance nº. 204/2016 of the Brazilian Ministry

of Health[6, 7].

Only mammals are transmitters and develop the disease of rabies virus, becoming vectors. Rabies presents three transmission cycles: urban, wild, and rural. Domestic (mainly dogs and cats) or wild (bats, monkeys, and foxes) animals are the major viral reservoirs and transmit the disease to humans and large animals, such as cattle and horses[1, 8, 9]. In Brazil, bats are key agents in the wild cycle, while in municipalities, dogs are the main cause of infections[5, 10].

Human rabies is a lethal disease since treatment is nonspecific. However, unlike other zoonoses, human rabies could be fully prevented with the control of animal reservoirs. In Brazil, over 2,500,000 doses of Fuenzalida & Palacios-type and cell culture vaccines are administered annually for post-exposure treatment and immunization of professionals at-risk[8, 11, 12].

The control of domestic animals comprehends the reduction of directly involved reservoirs and vaccination of susceptible individuals, especially in endemic areas, following recommendations of the World Health Organization (WHO). Thus, rabies associated with wildlife and non-hematophagous bats cannot be prevented[13, 14]. An extensive vaccination program reduced the incidence of rabies transmitted by dogs in Brazil; however, rabies transmitted by bats (particularly *Desmodus rotundus*) remains endemic, mainly in the Northern and Northeastern regions[15-17].

In 1973, the National Program for Human Rabies Prophylaxis was created in Brazil to reduce the number of human cases by controlling zoonosis in domestic animals and performing post-exposure prophylaxis in individuals bitten and in contact with infected animals. A main objective was to keep 70% of dogs vaccinated, the minimum percentage to interrupt the epidemiological chain of disease transmission[12, 18].

Rabies in Brazil demand improvement of surveillance measures for the urban cycle, implementation in the wild and aerial cycles, and reinforcement of the importance of human prophylaxis to prevent new cases[12, 14]. Changes in habitat and food availability for bats, disordered occupation by human action, and low adherence to vaccination are considered risk factors. The creation of programs focused on rabies control is associated with different animal species infected by the virus and is responsible for its dissemination. In most Brazilian cities, 80% of cases in the urban cycle are sustained by dogs[6].

The United Against Rabies Initiative of 2018, a collaboration between the WHO, the Food and Agriculture Organization of the United Nations, the World Animal Health Organization, and the Global Alliance for Rabies Control, launched a global strategic plan to cease human deaths from canine rabies until 2030[19,20]. This study aimed to report the number of cases of human rabies from 2013 to 2017 in the Northeast region of Brazil and identify factors correlated to the distribution in the epidemiological panorama

## METHODS

The present study consisted of a descriptive analysis of epidemiological data on human rabies in the Northeast region of Brazil from 2013 to 2017. The database from the Notifiable Diseases Information System (SINAN) [21], managed by the Brazilian Ministry of Health, was accessed using the search terms “region/state of notification” and “year of first symptoms”. The search terms “age group”, “sex”, and “residence area” were also included in the analysis for individuals with a positive diagnosis.

The “Brazil in Synthesis” database, managed by the Brazilian Institute of Geography and Statistics[22], was accessed to evaluate the relevance of the socioeconomic factors according to the Human Development Index (HDI) of regions affected by human rabies. Populational and territorial information was retrieved from the 2010 Census.

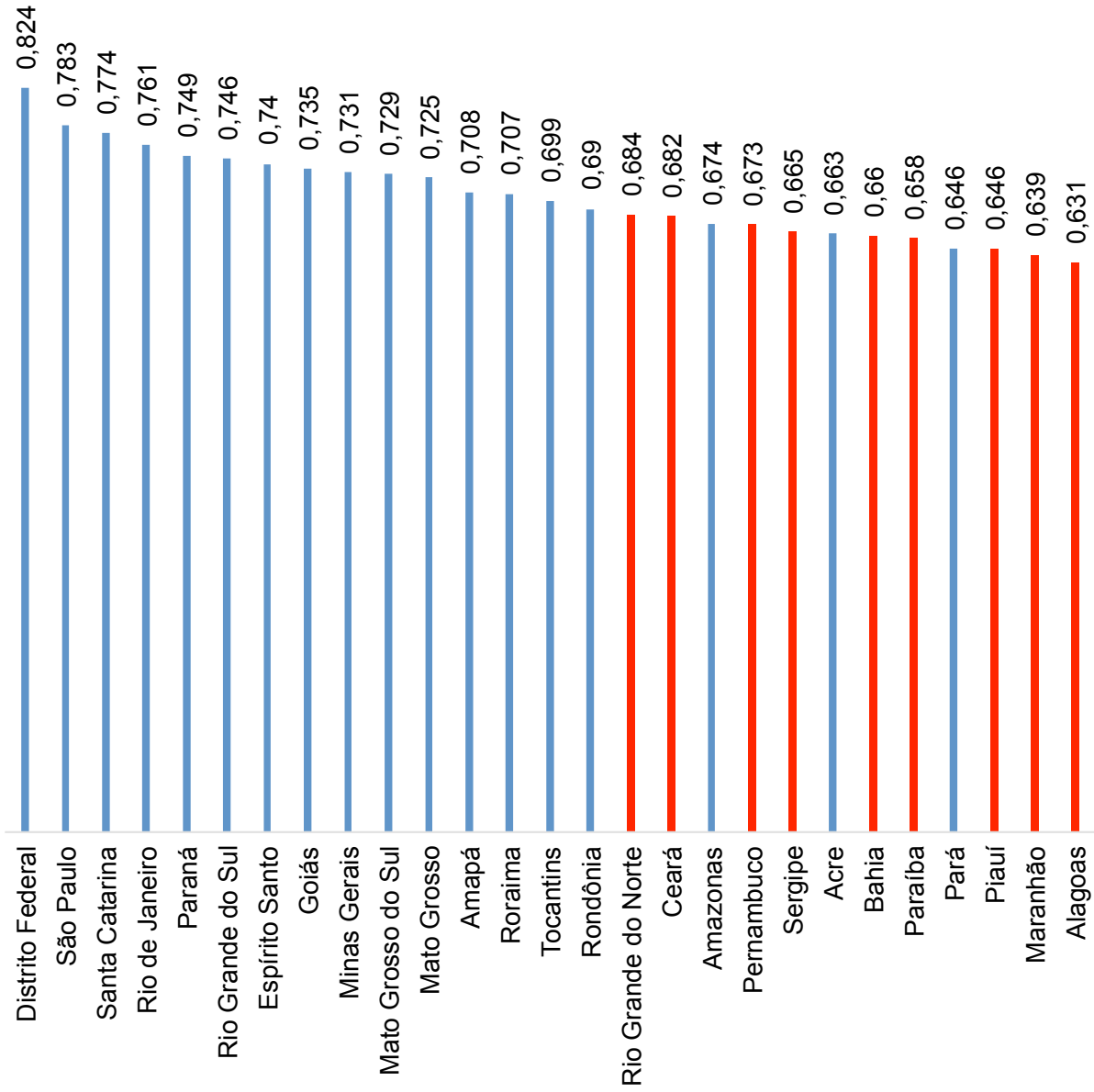
## RESULTS

According to the WHO[20], rabies is responsible for 59,000 human deaths per year worldwide, especially in Asia (35,172) and Africa (21,476), affecting mainly low-income populations from rural areas.

The Northeast region of Brazil has over half the confirmed cases of human rabies, in-

cluding nine states: Alagoas, Bahia, Ceará, Maranhão, Paraíba, Pernambuco, Piauí, Rio Grande do Norte, and Sergipe. This region is the third-largest, with a territory of 1,302,679 km$^2$, and has the second-largest population, with 49,963,590 inhabitants. However, Northeastern states occupy the lowest ranks according to HDI (Figure 1), which assesses the progress of a population considering family income, education, and health[23].

**Figure 1.** Brazilian ranking of Human Development Index (HDI) by state.




The HDI values are presented on top of the bars corresponding to each state. The bars representing the Northeastern states are highlighted in red). Source: IBGE, 2010.

According to the SINAN database (2018)[21], between January 2013 and December 2017, 15 cases were confirmed in Brazil, with nine (60%) in the Northeast, five (33%) in the North, and one case (7%) in the Central-West region; the South and Southeast regions did not report human cases. According to these results, the Northeast region comprised over half the confirmed cases. The distribution of cases is shown in Table 1.

**Table 1.** Distribution of confirmed cases of human rabies in the Northeast region of Brazil.

| State | Year of the last case before 2013 | Number of cases | | | | | Total |
|---|---|---|---|---|---|---|---|
| | | 2013 | 2014 | 2015 | 2016 | 2017 | |
| Maranhão | 2012 | 3 | - | - | - | - | 3 |
| Piauí | 2001 | 2 | - | - | - | - | 2 |
| Ceará | 2012 | - | - | - | 1 | - | 1 |
| Rio Grande do Norte | 2010 | - | - | 1 | - | - | 1 |
| Pernambuco | 2008 | - | - | - | - | 1 | 1 |
| Bahia | 1999 | - | - | - | - | 1 | 1 |
| **Total** | - | 5 | - | 1 | 1 | 2 | 9 |

Source: SINAN (2018).

The Maranhão state was the most affected, with three cases in 2013, without further cases until 2017. Of the three cases, two were registered in the municipality of Humberto de Campos and one in the capital, São Luís. Before the analyzed period, two cases were confirmed at São Luís in 2012.

The Piauí state registered two cases in 2013, with one case at the municipality of Parnaíba and the other at the capital, Teresina. Until 2013, the last confirmed cases occurred 12 years before at the municipalities of Anísio de Abreu and Bonfim do Piauí, one case each.

The Ceará state had one confirmed case of human rabies at the capital, Fortaleza, in 2016[21]. Before this, the last case was in 2012 in the municipality of Barbalha.

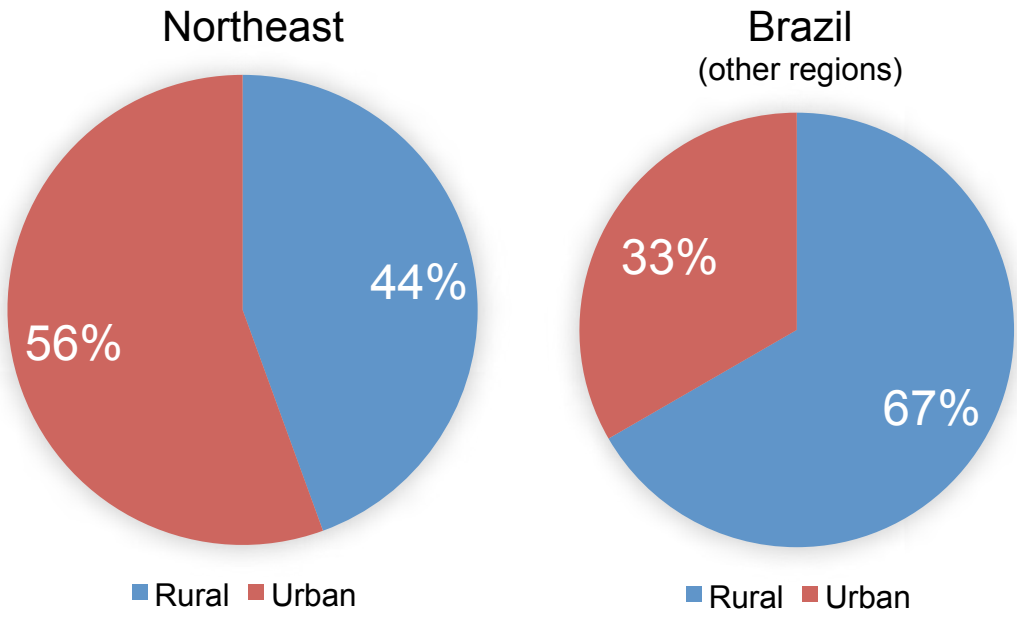
The Rio Grande do Norte state registered one case in 2015 at the capital, Natal. Before this episode, the last confirmed case was at the municipality of Frutuoso Gomes in 2010.

The Pernambuco state had one case of human rabies registered in 2017 at the capital, Recife that progressed to death. Before 2017, the last case was also registered at Recife in 2008.

Similarly, the Bahia state reported one confirmed case in 2017 in the municipality of Paramirim. Until 2017, the last three registered cases were at the municipalities of Dias d'Ávila, Itororó, and the capital, Salvador, in 1999.

Concerning the area of residence of infected individuals, from the nine cases in the Northeast region, four (44%) were registered in rural and five (56%) were in urban areas. A different proportion compared with other cases in Brazil; from six cases, four (66%) were registered in rural areas, and two (33%) were in urban areas (Figure 2).

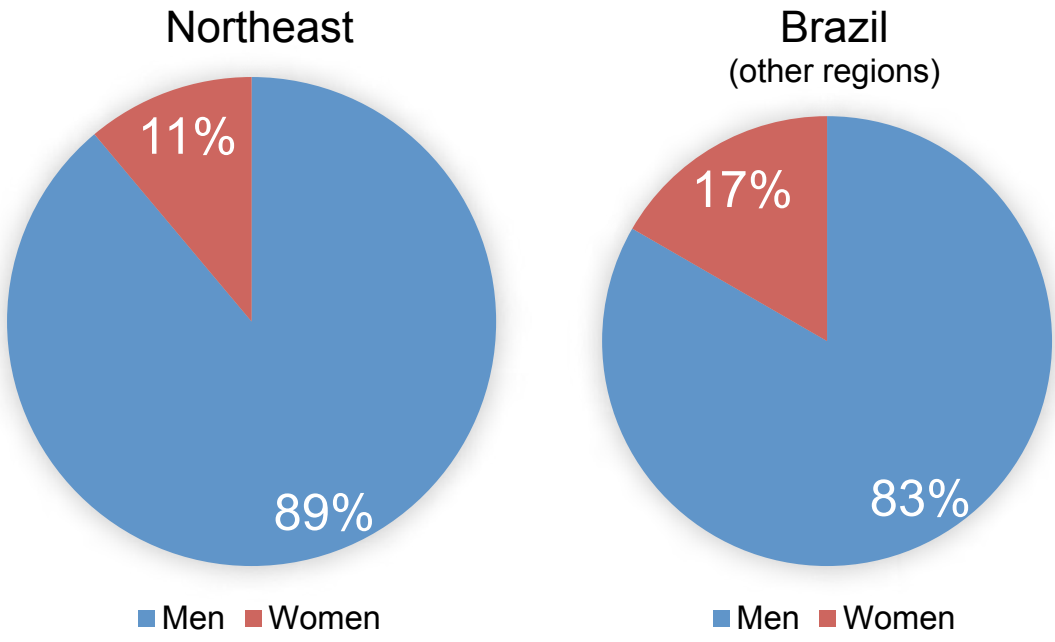
**Figure 2.** Percentages of confirmed cases of human rabies by area of residence in the Northeast and other regions of Brazil (North, Central-West, South, and Southeast).




Source: SINAN (2018).

Regarding sex, the Northeast region showed a significant disparity between men and women. Only one woman (11%) was diagnosed with human rabies in the municipality of Recife in 2017; the other eight cases (89%) were registered in men. This predominance in men was similar in other regions, with five (83%) cases in men and one case (17%) in a woman (Figure 3).

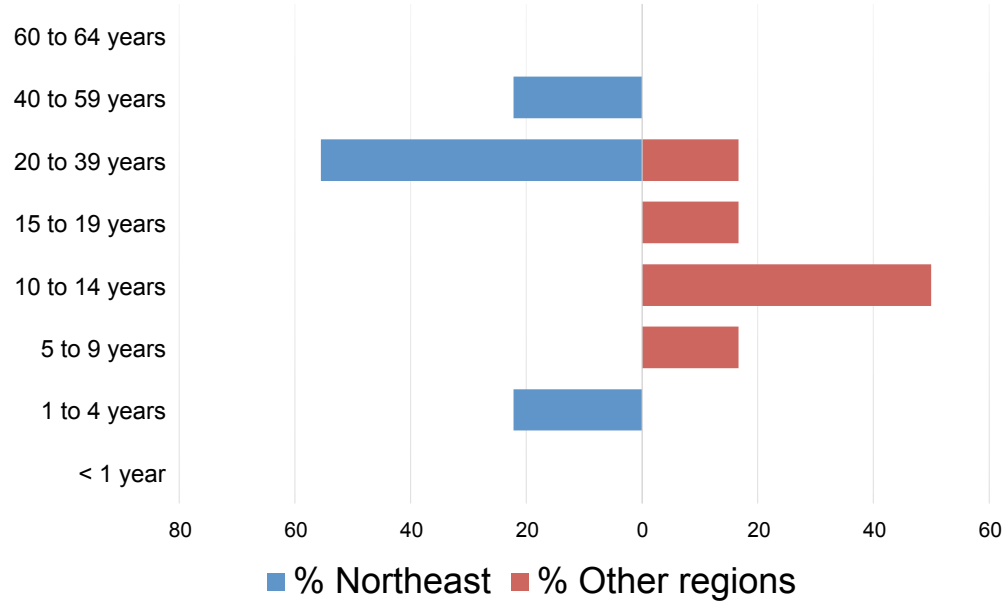
**Figure 3.** Percentage of confirmed cases of human rabies by sex in the Northeast and other regions of Brazil (North, Central-West, South, and Southeast).




Source: SINAN (2018).

The age group analysis showed that most cases in the Northeast region were in individuals aged 20 to 39 years, with five confirmed cases (56%). Additionally, two cases (22%) were registered in individuals aged from one to four years and two (22%) in the age group of 40 to 59 years. The other Brazilian regions had most cases between 10 and 14 years, encompassing three cases in the Amazon region and one confirmed case in the age groups of 5 to 9 years, 15 to 19 years, and 20 to 39 years (Figure 4).

**Figure 4.** Percentages of confirmed cases of human rabies by age group in the Northeast and other regions of Brazil (North, Central-West, South, and Southeast).




Source: SINAN (2018).

Last, from nine confirmed cases in the Northeast region, five acquired rabies from unvaccinated animals, and the other four did not have this information. This pattern was reflected in other regions of Brazil; from six cases of human rabies, four were acquired from unvaccinated animals, and the other two cases the immunization status was unknown.

## DISCUSSION

A significant reduction in cases of human rabies was observed in Brazil over the past decades, considering absolute numbers. In 1990, 70 cases were registered, which was 467% higher than the total cases between 2013 and 2017[18]. This reduction reflects public health policies such as the implementation of vaccination programs for dogs and cats and administration of post-exposure prophylaxis24.

Otherwise, on the expressive reduction in notification numbers, this study observed that between 2013 and 2017, considering the confirmed cases, 60% occurred in the Northeast region, a percentage close to the 50% observed from 1996 to 2001[25]. This result highlights that human rabies remains a challenge for the health authorities of this region.

A control measure against rabies dissemination is the immunization of dogs and cats identified as potential domestic transmitters. Thus, some states in the Northeast region emphasized that vaccination campaigns met the goals for national immunization. Indeed, from 1982 to 2003, a reduction of 91% of human rabies cases transmitted by dogs in Latin America was observed due to efforts between countries[24]. Changes in the epidemiological transmission pattern of rabies in Latin America were evidenced in 2004 since hematophagous bats (Desmodus rotundus) were the primary transmitters to humans[24]. In this context, the present cycle of human rabies in the Northeast region of Brazil may be maintained by synanthropic animals, such as hematophagous and insectivorous bats, whose presence was

documented in several municipalities of this region[26].

Regarding the residence area of infected individuals, the number of cases in rural areas of the Northeast equaled other Brazilian regions (four cases). This finding corroborates previous studies, which documented human rabies in rural areas in the Maranhão state16. Additionally, researchers alerted on the circulation of rabies virus in the semiarid region of Paraíba, involving cattle, horses, goats, and foxes[27-29]. A study documented the presence of the same rabies virus lineage in livestock and in hematophagous and insectivorous bats in Maranhão e Paraíba states, suggesting bat attacks on herds and subsequent infection[30].

Moreover, the higher number of cases of human rabies in urban areas in the Northeast region (five cases) compared with other Brazilian regions (two cases) is noteworthy. This finding might arise from bats in large urban centers, where they adapt to urban conditions, find refuge and food, and increase their contact with humans and domestic animals, raising the chances of infection[26]. However, a greater population of bats does not reflect an increase in rabies dissemination, which is conditioned to virus circulation in the environment[31].

The socioeconomic development could be correlated to the higher prevalence of human rabies in the Northeast regions. Studies demonstrated an increased transmission of rabies in regions of greater social vulnerability, which is associate with lower levels of education on preventive measures and, consequently, more susceptibility to infections[25, 31]. Additionally, underreporting may occur since the population does not recognize licks and scratches as infection pathways, and inadequate conduct on post-exposure prophylaxis of healthcare professionals is also an issue[32, 33].

Most diagnoses in the Northeast region were in adults aged from 20 to 39 years (five cases), corroborating a previous study in the Pernambuco countryside[34]. The exposition during work and discontinuation of post-exposure prophylaxis may explain the higher prevalence in adults[35, 36]. This proportion differs from other Brazilian regions that showed a higher prevalence in children aged from 10 to 14 years (three cases), resembling indicators of the 1990s, probably linked to greater exposure to animals during plays[18].

Regarding sex, the data indicate a high incidence of rabies in men in all Brazilian regions. This finding differs from the literature, which showed homogeneous post-exposure prophylaxis percentages between men and women[36]. However, a higher number of interruptions in post-exposure prophylaxis in men may explain this result[36].

In the Northeast and other regions of Brazil, most transmissions were from unvaccinated animals (55% and 67%, respectively), and in the remaining cases, the immunization status was unknown (45% and 33%, respectively). This demonstrates that, despite high vaccination coverage, animals lack immunization, and patients report insufficient information to healthcare systems regarding the immunization status of domestic animals responsible for aggressions, which would facilitate the implementation of post-exposure prophylaxis[37].

## CONCLUSION

The higher prevalence of human rabies in the Northeast region comprehends a multifactorial approach. Lower levels of socioeconomic development, lack of information on rabies transmission and disease lethality, underreporting of suspected cases, inadequate prophylactic care by healthcare professionals, and discontinuation of voluntary immunization schedules may be responsible for the numbers observed.

Moreover, since most cases in the Northeast region were from rural areas, it is crucial to emphasize to these populations the measures to handle animals that are economically valuable and discourage the breeding of wildlife, which may be infected and responsible for transmission to humans.

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ORIGINAL ARTICLE

# UNDERDIAGNOSIS: A LIMITATION TO THE FOLLOW-UP OF PATIENTS WITH COPD ASSOCIATED WITH ALPHA-1 ANTITRYPSIN DEFICIENCY

*Subdiagnóstico: uma limitação ao seguimento dos pacientes com DPOC associados à deficiência de alfa-1*

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## ABSTRACT

Alpha-1 antitrypsin deficiency (AATD) is a rare autosomal codominant hereditary disorder that primarily affects the lungs and liver. The only Brazilian study reporting the prevalence of AATD estimates that 2.8% of patients with chronic obstructive pulmonary disease (COPD) have this disorder. Thus, this case report aimed to demonstrate the need to investigate AATD in patients with COPD, as the underdiagnosis and subsequent lack of prevention and treatment lead to unfavorable prognostic outcomes.

**Keywords:** Alpha-1-Antitrypsine; COPD; Genotyping techniques; Neutrophil elastace; Spirometry

## RESUMO

A deficiência de alfa-1 antitripsina (DAAT) é um distúrbio hereditário codominante autossômico raro que afeta principalmente os pulmões e o fígado1. O único estudo brasileiro que relata a prevalência de DAAT estima que 2,8% dos pacientes com doença pulmonar obstrutiva crônica (DPOC) apresentam essa deficiência. O objetivo deste relato de caso consiste em demonstrar a necessidade de investigar a DAAT em pacientes portadores de DPOC, evitando o subdiagnóstico e a não realização de medidas preventivas e de tratamento específico, que quando não implementados leva a desfechos prognósticos desfavoráveis.

**Palavras-chave:** DPOC; Alfa-1-antitripsina; Técnicas de genotipagem, Espirometria; Elastase neutrofílica

## INTRODUCTION

Alpha-1 antitrypsin deficiency (AATD) is a rare hereditary autosomal codominant disorder that affects mainly the lungs and the liver.[1] Alpha-1 antitrypsin (AAT) is part of the superfamily of serine protease inhibitors, and it is encoded by the SERPINA1 gene, located on the long arm of chromosome 14 (14q32.1). The main function of AAT is to inhibit several enzymes, including trypsin, neutrophil elastase, and protease-3.[1,2]

The AAT deficiency causes pulmonary emphysema due to an imbalance in the protease-antiprotease relationship, as reduced serum levels of this protein (or dysfunctional molecules) are insufficient to protect the lungs from the elastolytic action of neutrophil elastase and other damages.[2,4] Thus, the lung lesion would be a consequence of increased damage factors (smoking, infections, and occupational factors), or reduced protection (i.e., serum AAT levels) (or both), accelerating lung damage.[3]

In Brazil, the underdiagnosis of AATD is mainly due to poor medical knowledge about the condition, the diagnostic tests required, and their limited availability. The diagnosis is confirmed when the test detects reduced AAT serum levels, followed by the identification of specific alleles via phenotyping or genotyping (or both). The normal serum AAT levels range between 120 and 220 mg/dL; levels below 50 mg/dL characterize severe deficiency.[2,3,4]

AAT is an acute phase reactant, similar to C-reactive protein (CRP) and amyloid A, and its plasma levels increase in response to inflammation or infection. A normal CRP level confirms that AAT levels are elevated. However, AAT levels could be falsely increased when CRP is elevated, requiring a new test during clinical stability.[5]

Protein phenotyping uses isoelectric focusing electrophoresis to identify the most common AAT variants (S, Z, and M). Although this test is the gold standard for detecting AATD variants, it requires expertise in interpretation and has limitations. When the diagnosis is inconclusive (null, rare, or very rare variants), genotyping is performed.[5]

Genotyping uses CRP to identify the most common AATD alleles, mainly S and Z. Gene sequencing may be needed when null or deficient variants besides S and Z are suspected to be present. Fast genotyping methods can be used to detect the most common alleles (PiS and PiZ); however, misdiagnosis may occur since these tests do not include rare or null alleles. The molecular analysis by direct SERPINA1 gene sequencing may be used to identify rare alleles and null variants and characterize novel mutations.[5]

One of the tests available in Brazil is the A1AT genotyping, which simultaneously analyzes the 14 most prevalent AATD mutations using DNA extracted from buccal swabs or blood collected on filter paper.[5] Nearly 80% of patients are identified via investigation of respiratory symptoms, whereas only 3% of diagnoses are attributed to liver disease.[3]

Given that AAT gene mutations are found in about 1.0% to 3.0% of patients with COPD, this case report presents several clinical and imaging aspects of a patient with a long-standing, early-onset COPD diagnosis who had never been screened for AATD.[1]

This case report aimed to highlight the need to investigate AATD in patients with COPD, preventing underdiagnosis and ensuring proper prevention and treatment to avoid poor prognostic outcomes.

## CASE REPORT

Male patient, 63 years old, with a medical history of systemic arterial hypertension, mild obstructive sleep apnea syndrome, and significant exertional dyspnea. He was diagnosed with COPD 30 years ago, was a former smoker with an 80-pack-year history, and was abstinent for 10 years. The patient was referred on 12/03/2019 to the Emergency Department of the State Public Servants' Hospital.

In the emergency, the dyspnea of the patient worsened, and he presented a productive cough with increased yellow or green sputum . On physical examination, the patient was dyspneic (2+/4+), with $SpO_2$: 89% to 90% on room air; HR: 116 bpm; BP: 190 X 110 mmHg; and temperature: 37.5ºC. Pulmonary auscultation revealed universally reduced vesicular breath sounds, rhonchi at the bases, and discrete diffuse expiratory wheezing.

His medical history included four previous hospitalizations for COPD exacerbations in the past year; the most recent occurred two months prior. He was under the care of a pulmonologist and was using inhaled Salmeterol (50 mcg) and Fluticasone (500 mcg) twice a day, along with Tiotropium 2.5 mcg (two inhalations once daily). He also used a short-acting bronchodilator as needed, reporting daily use of four to six doses.

A chest tomography (CT) from October 2019 showed centrilobular and paraseptal emphysematous changes in the upper lung, along with multiple emphysematous alterations in the lung bases, architectural distortion in the lower lobes, middle lobe, and lingula, as well as cicatricial atelectasis and bronchiectasis in the lower lobes.

A spirometry performed in September 2019 showed FVC: 1.32 L (34%), $FEV_1$: 0.65 L (21%), and $FEV_1$/FVC: 49.2 (62%) pre-bronchodilator; and FVC: 1.39 L (36%), $FEV_1$: 0.77 L (25%), and $FEV_1$/FVC: 55.4 (69%) post-bronchodilator. These results characterized a severe obstructive ventilatory disorder with reduced FVC and no significant bronchodilator response.

With a presumptive diagnosis of COPD exacerbation, the patient was admitted and started on broad-spectrum antibiotic therapy with piperacillin-tazobactam due to the history of previous hospitalizations, alongside other standard measures for an infectious COPD exacerbation. Given the CT findings and the severity of the disease progression, a genotyping test for AATD and serum AAT measurement were performed using an oral swab sample.

During hospitalization, the patient improved in dyspnea, returning to his baseline level with moderate exertion (mMRC: 3). He also reduced cough and sputum production. He was discharged in good general condition, without signs of infection or complaints, maintaining preserved physiological habits and adequate oral food intake.

At a follow-up appointment on 12/26/2019, serum AAT levels and genotypic testing results confirmed the diagnosis of AATD with the PI*-ZZ genotype. After reassessment, a weekly intravenous AAT replacement therapy was added to his treatment regimen. Over one year of follow-up, the patient remained clinically stable, with no further exacerbations.

This case report was approved by the research ethics committee of the Faculdade de Medicina de Olinda (CAAE: 50086721.3.0000.8033).

## COMMENTS

ATTD is considered the most important genetic cause of respiratory disorders in adults, particularly COPD with an emphysematous phenotype. Several mutations on the SERPINA1 gene cause it and have several clinical implications.[1]

The rate of lung function decrease among smokers with COPD associated with AATD is significantly higher than in COPD cases with normal AAT levels. This results from the combined effects of cigarette smoke, reduced antiproteinase activity of the AAT, and persistent pulmonary inflammatory infiltration.[6]

The global database of individuals affected by AATD is limited, and for a long time in Europe, researchers considered that this disease affected only white individuals and their descendants. However, recent studies demonstrated that this disease is present among many populations, including Black Africans, Arabs, and Jews in the Middle East, white individuals in Australia/New Zealand, Europe, and North America, as well as Central, East, and Southeast Asians.[7]

Epidemiological studies estimate that AATD affects about 1 in 2,000 to 5,000 live births. Moreover, the only Brazilian study reporting AATD prevalence estimated that 2.8% of patients with COPD present this disorder. The Platino study revealed that 15.8% of patients aged 40 years or older had COPD in the city of São Paulo, suggesting a significant number of AATD underdiagnosis.[3]

The criteria for suspecting and investigating AATD include any patient diagnosed with COPD, especially those with early-onset emphysema (before age 45); bronchiectasis of unknown cause; adults with asthma exhibiting a progressive obstructive pattern of evidence of emphysema; consanguineous relatives of AATD patients; individuals with family members with chronic cough and dyspnea; and individuals with chronic liver disease of unknown origin, lacking an alpha-1 glycoprotein peak, or with panniculitis or vasculitis of unknown cause.[1,8,9]

The patient analyzed in this case had been diagnosed with COPD at age 33, presenting severe symptoms and a chest CT scan showing widespread emphysema, especially in the basal lung. Nevertheless, he was never screened for AATD, leading to a missed diagnosis for 30 years.

Since COPD alone and COPD with AATD affect the body differently, they lead to different disease progressions, outcomes, and treatment responses. Therefore, early diagnosis of AATD changes the natural history of the disease, improving patient outcomes by allowing preventive measures and identifying those who may benefit from specific therapy. [5]

Thus, upon early identification of COPD-AATD, standard therapy (i.e., smoking cessation, vaccination, bronchodilator use, pulmonary rehabilitation, and long-term home oxygen therapy when indicated) should be implemented. Additionally, specific therapy involving AAT replacement via the administration of purified, concentrated human plasma-derived AAT may be needed in selected patient groups.[9] Therefore, a thorough investigation of clinical history and AATD as a potential diagnosis is essential.[6]

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ORIGINAL ARTICLE

# DEMYELINATING DISEASE IN A PATIENT WITH PRIMARY SJÖGREN'S SYNDROME: A CASE REPORT

*DOENÇA DESMIELINIZANTE EM PACIENTE COM SÍNDROME DE SJÖGREN PRIMÁRIA: RELATO DE CASO*

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## ABSTRACT

This report describes the case of a patient with primary Sjögren's Syndrome (SS) associated with demyelinating neurological involvement. Data were obtained using medical records, patient interviews, photographic documentation of imaging exams, and a brief literature review. Neurological manifestations of SS are rare and present a wide clinical spectrum, including demyelinating features that resemble multiple sclerosis and neuromyelitis optica. Treatment of the neurological manifestations is often based on an extrapolation of other autoimmune diseases, including rheumatoid arthritis and systemic lupus erythematosus. Management may require oral or intravenous immunosuppressive therapy, depending on symptom severity.

**Keywords:** Neurological Manifestations; Neuromyelitis Optica; Sjogren Syndrome

## RESUMO

Relatamos o caso de uma paciente portadora de Síndrome de Sjögren Primária com manifestações neurológicas de característica desmielinizante. As informações foram obtidas por meio de revisão do prontuário, entrevista com a paciente, registro fotográfico dos exames de imagem e, por fim, breve revisão da literatura. As manifestações neurológicas da Síndrome de Sjögren são raras e apresentam um amplo espectro clínico, incluindo manifestações desmielinizantes que simulam a esclerose múltipla, além de neuromielite óptica. O tratamento dos sintomas neurológicos se baseia numa extrapolação de outras doenças autoimunes, como a artrite reumatoide e lúpus eritematoso sistêmico, e preconiza o uso de imunossupressores orais e venosos, a depender da gravidade dos sintomas.

**Palavras-chave:** Manifestações neurológicas; Neuromielite óptica; Síndrome de Sjögren

## INTRODUCTION

Sjögren's syndrome (SS) is an autoimmune epithelitis, defined by lymphocytic infiltration of exocrine glands and the presence of specific antibodies. This condition mainly affects women aged between 40 and 55 years. Besides the ocular and oral dryness, typical symptoms of SS, patients may present extraglandular manifestations involving the kidneys, lungs, hematologic system, skin, and nervous system.[1] Neurological involvement may include sensory and motor impairment, along with central nervous system (CNS) manifestations, such as myelitis, cerebral vasculitis, seizures, organic brain syndrome, and neuromyelitis optica spectrum disorders (NMOSD).[2,3]

The etiopathogenesis of SS involves an autoimmune reaction potentially initiated by environmental factors (e.g., viral infections) in genetically susceptible patients. This reaction may cause dysregulation and hyperactivity of B lymphocytes, leading to lymphocytic infiltration of the exocrine glands, and possible degeneration, necrosis, and atrophy of the acinar glands. Clinically, this glandular damage impairs lacrimal and salivary function, which contributes to xerophthalmia and xerostomia, present in about 95% of patients.[4]

Diagnostic criteria for SS have not yet been established. However, the diagnosis should be considered in patients with sicca symptoms combined with at least one of the following conditions: (a) positive serologic testing for anti-SS-A or anti-SS-B antibodies; (b) a positive salivary gland biopsy demonstrating lymphocytic inflam-

matory infiltration in exocrine glands; or (c) systemic extraglandular manifestations.[5]

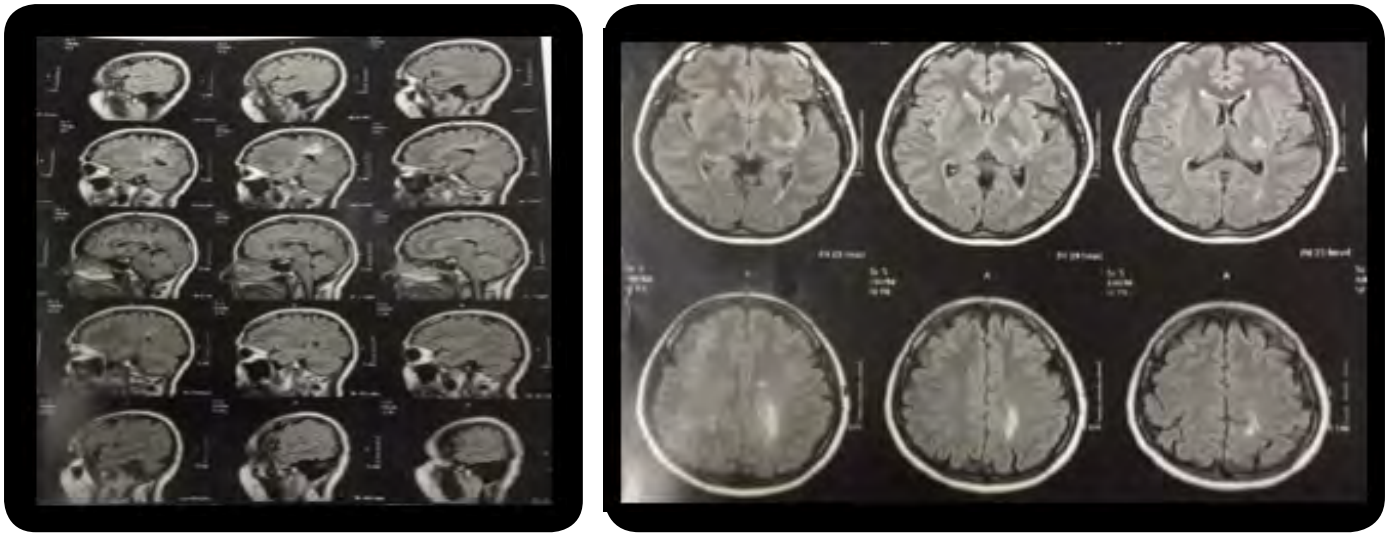
The following recommendations of the European League Against Rheumatism (EULAR) should be considered when managing patients with systemic disease: (a) adapt the management of the systemic disease according to organ-specific severity using the EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI) (EULAR Grade C, Level 4); (b) use the minimum effective dose and shortest duration needed of glucocorticoids to control active systemic disease (EULAR Grade C, Level 4); (c) consider the use of synthetic immunosuppressive agents as corticosteroid-sparing options (EULAR Grade C, Level 4); (d) consider B-cell-targeted therapies for patients with severe refractory systemic disease, with no evidence supporting one treatment over the other (EULAR Grade B, Level 1b); (e) after sequential (or combined) use of glucocorticoids, immunosuppressants, and biologic medications, an organ-specific systemic intervention may be considered (EULAR Grade D, Level 5).[7]

This report described a clinical case involving primary SS presenting with demyelinating neurological manifestations and provides a review of concepts related to this topic.

## CASE REPORT

E.B.S., a 49-year-old female, initially reported headache, paresthesia, and eventual limb weakness. Magnetic resonance imaging (MRI) revealed hyperintensities in the corticospinal tract at the level of the cerebral peduncles, periventricular and subcortical white matter, and the corpus callosum. A cavitated lesion was also observed, extending from the subependymal region to the subcortical area of the inferior parietal lobe, suggesting multiple sclerosis. Then, the patient developed blurred vision and ocular hyperemia, predominantly in the right eye. A diagnosis of optic neuritis was established and treated with intravenous methylprednisolone pulse therapy. Despite treatment, the condition progressed to visual loss in the right eye and right-sided hemiparesis, requiring plasmapheresis and cyclophosphamide therapy.

Due to the persistent motor and visual impairments, rituximab therapy was initiated, followed by maintenance therapy with azathioprine. The motor function improved; however, visual loss in the affected eye persisted. Follow-up MRI revealed hyperintense lesions in the white matter of both cerebral hemispheres and signal alterations in the spinal cord at the C6 and C7 levels (Figures 1, 2, and 3). Oligoclonal band testing in cerebrospinal fluid (CSF) and serum anti-aquaporin-4 antibody (AQP4-IgG) yielded negative results. Given the presence of ocular and oral dryness symptoms, an investigation for SS was conducted. The results included positive anti-Ro/SSA antibodies, an antinuclear antibody (ANA) titer of 1:320 with a fine speckled nuclear pattern (FSNP), and a salivary gland biopsy consistent with chronic lymphocytic sialoadenitis, confirming the diagnosis.



**Figures 1 and 2.** Brain MRI in fluid-attenuated inversion recovery (FLAIR) sequence showing hyperintense signal in the corticospinal tract at the level of the cerebral peduncles, periventricular white matter, and corpus callosum. A cavitated lesion extends from the subependymal region to the subcortical area of the inferior parietal lobe.

**Figure 3.** T2-weighted brain MRI: Signal alteration in the spinal cord at the C6 and C7 levels.

Ethical aspects of this study followed the recommendations of resolution No. 510, dated April 7, 2016, of the Brazilian national health council, which establishes specific ethical guidelines for the human and social sciences. The study was approved by the research ethics committee of the Faculdade de Medicina de Olinda (no. 46365721.9.0000.8033).

## DISCUSSION

This report described the case of a 49-year-old female who presented an acute neuro-ophthalmologic syndrome. Neuroimaging findings suggested a demyelinating disease within the multiple sclerosis spectrum. During diagnostic evaluation, the presence of xerostomia and xerophthalmia raised the suspicion of SS. The diagnosis was confirmed by positive anti-Ro/SSA antibodies, an ANA titer of 1:320 FSNP, and a salivary gland biopsy revealing chronic lymphocytic sialadenitis.

Neurological manifestations occur in about 20% of patients with primary SS, with CNS involvement occurring in about 3.6%.2 In 80% of patients with neurological symptoms, CNS involvement may precede the primary SS diagnosis by up to two years. These clinical presentations may range from asymptomatic MRI findings to symptomatic lesions, including meningitis, seizures, cerebral vasculitis, or myelitis.[8]

NMOSD is a group of CNS disorders characterized by severe immune-mediated inflammation, demyelination, and axonal damage. These disorders may occur as primary conditions or associated with autoimmune rheumatic diseases (e.g., SS and systemic lupus erythematosus), with or without the presence of AQP4-IgG. These antibodies target aquaporin channels, disrupting the regulation of intra and extracellular water balance. This process strongly affects the optic nerves and the spinal cord.5,9 Besides the optic nerve and spinal cord, the central medulla, diencephalon, hypothalamus (areas with high aquaporin-4 expression), and subcortical white matter may also be affected in up to 85% of cases throughout the disease. Pathogenic mechanisms include immune complex-mediated vasculitis and antiphospholipid antibodies associated with stroke, migraine, seizures, and transverse myelitis.5 Previous studies support the hypothesis that anti-Ro/SSA antibodies bind to endothelial cells and contribute to the inflammatory process.

Wingerchuk *et al.* (2015) established the International Panel for NMO Diagnosis (IPND) to revise the diagnostic criteria and support clinical decision-making. The new nomenclature distinguishes NMOSD based on the presence (or absence) of AQP4-IgG while also considering the exclusion of alternative diagnoses. When AQP4-IgG is positive, diagnostic criteria include clinical or MRI findings involving the optic nerve, spinal cord, area postrema, brainstem, diencephalon, or cerebrum. When AQP4-IgG is negative or testing is unavailable, diagnosis requires strict clinical criteria combined with characteristic neuroimaging findings.[3]

The combination of clinical presentation, CSF analysis with oligoclonal band testing, MRI findings, AQP4-IgG testing, and therapeutic response are key factors in distinguishing NMOSD from multiple sclerosis, its primary differential diagnosis.[3,7] Additional differential diagnoses include inflammatory, infectious, genetic, metabolic, and neoplastic disorders.[3,4]

The epidemiology of neurological manifestations of SS has not been fully elucidated due to selection biases in patient inclusion criteria. However, CNS manifestations are rare and may precede sicca symptoms. Among these

manifestations, NMOSD may occur as a manifestation of SS or as a coexisting condition. The main differential diagnosis includes multiple sclerosis, CSF, MRI, and antibody findings. Treatment encompasses corticosteroid therapy, plasmapheresis, immunoglobulin, cyclophosphamide, rituximab, azathioprine, and mycophenolate mofetil. In patients with demyelinating diseases who exhibit an inadequate therapeutic response, the diagnostic investigation must be expanded, as they may represent an initial manifestation of an autoimmune rheumatic disease, with an emphasis on SS.[2,3,8]

## CONCLUSION

Although neurological manifestations are rare, their presence may indicate an underlying autoimmune condition, including SS. In the presented case, atypical CNS involvement, particularly NMOSD preceding sicca symptoms, raised the suspicion of an autoimmune disease. The detection of specific autoantibodies and salivary gland biopsy subsequently confirmed the diagnosis of primary SS.

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# SURGICAL RESECTION OF A DOPAMINE AGONIST-RESISTANT MACROPROLACTINOMA: A CASE REPORT

*Ressecção Cirúrgica de Macroprolactinoma Resistente a Agonista Dopaminérgico: Estudo de Caso*

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## ABSTRACT

Prolactin-secreting pituitary tumors account for approximately 50% of all pituitary adenomas, of which 10% are macroadenomas. A 63-year-old woman reported a decrease in visual acuity for about six months and sporadic headaches. The patient was evaluated by endocrinology due to hyperprolactinemia and underwent magnetic resonance imaging (MRI) that identified an expansive formation of pituitary tissue, suggesting a pituitary adenoma. The treatment was performed with oral cabergoline without control of hyperprolactinemia. A control MRI showed tumor enlargement, leading to surgical resection of the pituitary tumor via a transnasal transsphenoidal approach. Macroprolactinomas are prolactin-secreting tumors with clinical first-line treatment using dopaminergic agonists. Surgical resection is rare and is reserved for cases refractory to medical therapy.

**Keywords:** Adenoma; Neurosurgery pituitary diseases; Pituitary gland; Pituitary neoplasms.

## RESUMO

Os tumores hipofisários secretores de prolactina compreendem cerca de 50% de todos os adenomas hipofisários, dentre os quais apenas 10% são macroadenomas. Paciente do sexo feminino, 63 anos, referia diminuição da acuidade visual havia cerca de 06 meses e cefaleia esporádica. Foi avaliada pela endocrinologia devido à hiperprolactinemia, tendo sido submetida a exame de imagem que detectou a presença de formação expansiva ocupando tecido hipofisário, sugestivo de adenoma hipofisário. Foi então tratada com cabergolina oral, sem controle da hiperprolactinemia. A ressonância magnética de controle, feita havia seis meses, revelou aumento nas dimensões do adenoma, e a paciente foi submetida a tratamento cirúrgico de ressecção do tumor hipofisário por via transnasal-transfenoidal. Os macroprolactinomas são tumores secretores de prolactina, cujo tratamento de primeira escolha é clínico, com agonistas dopaminérgicos. O tratamento de ressecção cirúrgica é raro e indicado para os casos que não respondem ao tratamento clínico.

**Palavras-chave:** Hipófise; Adenoma; Doenças da hipófise; Neoplasias hipofisárias; Neurocirurgia.

## INTRODUCTION

Pituitary adenomas are common intracranial tumors. Although mostly benign, they cause clinical symptoms due to the overproduction or deficiency of hormones and tumor mass[1].

Pituitary adenomas are classified as microadenomas (< 10 mm), macroadenomas (≥ 10 mm), and giant adenomas (≥ 40 mm)[2,3]. Approximately two-thirds of these tumors release an excess of hormones[4].

Prolactin-secreting pituitary tumors, or prolactinomas, are more frequent in women aged 20 to 50 years and comprise 50% of all pituitary adenomas. However, only 10% of prolactinomas are macroadenomas[4].

Clinical treatment is the first-line approach for hyperprolactinemia, including tumors, with a success rate of up to 90% and tumor reduction of 60%. Surgery is reserved for cases refractory to medical therapy[5].

This study aimed to present a case report on the surgical resection of a dopamine agonist-resistant macroprolactinoma.

## CASE REPORT

This ethics committee for research involving human beings of the Olinda School of Medicine (FMO) approved this case report under the number 4646864.

A 63-year-old woman reported an undefined decrease in visual acuity and difficulty in reading and watching television that started six months ago. In addition, the patient reported sporadic headaches.

An endocrinologist evaluated the patient two years earlier for hyperprolactinemia. Brain magnetic resonance imaging (MRI) showed an expansive formation on the pituitary tissue, suggesting a pituitary adenoma. The patient was treated with oral cabergoline without hyperprolactinemia control.

After 18 months of the diagnosis, a control MRI showed growth of the pituitary adenoma. The expansive formation measured 2.1 x 2.0 x 1.6 cm, occupying almost all pituitary tissue and extended into the suprasellar cistern, causing cranial displacement of the optic chiasm. A slight lateral bulging was evidenced, shifting the internal carotid arteries near the origin of the middle cerebral arteries without vascular involvement. Additionally, a lowering of the sellar floor was observed without signs of erosion or bone destruction. The diagnosis was of a pituitary lesion suggestive of pituitary macroadenoma (Figure 1).

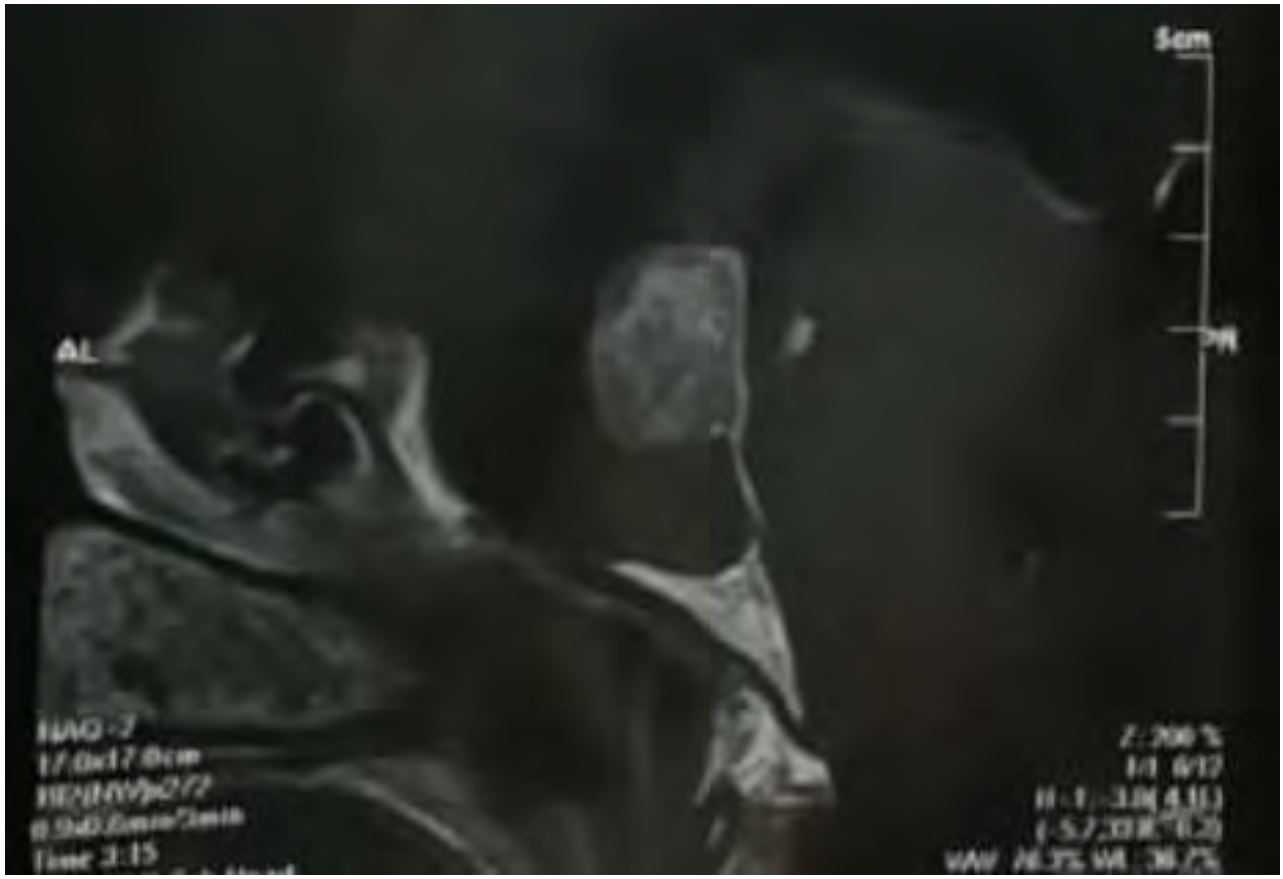


**Figure 1.** MRI of the sella turcica with contrast, sagittal section, demonstrating expansive formation measuring approximately 2.1 x 2.0 x 1.6 cm, suggestive of macroadenoma.

The patient underwent a visual campimetry exam, which showed bilateral heteronymous hemianopsia. A neurologic exam confirmed the visual field alteration, characterized by the bitemporal heteronymous hemianopsia, evidenced in the visual campimetry. Other noteworthy alterations were not observed.

The patient underwent endoscopy-guided transnasal transsphenoidal surgery for pituitary tumor resection, with no surgical complications. In the early postoperative period, hemianopsia regressed, and prolactin levels normalized. Postoperative MRI did not show evidence of the tumor, with preserved pituitary parenchyma and postsurgical scar changes (Figure 2).

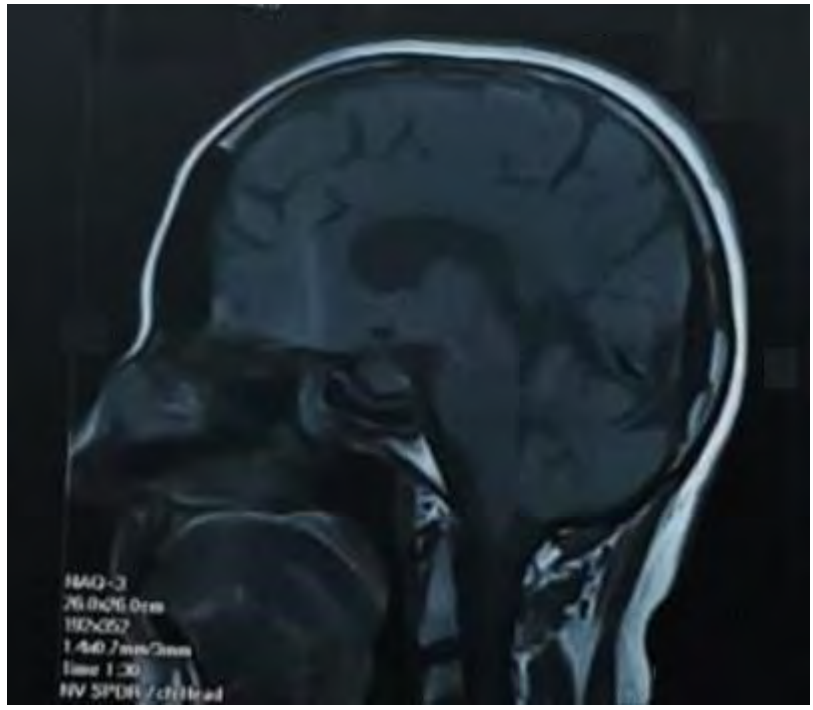

**Figure 2.** Brain MRI in a sagittal section, showing pituitary parenchyma preserved and postsurgical scar changes.

## DISCUSSION

High prolactin levels inhibit the hypothalamic-pituitary axis, resulting in libido loss, infertility, and osteoporosis in both sexes; oligomenorrhea, amenorrhea, and galactorrhea in women; and erectile dysfunction in men[6-8].

Prolactinomas are among the most common causes of hyperprolactinemia, typically increasing plasma prolactin levels beyond 50 µg/mL. Therefore, a brain and sella turcica assessment should be conducted via imaging exams in a suspected prolactinoma or with increased levels of prolactin[5].

More than 90% of the prolactinomas are microadenomas[9]. The MRI exam determines the presence and size of a tumor. However, when the tumor is not observed, hyperprolactinemia is classified as idiopathic. Additionally, a non-secreting macroadenoma may elevate prolactin levels due to its secretion inhibition, compressing the pituitary stalk or the hypothalamus. A prolactin level superior to 200 µg/L is generally related to prolactinoma production rather than pituitary stalk compression[10]. In the presence of a large tumor (> 3 cm), the extremely increased prolactin levels (> 10000 µg/L) rarely saturate assay antibodies, leading to false low or normal values ("hook effect"). Prolactin levels should be reassessed using a 1:100 dilution to avoid misinterpretation[7,8].

The treatment aims to restore normal gonadal function and fertility and reduce tumor size in patients with macroadenomas[7, 8]. Patients with mild eugonadal symptoms (e.g., women with mild galactorrhea and regular menstruation) and normal or with microadenomas in MRI might follow with observation, monitoring prolactin levels every 6 to 12 months.

When prolactinemia increases or symptoms develop due to hyperprolactinemia, a follow-up MRI should be performed to assess tumor size and initiate treatment. Only 5% to 10% of the microprolactinomas grow throughout 10 years[6]. Women with oligomenorrhea or amenorrhea who do not wish to conceive may use oral contraceptives or estrogen-progestin therapies as treatment options[7, 8].

The clinical treatment for prolactinomas is performed with dopamine agonists that activate dopamine receptors in the tumor. Considering its high efficacy and tolerability, cabergoline is more effective than bromocriptine in normalizing prolactin levels and reducing tumor size, with lower adverse effects[6-8]. However, 15% to 20% of patients, especially those with macroadenomas, may require larger doses

than conventional to ensure control[11,12].

Although a three- to six-fold increased risk of cardiac valve abnormalities was observed in patients with Parkinson's disease who received high doses of cabergoline for more than six months[13], this adverse effect was not demonstrated in patients with prolactinomas treated with conventional doses14. Since the threshold for risk of valve abnormalities is unknown, annual echocardiograms are recommended for patients exceeding the weekly dose of two milligrams[15]. Additionally, dopamine agonists may induce compulsive behaviors (e.g., excessive gaming, hypersexuality) in approximately 5% of patients, and they should be warned of this adverse effect[4].

Transsphenoidal surgery is a therapeutic option and may achieve prolactin normalization in 65% to 85% of microadenoma and in 30% to 40% of macroadenoma cases, with a recurrence rate of 20% in 10 years[6]. Radiotherapy is reserved for rare cases (< 5%) of hyperprolactinemia and uncontrolled tumor growth despite dopamine agonists or surgery[7, 8]. In aggressive prolactinomas and pituitary carcinomas, the alkylating agent temozolomide has been used with limited success[15].

## CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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ORIGINAL ARTICLE

# PRIMARY HEALTH CARE IN THE FIGHT AGAINST COVID-19: AN EXPERIENCE REPORT

*ATENÇÃO PRIMÁRIA À SAÚDE NO ENFRENTAMENTO AO COVID-19: RELATO DE EXPERIÊNCIA*

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## ABSTRACT

The COVID-19 pandemic has been causing thousands of cases worldwide, and it is considered one of the greatest global health problems of the century, challenging managers to establish measures to contain its impacts in the several scenarios affected. The problematization methodology based on the Maguerez Arch was used to identify the problem, the hypothesis of the solution, and the application to reality. According to the World Health Organization, until May 2021, around 16 million cases were confirmed in Brazil; of these, 472,000 cases were registered in the state of Pernambuco. These numbers show the seriousness of the COVID-19 pandemic and indicate that emergency measures must be taken to contain the virus spread. Primary health care should be considered an important support tool in emergency situations to contain the pandemic using special strategies.

**Keywords:** Covid-19; primary health care; basic health unit.

## RESUMO

A pandemia de COVID-19, responsável por milhares de casos que assolaram o mundo e que continua causando vítimas dia após dia, caracteriza-se como um dos maiores problemas sanitários em proporção global do século. Essa circunstância desafia os gestores a estabelecerem medidas para contenção de seus impactos nos diversos cenários acometidos por ela. Utilizou-se a metodologia da problematização, baseado no Arco de Maguerez para identificação do problema até a hipótese de solução e aplicação à realidade. Segundo a Organização Mundial de Saúde, até maio de 2021, aproximandamente 16 milhões de casos foram confirmados no Brasil e, desses, 472 mil foram registrados no estado de Pernambuco. Esses números evidenciam a gravidade da pandemia e indicam a necessidade de que sejam tomadas medidas emergenciais, a fim de refrear a disseminação do vírus. A Atenção Primária à Saúde deve ser considerada uma importante ferramenta de suporte diante de situações emergenciais e para a contenção da pandemia utilizando estratégias especiais.

**Palavras-chave:** Covid-19; Atenção primária à saúde; Unidade básica de saúde

## INTRODUCTION

The coronavirus disease (COVID-19) pandemic, which has been ravaging the world since November 2019, has created a serious public health crisis due to its high transmissibility and mortality. Considered one of the greatest global health problems of the century, the thousands of cases of COVID-19 continue to challenge managers in the economic, social, and health spheres, requiring measures to contain it and minimize the social impact[1-2].

From the start of the pandemic until May 2021, according to the World Health Organization (WHO), more than 168 million cases had already been recorded[3]. Of these, about 16 million had been confirmed in Brazil[4], with 472,000 in the state of Pernambuco[5]. These data prove the seriousness of the pandemic and indicate that emergency measures must be taken to prevent the virus from spread.

Brazil has an extensive Primary Health Care (PHC) network, which is the first level of healthcare guided by the principles of equity, universality, and comprehensiveness proposed

by the Unified Health System (SUS). PHC is composed of a set of health actions[6] that encompass activities ranging from promotion and prevention to disease control and treatment, palliative care, and rehabilitation. It aims to act in a sustainable, responsible, effective, and efficient way to provide intersectorial and comprehensive care for the main causes of health problems and risks and improve the well-being of individuals and the community[7].

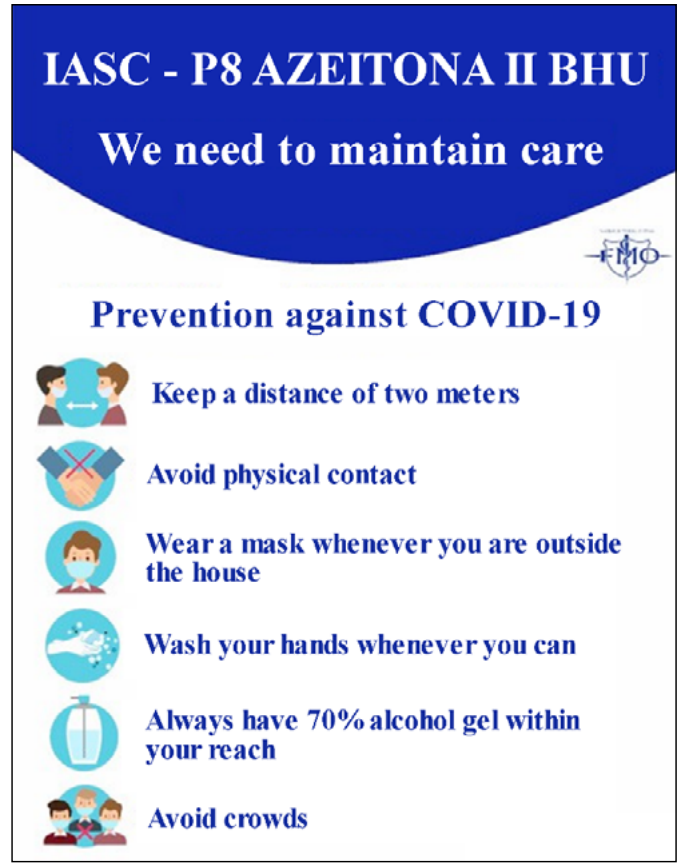
This report described an experience of the PHC in the fight against COVID-19, adopting viable and cost-effective methods that can be implemented in basic health units (BHU) to raise awareness and guide the population.

## EXPERIENCE REPORT

The problematization methodology based on the Arc of Charles Maguerez was used to recognize the content to be performed in this study, which establishes five stages: 1) Observation of reality and definition of the problem; 2) Key points; 3) Theorizing; 4) Hypotheses for a solution; and 5) Application to reality[8]. This methodology allows the revisitation of reality, identifying failures in some areas, and planning and intervening using strategies to mitigate the problem.

Given the activities in professional practice and the declaration of the pandemic by the WHO, immediate low-cost solutions and measures were sought within the PHC to prevent the spread of COVID-19. These measures aimed to raise awareness among the population, reduce the infection rate, and avoid overcrowding in BHUs, which could also reduce the overload of services from the medium and high complexities of public and private health systems. As a result, broad-spectrum and efficient actions were crucial to reach a greater number of citizens and reduce the spread of the virus.

Medical students working at the Azeitona II BHU, which provides comprehensive health care services, conducted the action by providing information and guidance on the correct use of masks; encouragement to maintain actions to protect against COVID-19 by distancing themselves, avoiding physical contact and crowds; and instructions to wash their hands whenever possible, or to use alcohol gel (70%) when accessible. All this guidance was given verbally and using banners and booklets, which were available at the BHU (Figures 1 and 2).



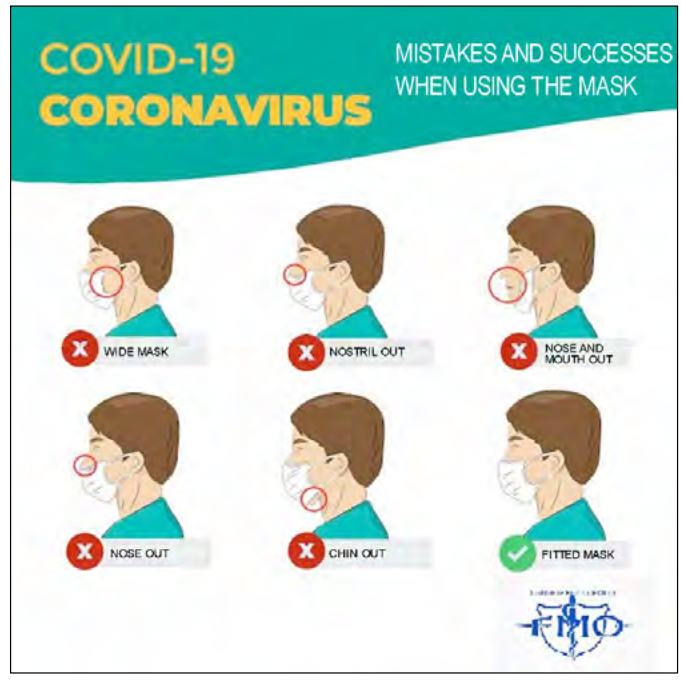




**Figure 1.** Banner displayed at the project. Source: Personal archive.
**Figure 2.** Booklets made available as part of the project. Source: Personal archive.

Since the action was performed on a day with spontaneous demand, it did not reach many individuals from the community, resulting in a reduced disclosure of educational measures. Besides the short period available for the theoretical and practical activities at the BHU, another challenge faced was the resistance of the community health agents; they did not use the proposed material to instruct the community. The collaboration of the agents would have helped disseminate the guidelines and could possibly improve the adherence of individuals to educational measures.

## COMMENTS

PHC should be considered an important support tool in emergencies to contain the pandemic using special strategies[9]. At this level of healthcare, safe and quality care, data-based planning, restructuring of services, allocation of funds, and new strategies are essential to reach as many citizens as possible.

Proposals at the PHC in the midst of the pandemic include, among many measures, the reorganization and restructuring of BHUs; the opening of new beds and adequate space to receive suspected cases; funding directed to personal protective equipment for professionals; training for healthcare professionals, including community health workers; large-scale diagnostic tests; structures for conducting complementary tests; stocks of medicines; information and guidance campaigns for citizens; and tele-service[10].

Considering the observations and actions conducted at the BHU Azeitona II, the important role that PHC plays in combating the COVID-19 pandemic is reinforced, evidencing its positive impact in the PHC on community health[11].

Therefore, the experience was important for better understanding and deepening knowledge for the group that proposed it, considering the perception of the needs of a community and the possible impact of educational actions implemented by the BHU, but also for the population that benefited from these educational measures.

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# ASSESSMENT OF GLOMERULAR FILTRATION RATE AS AN INDICATOR OF LOSS OF RENAL FUNCTION IN PATIENTS WITH HYPERTENSION AND DIABETES

*AVALIAÇÃO DA TAXA DE FILTRAÇÃO GLOMERULAR COMO INDICADORA DA PERDA DE FUNÇÃO RENAL EM PACIENTES COM HIPERTENSÃO E DIABETESS*

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## ABSTRACT

**Introduction:** The glomerular filtration rate (GFR) assesses kidney function and the extent of a chronic dysfunction. The GFR changes over the years, allows early recognition of dysfunctions, and determines its severity. Thus, the determination of GFR supports clinical decisions, such as prognosis, treatment, and possible complications. **Objectives:** This study aimed to assess the GFR in patients with type 2 diabetes mellitus and systemic arterial hypertension to determine their cardiovascular and nephrological risk due to the pattern of loss of renal function. **Methods:** Patients selected were aged ≥ 45 years and from the clinical school Dr. Carlos Brandt, at the Faculdade de Medicina de Olinda. The GFR was determined using the CKD-EPI equation, recommended by the National Kidney Foundation of the USA.

**Keywords:** Diabetes mellitus; Glomerular filtration rate; Systemic arterial hypertension,

## RESUMO

**Introdução:** A determinação da taxa de filtração glomerular é uma maneira de avaliar a função renal, que pode estabelecer a extensão de disfunção renal crônica. É uma determinação que se modifica ao longo dos anos, pois permite reconhecer disfunções ainda em fase precoce determinando o grau de severidade da disfunção, e assim auxilia na tomada de decisão clínica, podendo influenciar o tratamento, estabelecendo o prognóstico e antecipando complicações futuras. **Objetivos:** O intuito desse trabalho foi avaliar a taxa de filtração glomerular em pacientes da clínica escola Dr. Carlos Brandt da Faculdade de Medicina de Olinda portadores de diabetes mellitus e hipertensos com idades igual ou superior a quarenta e cinco anos pela equação CKD-EPI, atualmente recomendada pela Fundação Nacional de Rins dos EUA, com o objetivo de avaliar os riscos cardiovasculares e nefrológicos em decorrência do padrão de perda da função renal.

**Palavras-chave:** Diabetes mellitus; Hipertensão arterial sistêmica; Taxa de filtração glomerular

## INTRODUCTION

The glomerular filtration rate (GFR) is used to assess kidney function and the extent of chronic kidney disease (CKD). The determination of GFR changes over the years, allows early recognition of dysfunctions, and determines its severity. Thus, aids clinical decision-making, influences treatment, and establishes a prognosis and possible complications.[1]

The Kidney Disease (KDIGO) recommends the CKD-EPI equation from 2021 to estimate GFR (ml/min/1.73 $m^2$). Healthy individuals show a GRF ≥ 90, which is considered normal. Values between 60 and 89 without kidney damage are considered normal, particularly in older individuals and children. These values are associated with kidney damage (e.g., proteinuria) for three or more months, suggesting an initial kidney disease. A GFR < 60 for three or more months already indicates CKD.[1]

CKD is defined by its cause and abnormalities of function or morphology persisting for

more than three months, with implications for health. In addition, CKD is characterized as an estimated GFR (eGRF) < 60 mL/min or alterations in the urine test, especially albuminuria (30 mg/ 24h or albuminuria and creatinuria ratio of 30 mg/g), or renal morphology (GR: I; NE: C).[2] The classification and prognosis of CKD is based on eGFR and albuminuria values. Systemic arterial hypertension (SAH) is a cause and consequence of CKD and progressively increases together with the decline in kidney function, affecting 90% of patients in stage five (GR: I; NE: A).[3,4]

The classification or staging of CKD allows stratification of the progression risk and complications. The KDIGO guidelines from 2012 state that when patients are diagnosed with the described criteria, staging should follow the cause of the disease, eGFR (in six categories or G stages), and albuminuria (three categories or A stages).[5]

In clinical practice, the qualitative assessment of the excretory capacity of the kidney uses the plasmatic concentration of creatinine.[6] A simpler method compared with the endogenous creatinine clearance test with 24-hour urine collection, which is more accurate but with laborious execution and prone to errors. The GFR is determined using calculations based on age and sex, factors known to affect the result.[7,8]

Albuminuria or proteinuria (expressed in mg/g of creatinine) was categorized as A1 (normal or slightly increased, < 30 mg/g), A2 (moderately increased, between 30 and 300 mg/g) and A3 (markedly increased, > 300 mg/g), replacing the terms normoalbuminuria, microalbuminuria, and macroalbuminuria.[9]

Therefore, this study aimed to assess the GFR in patients with type 2 diabetes mellitus (DM) and SAH to establish a correlation and investigate future consequences on quality of life.

## METHODS

A quantitative epidemiological, cross-sectional, and analytical study was conducted to assess the GFR using the CKD-EPI equation of patients with type 2 DM and SAH. The study was performed with patients from the clinical school Dr. Carlos Brandt at the Faculdade de Medicina de Olinda, Pernambuco, Brazil.

The study included patients of both sexes and aged ≥ 45 years. Patients with known advanced kidney disease (GFR < 30 ml/min/1.73m$^2$) and on dialysis were excluded from the study.

A clinical file was created with information on age, sex, race, levels of blood pressure, urea, creatinine, fasting blood glucose, glycated hemoglobin, and anthropometric data (weight and height) to calculate body mass index (BMI).

The GFR was calculated in the National Kidney Foundation application, with values expressed as ml/min/1.73m$^2$, and categorized according to the degree of reduction in kidney function following the criteria of updated guidelines.

The data was compiled for statistical analysis to identify the prevalence of patients with reduced GFR, correlating with the main risk factors.

The statistical analysis was performed using the Predictive Analytics Software (PASW® STATISTIC, version 17.0). Initially, a descriptive analysis was used for the maximum and minimum values, mean, and standard deviation for quantitative variables. For the qualitative variables, the absolute and relative values were described. Pearson's Chi-squared test was used to verify the association between variables. The confidence interval established was 95%.

The study was approved by the institutional review board of the Faculdade de Medicina de Olinda (no. 4.789.832).

## RESULTS

A total of 99 patients were included in the final sample. Ages ranged from 45 to 86 years (mean age 66 ± 10.3 years); 69.7% (n = 70) were women and 30.3% (n = 30) were men. Regarding race, 53.5% (n = 54) were white, 44.4% (n = 44) black, and 2.0% (n = 2) brown. Among them, 55.6% (n = 56) had type 2 DM, 92.9% (n = 93) had SAH, and 37% had both comorbidities. In addition, 9.1% (n = 9) had an acute myocardial infarction, and 5.1% (n = 5) had undergone a cardiac procedure, surgical or percutaneous revascularization.

Concerning medication, 8.1% (n = 8) used sulfonylureas, 34.3% (n = 34) metformin, 4.0% (n = 4) Hagedorn neutral protamine insulin, and 1.0% (n = 1) regular insulin. In addition, 33.3% (n = 33) used beta-blockers, 34.3% (n = 34) calcium channel blockers, 54.5% (n = 54) diuretics, 15.2% (n = 15) angiotensin-converting enzyme inhibitors, 62.6% (n = 62) angiotensin receptor blockers, and 3.0% (n = 3) direct vasodilators.

The anthropometric assessment showed that weight ranged from 49 to 109 kg (73± 14.1), and based on BMI, 37% were obese, 24% were

grade I, 7% were grade II, and 6% were grade III. Laboratory tests showed urea levels between 17 and 108 (39.18 ± 15.15), creatinine levels between 0.50 and 2.11 (0.98 ± 0.27); glucose levels between 9.30 and 296 (123.85 ± 49.84), and glycated hemoglobin levels between 4.20 and 10.80 (6.41 ± 1.50).

Based on the eGFR application, the CKD-EPI equation ranged between 32 and 130.20 (72.45 ± 19.58), and the Cockcroft-Gault equation ranged between 27.48 and 206.1(74.42 ± 28.18). The CDK-EPI equation showed 20% (n = 20) of patients classified as G1 (GFR ≥ 90) with 11% (n = 11) women and 9% (n = 9) men, 55% (n = 51) as G2 (89 ≤ GFR ≤ 60) with 42% (n = 42) women and 13% (n = 13) men, and 25% as G3 (59 ≤ GFR ≤ 30) with 18% (n = 18) women and 7% (n = 7) men, without patients as G4 (29 ≤ GFR ≤ 15) or G5 (GFR < 15).

This study investigated the association between sociodemographic (age, sex, and BMI), morbidity variables (SAH and DM), and outcomes in the reduction of GFR. A significant association was not observed between SAH and reduction in GFR (p = 0.099) and between DM and reduction in GFR (p = 0.288) and BMI (p = 0.454). In contrast, G2 and G3 were significantly associated with age > 60 years (61.4%, p = 0.032), and the best GFR rates (G1) were related to age < 60 years.

## DISCUSSION

This quantitative epidemiological, cross-sectional, and analytical study assessed the GFR in patients with type 2 DM and SAH using the CKD-EPI equation to evaluate cardiovascular and nephrological risks related to the loss of renal function. The National Kidney Foundation of the United States of America recommends the CKD-EPI equation to estimate the GFR using the values of serum creatinine, age, and sex[1]. This study associated sociodemographic and morbidity variables with the reduction in GFR. However, only age > 60 years was significantly associated with the different stages of GFR, which helps to identify vulnerable patients that require monitoring and treatment targets.

SAH was correlated with GFR to investigate consequences in the quality of life of the patients since it is the most important risk factor for the progression of kidney damage.[10] The impact of uncontrolled blood pressure in the glomerular hemodynamics has a direct effect on factors associated with kidney damage, such as the activation of the renin-angiotensin system and proteinuria, which require appropriate pressure adjustments to be controlled.[11]

Type 2 DM is independently associated with a significant increase in mortality due to cardiovascular and renal causes. Diabetes kidney disease is a complication of DM characterized by impaired kidney function, with high morbidity and mortality rates, and the leading cause of kidney failure worldwide. Between 20% and 50% of patients with DM are estimated to develop kidney disease, affecting around 30% of patients with type 1 DM and being the main cause of death, while the prevalence ranges from 20% to 50% in patients with type 2 DM.[12]

Regarding sociodemographic variables, BMI is an important indicator of CKD risk factors, especially associated with increased abdominal circumference, although independent of GRF decline.[13] Moreover, the association of increased GFR with age is widely documented in relation to other risk factors for CKD. Kidney function is stable between childhood and adulthood, and GFR declines one mL/min/1.73 m² per year after 30 years old in healthy people.[14] Decreased kidney function occurs due to changes in the structure of the kidney associated with aging.

Thus, although this study only significantly associated age with decreased GFR, the literature confirms that other variables assessed are related to the decline in GFR. A potential limitation of this study was that the patients assessed may not represent the total population in the routine clinical setting.

## CONCLUSION

The study assessed the GFR in patients with type 2DM and SAH using the CKD-EPI equation. The data showed an association between the decrease in GFR and age. Thus, anthropometric data and comorbidities were not associated with GFR, showing that these variables did not influence the decline in kidney function. This data shows the importance of monitoring and assessing GFR in patients with DM and SAH along with aging.

The association of SAH and DM was more frequent with increased age, especially over 60years, an important consideration given the relevance of these factors in the progression of CKD and increased cardiovascular risk. Furthermore, levels of glycemia, glycated hemoglobin, and blood pressure were not within target for most patients.

In conclusion, monitoring renal function in older patients is essential to reduce the risk of total kidney failure and to establish conservative approaches to control this function. In addition, the referral of patients to services could delay the progressive loss of renal function and the need for renal replacement therapy, dialysis, and transplantation.

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# IMPACTS OF THE COVID-19 PANDEMIC ON THE MENTAL HEALTH OF HEALTHCARE PROFESSIONALS IN BRAZIL: AN INTEGRATIVE REVIEW

*IMPACTOS DA PANDEMIA DE COVID-19 NA SAÚDE MENTAL DOS PROFISSIONAIS DE SAÚDE DO BRASIL: UMA REVISÃO INTEGRATIVA*

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## ABSTRACT

**Introduction:** The COVID-19 pandemic exposed insecurities, adversities, and fears that the international community had not experienced for decades. Pandemics lead to sudden changes in daily life, generating consequences that may exceed the coping capacity of those affected. Therefore, this study aimed to review the psychological impacts resulting from this reality. **Objective:** To conduct a review and demonstrate the impacts of the COVID-19 pandemic on the mental health of healthcare professionals in Brazil. **Methods:** This integrative review included studies published in English and Portuguese between January 1, 2020, and February 10, 2020. Two databases were searched (SciELO and PubMed) using the following descriptors: mental health, covid-19, health workers, and Brazil. **Results:** Thirty-nine studies were identified, and 12 met the eligibility criteria. **Conclusion:** A clear association between the COVID-19 pandemic and the worsening of the mental health of healthcare professionals in Brazil was observed. A high demand for psychological care services due to the long-term effects of the pandemic on the mental health of this population should be expected in the future. Further research is needed to develop strategies to mitigate this adversity.

**Keywords:** COVID-19; Brazil; Mental health; Health personnel.

## RESUMO

**Introdução:** A pandemia da COVID-19 trouxe à tona inseguranças, adversidades e medos que a comunidade internacional não experienciava havia décadas. Pandemias implicam mudanças bruscas no cotidiano da sociedade. Essas implicações geram impactos que podem ultrapassar a capacidade de enfrentamento daqueles que as vivenciam. **Objetivo:** Realizar uma revisão integrativa e demonstrar os impactos da pandemia da COVID-19 na saúde mental dos profissionais de saúde do Brasil. **Métodos:** Trata-se de uma revisão integrativa, na qual foram analisados estudos publicados em língua inglesa e portuguesa, entre 1º de janeiro de 2020 e 10 de fevereiro de 2021, tendo como referência a base de dados SciELO e PubMed, empregando os seguintes descritores: Mental Health, COVID-19, Health Workers, Brazil. **Resultados:** Dos 39 estudos identificados após a remoção de duplicatas, 12 preencheram os critérios de elegibilidade. **Conclusões:** Há uma notória associação entre a pandemia de COVID-19 e o agravo da saúde mental dos profissionais de Saúde do Brasil. No futuro, poderá haver alta demanda nos serviços de atenção psicológica devido às consequências dos impactos da pandemia na saúde mental da população estudada, fato que torna necessárias a realização de pesquisas e a elaboração de estratégias para reverter essa adversidade.

**Palavras-chave:** COVID-19; Brasil; Saúde mental; Profissionais da saúde.

## INTRODUCTION

The World Health Organization declared the COVID-19 pandemic in March 2020 due to its high infectious capacity. Over time, social, economic, and political repercussions corroborated the development of psychological disorders among healthcare professionals, compromising interpersonal relationships and triggering failures in healthcare[1-3].

Pandemics require sudden changes in routine, affecting the coping capacity of those who experience it. An increased incidence of mental disorders among the population is expected, a consequence that varies according to the magnitude of the event, the degree of social vulnerability, and the timing and quality of actions focused on mental health[4].

Since then, studies have aimed to discuss the consequences of the new pandemic and its association with the mental health of frontline healthcare professionals[2]. Among the main factors affecting mental health were poor work environment, risk of infecting themselves and others, fear of becoming ill, fear of death, despair, hopelessness, and coping with social distancing[2,5]. Studies reported the neglect of public policies related to mental support for healthcare professionals and how the increased demand for psychological care services for healthcare professionals was in course[2,6].

This study aimed to conduct an integrative review, summarizing the information in literature to identify the possible repercussions of the COVID-19 pandemic on the mental health of healthcare professionals in Brazil.

## METHODS

This integrative review of the literature combined studies with different methodologies and compared the occurrence of the disease among groups of individuals according to the guidelines found in scientific evidence. The following question guided the review: What are the impacts of the COVID-19 pandemic on the mental health of healthcare professionals in Brazil?

### Search strategy

Electronic searches were conducted in April 2020 on SciELO and PubMed databases using the following keywords: “mental health”, “COVID-19”, “health workers”, and “Brazil”. Keywords were combined using the Boolean operator “AND”.

In the first screening, titles and abstracts were reviewed using the eligibility criteria. Consequently, independent reviewers read all the articles in full. Figure 1 details the study flowchart.

The inclusion criteria were a) scientific articles; b) free full texts (original, review, experience report, update, or case study); c) studies that addressed the mental health of healthcare professionals; d) publication date between January 1, 2020, and February 10, 2021; and e) studies available in Portuguese and English. Studies that did not address the guiding question or duplicates were excluded.

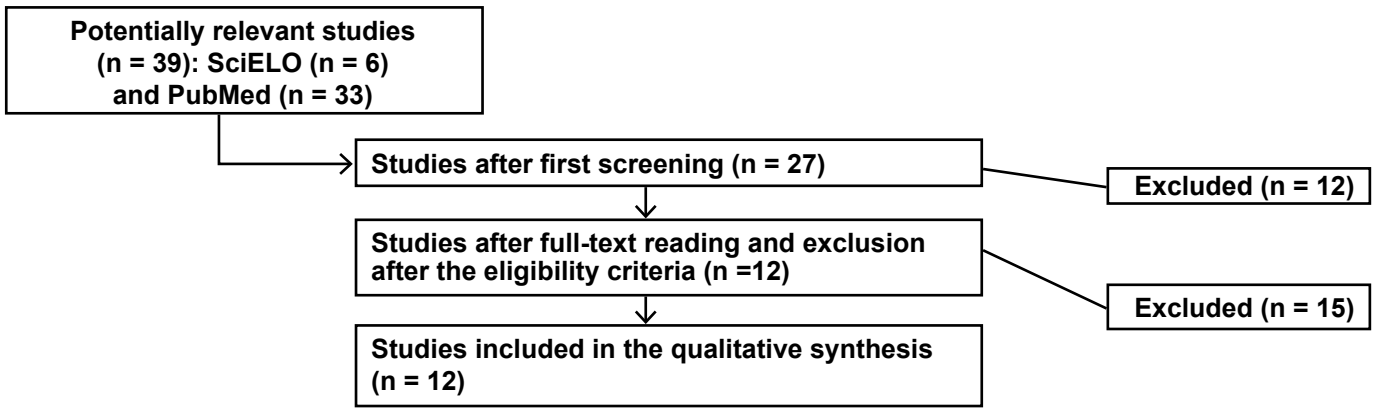


**Figure 1.** Study flowchart.

## RESULTS

| | TITLE | AUTHOR | OBJECTIVES | CONCLUSION |
|---|---|---|---|---|
| 1 | Saúde Mental dos profissionais de saúde no Brasil no contexto da pandemia de COVID-19 | Dantas E. (2021) | To discuss the nuances surrounding the challenges and possibilities related to the mental health of healthcare professionals in Brazil in the context of the COVID-19 pandemic[2]. | Currently, mental health actions are urgent and vital and must be one of the foundations of resilience in a society that will face a COVID-19 pandemic with definitive and unknown consequences for the mental health of healthcare professionals[2]. |
| 2 | The impact of the COVID-19 pandemic on the mental health of healthcare professionals | Ornell *et al* (2020) | To unravel the impacts of the COVID-19 pandemic on the mental health of healthcare professionals in Brazil[3]. | Healthcare professionals are particularly vulnerable to psychological distress, a fact that corroborates the development of psychological disorders. This reiterates the importance of intervention for the mental health promotion of these professionals[3]. |
| 3 | Escolhas de Sofia e a pandemia de COVID-19 no Brasil: reflexões bioéticas | Torres *et al* (2020) | To demonstrate how the pandemic affects the distribution of health resources in Brazil and highlight the ethical and psychological dilemmas experienced by healthcare professionals in the context of combating the disease[4]. | The pandemic has led to an increased demand for therapeutic equipment and brought bioethical dilemmas to Brazilian healthcare professionals, which may generate significant psychological disorders and marks in this population[4]. |
| 4 | Depressão e ansiedade em profissionais de enfermagem durante a pandemia da COVID-19. | Santos *et al* (2021) | To analyze the prevalence of symptoms of depression, anxiety, and the associated factors in a nursing staff during the COVID-19 pandemic[5]. | Female gender, brown color or race, monthly income of less than five minimum wages, and working in the private sector were factors related to a higher prevalence of symptoms suggestive of anxiety and depression disorders[5]. |
| 5 | Capacitação nacional emergencial em saúde mental e atenção psicossocial na COVID-19: um relato de experiência. | Noal *et al* (2020) | To highlight the approaches to mental health and psychosocial care developed to provide technical support based on scientific knowledge to healthcare professionals in this context[6]. | Indicators of mental health and psychosocial care in crises showed that mental health was directly impacted, with a gap in the creation of public mental health policies in Brazil aimed at health emergencies[6]. |
| 6 | Segurança dos profissionais de saúde no enfrentamento do novo coronavírus no Brasil. | Santana *et al* (2020) | To present the number of healthcare professionals affected by COVID-19 in Brazil, identify some measures to reduce vulnerability, and demonstrate the repercussions on the health of these professionals[7]. | The precarious condition of the environments where healthcare professionals work has been evidenced, which corroborates with a worsening of the physical integrity of these professionals and their health as a whole[7]. |
| 7 | Exposição às informações sobre COVID-19 em mídias digitais e suas implicações para funcionários do setor de saúde: resultados de uma pesquisa on-line. | Bazán *et al* (2020) | To estimate how the high consumption of information related to the novel coronavirus disease affects healthcare professionals during the pandemic[8]. | Approximately half of the participants complained of headaches (57.9%) and sleep disorders (49.5%). Among other symptoms, anxiety and exhaustion were the most frequently reported. Approximately a third of respondents felt stressed almost every day or always[8]. |

| | | | | |
|---|---|---|---|---|
| 8 | A saúde mental da enfermagem no enfrentamento da COVID-19 em um hospital universitário regional. | Dal'Bosco *et al* (2020) | To identify the prevalence and factors associated with anxiety and depression in nursing professionals who deal with COVID-19 in a university hospital[9]. | A prevalence of anxiety (48.9%) and depression (25%) was observed[9]. |
| 9 | The emotional impact of Coronavirus 2019-nCoV (new Coronavirus disease). | Lima *et al* (2020) | To analyze the emotional impact of the new coronavirus on the population[10]. | Patients and frontline professionals are vulnerable to the emotional impacts of the pandemic due to the potential stressors arising from this reality, which are underestimated, and the constant resilience of these professionals[10]. |
| 10 | Impact of COVID-19 on Mental Health in a Low and Middle-Income Country | Castro-de-Araujo *et al* (2020) | To identify the impacts of COVID-19 on mental health in low- and middle-income countries[11]. | The rapid spread of the pandemic has challenged the ability of countries to maintain their economies, a factor that has contributed to the prevalence of anxiety and stress throughout the population. Brazil is unprepared for the foreseeable consequences of the impacts addressed[11]. |
| 11 | When health professionals look death in the eye: the mental health of professionals who deal daily with the 2019 coronavirus outbreak. | Neto *et al* (2020) | To discuss the psychological aspects of healthcare professionals dealing with the COVID-19 pandemic on a daily basis[12]. | Intensive care physicians are on the edge of stress, especially when dealing with older patients and death; mental health care needs to be developed to reduce the impact of these issues[12]. |
| 12 | Psychiatric symptomatology associated with depression, anxiety, distress, and insomnia in health professionals working in patients affected by COVID-19: A systematic review with meta-analysis. | da Silva *et al* (2021) | To systematically analyze psychological symptoms, such as depression, anxiety, and insomnia, among healthcare professionals who deal with COVID-19[13]. | A strong association between COVID-19 and psychiatric repercussions in healthcare professionals was reported. Healthcare professionals had a higher level of indirect traumatization, in which the impact of psychological damage may exceed the tolerance and emotional resilience of these professionals[13]. |

## DISCUSSION

The number of studies investigating the psychological impacts of COVID-19 on healthcare professionals increased since the start of the pandemic[12]. Although the studies involved different perspectives, more homogeneous themes were discussed, such as stress factors associated with mental illness[2, 3].

The study by Dantas et al. (2021)[2] mentioned many factors, including fear of death, fear of infection and contaminating others, despair, hopelessness, and coping with social distancing. These factors corroborate the emergence of post-traumatic stress, depression and anxiety, and even suicidal behavior. The authors highlighted the importance of the Psychosocial Care Network as an excellent tool to support healthcare professionals and the psychological resilience as a strategy to combat the challenges arising from the pandemic. Dantas et al. also stated that a massive demand for mental health services might arise and should not be neglected, given the negative psychosocial repercussions that affect the community[2].

Ornell et al. (2020)[3] reported that during pandemics, people comply with social distancing to reduce infection rates, while healthcare professionals usually deal with the opposite due to the exponential demand. The monitoring of healthcare professionals in direct contact with infected patients is necessary, especially regarding symptoms of depression, suicide, and anxiety. On the other hand, the study highlighted Brazil as a country with severe socio-eco-

nomic inequalities and increased contamination curves; thus, establishing the need to create strategies for monitoring and promoting the mental health of frontline healthcare professionals, considering the high burden on them[3].

Torres et al. (2020)[4] highlighted how the need for decisions based on protocols represented one of the greatest bioethical challenges faced by healthcare professionals and may generate high levels of stress and psychological suffering. The study demonstrated how psychology, in the context of the pandemic, had the potential to reduce negative impacts and improve the communication between those involved. This process may promote the mental health of the population evaluated. The study also emphasized the unknown medium- and long-term negative impacts on the mental health of healthcare professionals and the undoubted need for psychological support[4].

Santos *et al.* (2021)5 reported that females, brown race, monthly income of three to four minimum wages, living with parents and siblings, and working in private practice and places without adequate structure were factors that influenced the prevalence of moderately severe to severe depression and anxiety among healthcare professionals. On the other hand, physical activity and talking to friends and family reduced the prevalence of symptoms of anxiety and depression in healthcare professionals. Therefore, actions aimed at improving working conditions and promoting physical activity may benefit the mental health of this population.

The overload of the Unified Health System was a consequence of governmental strategies to combat the pandemic, implying disturbances that exceeded the coping capacity of healthcare professionals. This situation triggered symptoms that already existed before the pandemic, such as stress, depression, and anxiety. Approximately one-third to half of the population affected may develop or increase mental disorders, an estimate that varies according to the degree of vulnerability and the quality of public psychosocial actions in response to the pandemic. In this context, the study indicated a gap in training and public health policies in Brazil aimed at health emergencies and highlighted the need to create strategies for training and monitoring healthcare professionals[6].

The precarious conditions of the environments in which healthcare professionals work contribute to the deterioration of physical integrity and health. A study7 reported that psychological repercussions are often underestimated during crises. According to the authors, reducing the triggers for healthcare professionals is necessary to maintain the entire health system and professionals and, consequently, combat the COVID-19[7].

High exposure to media information may be related to psychological distress. Spending more time consuming accurate and up-to-date information related to COVID-19 was a protective factor, although such exposure may increase the psychological distress of healthcare professionals. In the study, headaches, sleep disorders, anxiety, and exhaustion were among the symptoms resulting from this suffering[8].

An incidence of approximately 48.9% of anxiety and 25% of depression was observed among the healthcare professionals. In this context, conflicts of interest, the high technical and professional responsibility of these professionals, and incisive pressures may contribute to the emotional imbalance of nursing professionals. According to Bosco et al., healthcare professionals must be prepared to face the threat by seeking specialized psychological support and performing integrative activities (e.g., relaxation exercises and Reiki) to reduce the mental health impacts of the pandemic[9].

Patients and healthcare professionals are constantly tested for resilience and vulnerability to the emotional impacts of the pandemic, considering the underestimated potential stressors arising from this reality. According to a research published in the Lancet Psychiatry, older adults and immigrant professionals need special attention for mental health. In addition, many professionals often do not receive training in mental health and may have a feeling of collective hysteria, increasing the rates of anxiety, depression, and stress[10].

A study[11] described how the rapid spread of the pandemic has affected the economy in many countries, increasing the prevalence of anxiety and stress in the population. The study

also reported the relationships between mental disorders and cardiovascular and metabolic diseases and the possibility of progression of these symptoms (e.g., panic disorders). Another point evaluated was the approach to vulnerable populations, such as those affected by bipolar disorder. In these populations, loneliness and other stressors can be more incisive triggers of depressive syndromes[11].

Neto *et al.* (2020)[12] stated that the rapid growth of confirmed and suspected cases of COVID-19, work overload, shortage of protective equipment, and lack of specific medication contributed to increasing the emotional burden on healthcare professionals. This study also reported a high prevalence of COVID-19 among healthcare professionals, intensifying the uncertainties and anxiety regarding their profession. Neto et al. (2020) also indicated the need to develop mental health-related care, including the use of psychotropic drugs prescribed by specialized professionals for severe mental pathologies, follow-up with appropriate health services and facilities, development of psychological treatment plans for healthcare professionals, psychological electronic counseling, and the provision of psychological support from psychotherapeutic techniques based on the adaptive stress theory[12].

In their review, da Silva et al. (2021)[13] highlighted the prevalence of sleep disorders, anxiety, and depression associated with the high risk of infection, lack of sufficient biological protection measures, and mental suffering among healthcare professionals. The meta-analysis showed that healthcare professionals had a higher level of indirect traumatization, in which the impact of psychological damage exceeded their tolerance and emotional resilience[13].

## CONCLUSION

An important association between the COVID-19 pandemic and the worsening of mental health of healthcare professionals in Brazil was observed. The consequences of COVID-19 trigger the emergence and intensification of stress and anxiety. A high prevalence of serious symptoms of mental illness, such as anxiety, depression, and burnout syndrome, were observed among healthcare professionals. On the other hand, public health policies to combat this problem are neglected. The lasting impact of the pandemic on the mental health of healthcare professionals may lead to a significant increase in the demand for psychological care services, highlighting the need for research and strategic interventions to address this challenge.

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# BLUE NOVEMBER: WHY SCREENING FOR PROSTATE CANCER?

*NOVEMBRO AZUL: POR QUE RASTREAR O CÂNCER DE PRÓSTATA?*

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## ABSTRACT

This narrative review aimed to explore studies that addressed the importance of the integrality of the health of men, focusing on the prevalence and screening of prostate cancer. National and international full-text studies from the last ten years were randomly selected using the descriptors “Blue November”, “prostate cancer”, “screening”, “epidemiological data”, and “Ministry of Health” in the following databases: the Ministry of Health website, SciELO, and Google Scholar. After analytical, selective, and interpretive reading of the information, 32 studies were selected; 11 were included due to the delimitation and relevance of the theme, and 21 were excluded because they did not present enough data. The actions developed by the Blue November, from its essence to the present day, aimed to ensure the integrality of health of the men and became an important strategy for prostate cancer screening.

**Keywords:** Blue November; Prostate cancer; Screening; Epidemiological data; Ministry of Health.

## RESUMO

Trata-se de uma revisão narrativa da literatura, que objetivou explorar estudos que abordem a importância da integralidade da saúde do homem, dando foco referente à prevalência e rastreamento ao câncer de próstata. Artigos nacionais e internacionais com seus textos completos dos últimos dez anos, foram selecionados aleatoriamente através dos descritores “novembro azul”, “câncer de próstata”, “rastreamento”, “dados epidemiológicos” e “ministério da saúde”, nas seguintes bases de dados: site do Ministério da Saúde, SciELO (Scientific Electronic Library Online) e Google Acadêmico. Após leitura analítica, seletiva e interpretativa das informações buscando a melhor qualidade e relevância do assunto abordado para a construção da revisão, foram selecionados 32 artigos dos quais 11 foram incluídos pela delimitação e pertinência do tema e 21 foram excluídos, pois não apresentavam dados suficientes para o contexto. As ações desenvolvidas pelo movimento Novembro Azul, desde a sua essência até os dias atuais, visam garantir a integralidade da saúde do homem e se tornaram uma importante estratégia para o rastreio do câncer de próstata.

**Palavras-chave:** Novembro Azul; Câncer de próstata; Rastreamento; Dados epidemiológicos; Ministério da saúde.

## INTRODUCTION

In 1999, some USA entities mobilized to promote awareness for combating prostate cancer, with the government establishing the month of September as “National Prostate Cancer Awareness Month” in 2001[1].

The “Blue November”, although with another connotation and another name, began in 2003 with a group of Australian friends who gathered in a bar and realized that the use of mustaches was the only fashion of the Seventies that had not yet returned to the male public. For fun, they decided to start the following month with only the mustache grown; they would have a themed party at the end of the month to reward the best and the worst mustache. As it was in November, the game was called *Movember*, by the union of the words “mo”, referring to an Australian slang for mustache, and November. Therefore, “Blue November” came up with a proposal other than the one referred to today[2].

Global campaigns against breast cancer inspired the revival of the joke in the following year when they decided that *Movember* could help raise awareness about prostate cancer. This movement gained popularity and began fundraising for an organization dedicated to

treating this type of cancer, expanding each year in Australia and reaching supporters in other countries. In 2008, Brazil launched a campaign to raise awareness of the disease, initially promoted by the *Instituto Lado a Lado Pela Vida* (ILLPV), a non-profit organization. The campaign was originally named "One Touch, One Dribble" and was later renamed to "Blue November" in 2012[3]. To this day, the movement continues to occur as an engaging strategy for prostate cancer screening.

Cancer is the leading public health problem worldwide and is already among the top four causes of premature death (before the age of 70) in most countries. The incidence and mortality due to cancer have been increasing globally, partly due to aging, population growth, as well as the change in the distribution and prevalence of cancer risk factors, especially those associated with socioeconomic development. A transition of the main types of cancer occurred in developing countries: the types of cancer associated with infections reduced and those associated with improved socioeconomic conditions increased; the latter is related to the incorporation of habits and attitudes associated with urbanization (e.g., sedentary lifestyle and inadequate diet).

This literature review aimed to explore studies that addressed the importance of the integrality of human health, focusing on the prevalence and screening of prostate cancer.

## MATERIAL AND METHODS

This study provided a narrative review of studies that used descriptive and qualitative data, updated using bibliographic research. National and international full-text studies available *online* from the past decade were randomly selected from the Ministry of Health website, SciELO, and Google Scholar databases. Key descriptors used were blue November, prostate cancer, screening, epidemiological data, and Ministry of Health. An analytical, selective, and interpretive reading of the information was conducted to ensure the high quality and relevance of the theme. Out of the 32 studies reviewed, 11 were included based on their relevance, while 21 were excluded for lacking sufficient contextual data.

## EPIDEMIOLOGICAL DATA

Cancer surveillance seeks to manage non-communicable diseases and relies on morbidity and mortality information obtained from the Population-Based Cancer Records (RCBP), Hospital Cancer Records (RHC), and the Mortality Information System (SIM) of the Department of Informatics of the Unified Health System (DATASUS). This information provides subsidies for managers to monitor and coordinate cancer control, as well as the direction of research related to the disease.

The most recent global estimate from 2018 indicates the incidence of 18 million new cancer cases worldwide (17 million excluding non-melanoma skin cancers) and 9.6 million deaths (9.5 million excluding non-melanoma skin cancers). Lung cancer is the most common cancer (2.1 million), followed by breast cancer (2.1 million), colon and rectum cancer (1.8 million), and prostate cancer (1.3 million). Among men, the incidence of 9.5 million cases accounts for 53% of new cases, while women have 8.6 million new cases (47.0%). The leading cancers in men include lung (14.5%), prostate (13.5%), colon and rectum (10.9%), stomach (7.2%), and liver (6.3%). For women, the most common cancers are breast (24.2%), colon and rectum (9.5%), lung (8.4%), and cervical cancer (6.6%). In Brazil, an estimated 65,840 new prostate cancer cases are projected each year for the 2020-2022 triennium. This value corresponds to an estimated risk of 62.95 new cases per 100,000 men[4].

Excluding non-melanoma skin cancers, prostate cancer ranks as the most prevalent across all Brazilian regions, with an estimated risk of 72.35 per 100,000 in the Northeast, 65.29 per 100,000 in the Midwest, 63.94 per 100,000 in the Southeast, 62.00 per 100,000 in the South, and 29.39 per 100,000 in the North region.

According to global estimates, prostate cancer is the second most common cancer among men worldwide. About 1,280,000 new cases are expected, accounting for 7.1% of all cancer diagnoses. This value corresponds to an estimated risk of 33.1/100 thousand. The highest incidence rates of prostate cancer are

found in Australia, New Zealand, and European countries (North and East)[7,12].

In the United Kingdom, Japan, Costa Rica, and Thailand, the influence of the prostate-specific antigen (PSA) blood test on the trend of prostate cancer incidence rates is still being determined. Conversely, in the United States, this incidence has been decreasing since the 2000s due to reduced PSA screening. From 2011 to 2015, the rate decreased by around 7% per year[6,7,12].

In Brazil, prostate cancer was responsible for 15,391 deaths in 2017, translating to a risk of 15.25 per 100,000 men[8]. The main risk factor is age, with the incidence rising 50 years onwards[9]. Regarding the etiology, despite being a very common cancer, its causes remain poorly understood[11,13]. Additional risk factors include a family history of the disease, inherited genetic factors (e.g., Lynch syndrome and mutations in BRCA1 and BRCA2)[6], smoking, excess body fat[10], and exposure to aromatic amines, arsenic, and petroleum products.

## STRATEGIES FOR EARLY DETECTION OF PROSTATE CANCER

Early cancer detection is a strategy aimed at identifying tumors at their earliest stages, increasing the likelihood of successful treatment. Detection can be achieved via clinical, laboratory, or radiological exams for individuals exhibiting signs and symptoms of the disease (early diagnosis), or via periodic exams in those without signs or symptoms (screening) but belonging to higher-risk groups. These assessments involve a rectal examination and a blood test to evaluate PSA dosage[14].

The literature is not clear whether prostate cancer screening offers more benefits than risks. Therefore, the National Cancer Institute (INCA) does not recommend routine tests for this purpose. If men actively seek screening for this type of tumor, the Institute also recommends that they should be informed about the risks and possible absence of benefits of routine tests[14].

Early diagnosis of prostate cancer enables better treatment results and should be sought by investigating signs and symptoms, such as difficulty urinating, decreased urine output, the need to urinate more often during the day or at night, and blood in the urine[14]. Although these symptoms are not caused by cancer in most cases, they need to be investigated by a physician[14].

Based on the National Policy for Comprehensive Care in Men's Health (PNAISH)[15], which aims to promote health initiatives for men aged 20 to 59, the Ministry of Health advises that organized activities occur not just in November but year-round. These activities should cover violence and accident prevention, access and support services, and health matters like sexual and reproductive health, diabetes, and hypertension, among others.

## FINAL CONSIDERATIONS

The Blue November movement became an emblematic movement in many countries, focusing on various actions to ensure the integrity of the health of men, especially prostate cancer. Even now, the movement remains a compelling strategy for prostate cancer screening.

This literature review confirmed that, excluding non-melanoma skin cancer, prostate cancer is the leading cancer across all Brazilian regions, and the global estimate points to prostate cancer as the second most common among men, highlighting the need for proactive measures in prevention and early treatment.

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REVIEW ARTICLE

# COVID-19 AND KIDNEY INJURY: A LITERATURE REVIEW

*COVID-19 E LESÃO RENAL: UMA REVISÃO DA LITERATURA*

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## ABSTRACT

**Introduction:** Although the kidney injury associated with COVID-19 is not yet fully elucidated, it is recognized as a complex and multifactorial condition. Studies indicate that the prevalence of associated risk factors increases the propensity for kidney injury. Additionally, the early assessment and detection of kidney injury have been emphasized as crucial for predicting prognosis and clinical outcomes during the COVID-19 treatment. **Objective:** Discuss the association between kidney injury and COVID-19 infection, highlighting potential risk factors and clinical implications. **Materials and methods:** This literature review obtained data from studies published in the Scielo and PubMed databases between December 2019 and September 2020. **Results and discussion:** Multiple factors contribute to kidney injury in COVID-19, ranging from direct viral damage to nonspecific mechanisms that hinder overall health. Furthermore, preexisting conditions, such as advanced age and hypertension, have been associated with a higher risk of kidney complications and increased mortality. Therefore, a thorough investigation of the kidney stress induced by the virus (SARS-CoV-2) is essential to enable early diagnosis and prevent severe outcomes. Nevertheless, kidney function recovery remains challenging and requires specialized medical follow-up. **Conclusion:** Despite the growing evidence on the theme, further studies are needed to elucidate the pathophysiological mechanisms underlying COVID-19-related kidney injury, improve early detection strategies, and establish management protocols.

**Keywords:** COVID-19; Acute kidney injury; Pathophysiology; Mortality

## RESUMO

**Introdução:** A lesão renal na COVID-19 ainda não está totalmente elucidada, mas sabe-se que ela é diversa e multifatorial. Os estudos realizados apontam a prevalência de alguns fatores de risco associados a uma maior propensão para o desenvolvimento da lesão renal. Além disso, tem sido discutida nesse cenário a importância da avaliação e detecção precoce da lesão renal, o que auxiliaria na predição de prognóstico e, ainda, no desfecho clínico durante o tratamento da infecção pelo vírus. **OBJETIVO**: Discutir a relação entre o desenvolvimento da lesão renal em pacientes que foram infectados pelo vírus da COVID-19. **Materiais e metódos:** O presente estudo trata de uma revisão da literatura. Os dados apresentados provêm de artigos científicos publicados entre dezembro de 2019 e setembro de 2020. A busca de artigos científicos foi realizada nos bancos de dados SCIELO e PUBMED. **Resultados e discussão:** Sabe-se que vários são os fatores envolvidos na relação entre COVID-19 e lesão renal, desde danos diretos causados pelo vírus até mecanismos inespecíficos que desencadeiam uma série de prejuízos à saúde. Além disso, quando associada a fatores de risco como idade avançada e hipertensão, a infecção pelo coronavírus pode ocasionar complicações renais e aumento da mortalidade. Desse modo, mostra-se essencial o desenvolvimento de mecanismos para realização de uma investigação minuciosa do estresse renal causado pelo vírus com o intuito de auxiliar no diagnóstico precoce e na prevenção de quadros mais graves. Ainda assim, a recuperação da função renal é difícil e precisa de um acompanhamento com especialista para monitoramento da sua evolução. **Conclusão:** Por mais que diversos artigos tenham sido publicados, ainda se faz necessário o desenvolvimento de estudos que determinem com segurança os mecanismos fisiopatológicos, a detecção precoce da lesão renal e o seu manejo específico.

**Palavras-chave:** COVID-19; Lesão renal aguda; Fisiopatologia; Mortalidade.

## INTRODUCTION

Kidney injury associated with COVID-19 is not yet fully elucidated. However, this injury is known to be diverse and multifactorial, resulting from specific and nonspecific mechanisms. These mechanisms include the synergism effects of the direct cytopathic action of the virus (SARS-CoV-2) and the indirect cytokine-mediated damage caused by the systemic inflammatory response in patients with COVID-19. [2,3,7,6]

Studies have identified several risk factors associated with an increased susceptibility to kidney injury in infected patients, particularly chronic conditions, such as metabolic and cardiovascular diseases. [1,2,8,10]

Additionally, early assessment and detection of kidney injury have been recognized as crucial in patients with COVID-19, as those who develop early kidney injury tend to have a high risk of severe outcomes, increased mortality, and a low probability of kidney function recovery. [4,5,9]

The clinical outcome of kidney injury during COVID-19 infection has not yet been elucidated. While some patients experience kidney recovery, others do not, particularly those with preexisting comorbidities that predispose them to further kidney injury. [3,7]

Moreover, acute kidney injury (AKI) in COVID-19 infection has been associated with high mortality rates in intensive care units (ICU), and other conditions (e.g., proteinuria and hematuria) have also been related to increased mortality in patients with COVID-19.[2,3,4,7]

This study aimed to reinforce current knowledge and contribute new insights into the relationship between kidney injury and COVID-19, including its pathophysiology, risk factors, renal biomarkers, recovery potential, and associated mortality rates.

## METHODS

This literature review presented data obtained from studies published between December 2019 and September 2020.

The search was conducted in the SCIELO and PUBMED databases, using the following descriptors: “Kidney”, “Injury”, “COVID-19”, “Pathophysiology,” and “Mortality”. Titles and abstracts were screened, and those that met the inclusion criteria (i.e., publications available online in English or Portuguese) were selected.

Five thematic areas emerged from this selection: pathophysiology of kidney injury, associated risk factors, renal stress markers, kidney function recovery, and relationship with increased mortality. Among the 292 studies initially identified, 10 were selected in this review.

## RESULTS AND DISCUSSION

### Pathophysiology of kidney injury

Although the mechanisms underlying kidney injury in COVID-19 are unclear, the condition is recognized as diverse and multifactorial. Current evidence suggests that kidney injury results from specific and nonspecific mechanisms, including the synergism effects of direct viral cytopathic on the renal glomeruli and tubules and indirect cytokine-mediated injury due to the systemic inflammatory response in patients with COVID-19.[2,3]

The intracellular infection mechanism of SARS-CoV-2, although not fully elucidated, involves angiotensin-converting-enzyme 2 (ACE2) as a primary receptor facilitating viral entry into human cells. Similar to SARS-CoV, the Spike protein of SARS-CoV-2 binds to the ACE2 transmembrane protein on the host cell, enabling viral entry. This process enables the virus to release fusion peptides, allowing it to attach to the host cell membrane (i.e., a central mechanism in determining tissue tropism) and enter the cell. Notably, studies analyzing RNA sequencing data from patients with COVID-19 and AKI have revealed that ACE2 expression in the kidney is nearly 100 times higher than in the lung. Furthermore, SARS-CoV-2 exhibits an affinity for ACE2 receptors that is 10 to 20 times greater than that of SARS-CoV. Consequently, the SARS-CoV-2 can invade renal tubular cells by binding to ACE2, triggering cytotoxicity effects and impairing kidney function.[3,7]

The literature showed that patients with severe COVID-19, particularly those admitted to ICU, exhibit elevated levels of inflammatory cytokines. This cytokine storm, characterized by significantly increased levels of inflammatory mediators, aims to combat the virus by attack-

ing infected cells. However, the immune system fails to distinguish infected and healthy cells, leading to collateral tissue injury. In the kidney, these cytokines contribute to kidney injury by interacting with resident cells, promoting endothelial and tubular dysfunction.[2,3,6]

### Risk factors associated with kidney injury

Risk factors for AKI in patients with COVID-19 include advanced age, diabetes mellitus, cardiovascular diseases, hypertension, black race, and the need for mechanical ventilation and vasopressor support.[1,2,8]

AKI frequently occurs in patients with COVID-19, with an early presentation in the disease course and temporal association with respiratory failure, and it is associated with a poor clinical prognosis.[1,10]

### Markers of renal stress

Studies have established a strong association between kidney injury and COVID-19 infection. Identifying the risk of developing AKI in infected patients is crucial for prognosis and treatment optimization, as AKI in this context is a marker of poor clinical outcomes.[5,9]

Currently, AKI diagnosis relies on serum creatinine levels and urine output; however, these markers indicate kidney injury only after its occurrence. Therefore, newer biomarkers have received greater attention, including tissue inhibitors of metalloproteinase-2 and insulin-like growth factor-binding protein 7. These markers, the only renal stress indicators approved by the Food and Drugs Administration, can predict AKI onset by detecting tubular stress and injury. [4,5]

### Kidney function recovery

Evidence suggests that most patients with severe COVID-19 experience some degree of kidney injury, with some progressing to kidney failure.[3,7]

Studies on AKI outcomes and management of patients with COVID-19 are scarce. However, renal replacement therapy (RRT) has been widely employed, with some patients exhibiting partial recovery of renal function following viral and inflammatory responses. Despite this, the mortality rate remains high among patients requiring RRT, and the extent of renal function recovery remains uncertain. [3,7]

Studies emphasize that after the critical phase of infection and kidney injury, nephrological follow-up is essential to monitor the condition of the patient and prevent the recurrence of kidney injury.[7]

### Increased mortality in patients with kidney injury

Studies already show that preexisting comorbidities have been strongly associated with a higher mortality rate in patients with COVID-19, with kidney disease being a significant contributor.[7,4]

Besides the AKI during SARS-CoV-2 infection being associated with a high mortality rate in the ICU, other conditions also contribute to increased mortality.[2]

Stage 2 or higher AKI, along with the presence of proteinuria and hematuria and elevated baseline serum creatinine and urea levels, are factors associated with increased mortality in patients with COVID-19 with renal involvement.[3]

## CONCLUSION

Although patients with kidney injury present several defense mechanisms to counteract COVID-19 infection, the prognosis remains unfavorable when risk factors are present. In these cases, recovery rates decline while complications and mortality rates increase.

Therefore, despite the existing knowledge on the theme, systematic studies and analyses are needed to develop tools for the early detection of kidney injury. Additionally, establishing a standardized protocol for managing affected patients may help mitigate disease sequelae and reduce associated complications and mortality rates.

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REVIEW ARTICLE

# THE IMPACT OF COVID-19 IN OLDER ADULTS: A LITERATURE REVIEW

O IMPACTO DA COVID-19 NA POPULAÇÃO IDOSA: REVISÃO BIBLIOGRÁFICA

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## ABSTRACT

**Objective:** This study aimed to highlight the impact of COVID-19 in older adults, identifying the problems faced by this population during the pandemic. **Methods:** A bibliographic search was performed in the Scielo database in December 2020, using the Portuguese and Spanish languages, resulting in 1,643 studies. The insertion of a new filter, "COVID and elderly population", resulted in 71 studies. Those that included the terms "elderly people and COVID-19" in the title were selected; after removing duplicates, six studies were selected. **Results**: Older adults with multimorbidities presented an increased risk of severe COVID-19. The information disclosed by the countries was heterogeneous since they present unique characteristics, and the way the governments inform and prepare to receive older adults differs among countries. The pandemic also caused and amplified cases of violence against older adults, including discrimination against them. **Conclusion:** The COVID-19 virus pandemic caused and exacerbated several problems for older adults. The evaluated studies evidenced that older adults are part of the risk group and that the association of age and comorbidities increases the risk of complications. The presence of increased violence in different aspects and inappropriate communication in general, such as cybernetic and television fake news, was also evidenced. The Unified Health System plays an important role in the Family Health Strategy to alleviate social inequities, control chronic diseases and their prevention, reduce comorbidities, and diminish the susceptibility of older adults to diseases. The COVID-19 pandemic brought important reflections on implementing public social and health policies that ensure the clarification and rights of older adults.

**Keywords**: COVID-19; Elderly

## RESUMO

**Objetivo:** O presente estudo buscou evidenciar o impacto da COVID-19 na população idosa, identificando os problemas enfrentados por esse demográfico durante a pandemia. **Método:** Foi realizada busca bibliográfica na base de dados SciELO em dezembro de 2020, nos idiomas português e espanhol, resultando em 1.643 artigos. Após a inserção de novo filtro, "covid e idosos", o total foi reduzido para 71 artigos. Foram selecionados aqueles que continham no título "idoso e COVID-19" e, após desconsiderar artigos duplicados, foram selecionados 6 trabalhos que atendiam a todos os critérios. **Resultados:** Pessoas idosas com multimorbidades têm risco aumentado de apresentar a forma grave da COVID-19. Cada país veiculava informações heterogêneas sobre o tema, tendo em vista que as características de cada lugar são singulares e que há diferenças no comportamento de cada governo diante das informações e nos preparativos para atender à população idosa. A pandemia também ocasionou e amplificou casos de violência contra a pessoa idosa, inclusive a discriminação. **Conclusão:** A pandemia do vírus SARS-CoV-2 ocasionou e exacerbou diversos problemas na população idosa. Os trabalhos avaliados tratavam do fato de que os idosos constituem parte do grupo de risco e do aumento do risco de complicações com a associação de idade e comorbidades. Dentre os estudos, também foi evidenciado o aumento dos diversos aspectos da violência contra a pessoa idosa e da comunicação inapropriada, como as "Fake News" cibernéticas e televisivas. O Sistema Único de Saúde tem, a partir da estratégia de saúde da família, o importante papel de amenizar as iniquidades sociais e de controlar e prevenir doenças crônicas, diminuindo as comorbidades e a suscetibilidade de idosos a agravos. A pandemia trouxe à tona reflexões importantes sobre a implementação de políticas públicas sociais e de saúde que assegurem o esclarecimento e os direitos da população idosa.

**Palavras-chave:** COVID-19; idoso

## INTRODUCTION

The world has witnessed the evolution of an infectious pandemic named COVID-19, whose etiological agent is the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The first reports occurred in December 2019 in Wuhan (Hubei province, China) as a set of acute respiratory diseases that spread globally[1].

On January 1, 2020, the World Health Organization (WHO) promoted several actions to combat the outbreak due to the seriousness of the disease. On January 30, COVID-19 was already considered a public health emergency, and on March 11, it was characterized as a pandemic after infecting 118,000 people in 114 countries and causing 4,291 deaths[2-7]. This disease is highly infectious, and 20% of those infected develop respiratory problems[3].

The health systems of several countries collapsed due to a lack of infrastructure, human resources, equipment, and materials for the simultaneous care of thousands of infected people. In addition, the length of stay in the intensive care unit (ICU) has been extended, which increases the waiting time of critically ill patients[2]. This situation requires care protocols and makes health professionals decide who will receive the treatment that can avoid death [2,8]; the recommendation to not provide ventilators to people over 80 years old intensified this situation[2, 9].

The strong impact of COVID-19 on the population living in long-term care facilities is clear. In Brazil, estimates exceed 100,000 older adults affected, potentially the most fragile and vulnerable population. These estimates are based on a conservative assumption of total deaths, the increasing number of deaths, and others[4].

The high lethality of COVID-19 has been mostly associated with older adults or with the comorbidities most common among them[4,25,26]. Long-term care facilities are the homes of people at the most risk, and their proximity may aggravate the spread of SARS-CoV-2 infections[4, 27, 28].During the pandemic, violence against older adults has also been evidenced. Despite this, the discussion about strategies for dealing with it has been scarce worldwide[5].

The suspension of in-person activities, culminating in the closure of daycare centers, schools, and universities, and the interruption of professional activities and the transition to remote working, leads individuals to accumulate tensions inherent to full-time family life, often in precarious households with many residents[5, 7]. The fear of falling ill and losing loved ones, the reduced formal and informal social support, and uncertainty about the future are also concerns [5, 7]. Other aggravating factors worth mentioning are pre-existing discrimination against older adults and the lack of multidimensional, dynamic, and integrated protection policies to promote dignified and healthy aging [5, 32, 33].

Besides the social and economic vulnerability, most Brazilian older adults are isolated and abandoned by family members, who often lack the structural conditions to shelter and care for their relatives during old age [5, 34, 35].

Moreover, the increasing use of widely accessible social media worldwide leads to a quick spread of information, generally without adequate veracity verification [6, 42, 43]. The COVID-19 pandemic, declared in March 2020 by the WHO, amplified this situation, generating an “infodemic” phenomenon: an overload of information that hinders the disclosure of news from reliable sources [6, 44, 45].

This study found that older adults are at risk because of their age, and it increases with comorbidities. Moreover, they are more susceptible to violence in its various aspects and to be victims of the communication failures.

## METHODS

In December 2020, a bibliographic search in Portuguese and Spanish languages was conducted in the SciELO database, resulting in 1,643 studies. After inserting a new filter, “covid and elderly population”, the search yielded 71 studies. Studies whose titles included “COVID-19 and elderly population” were selected. After removing duplicates, six studies were selected.

## RESULTS

The studies on multimorbidities showed that older adults and those with chronic diseases were more likely to develop severe COVID-19[3, 10, 11, 12, 13, 14]. Multimorbidity (i.e., the presence of two or more chronic morbidities) is an important risk factor to be considered and is a predictor of risk of death [3,12,15]. Social determinants of health, such as male gender and advanced age, seems to be associated with mortality among hospitalized patients with COVID-19[1, 16]. Knowledge about the biological mechanism that increases the risk of infections among people with multimorbidity is still incipient. Despite this, an association exists between increased inflammation and decreased immune response [1, 17, 18, 19].

In Italy, the ethical issue was most evident, and they recommended the allocation of resources in the ICU; screening related to the age limit, the presence of comorbidities, and the functional status of any critically ill patient upon ICU admission; advanced medical care guidelines for patients with severe chronic diseases; and the application of palliative care after discontinuation of ICU treatment when serious complications arise[2, 20].

The United States attempted to maximize benefits by treating all patients equally, promoting and rewarding instrumental value, and prioritizing the lower-income population. The specific recommendations for allocating medical resources during the COVID-19 pandemic included maximizing benefits; prioritizing health professionals; avoiding allocating patients in order of arrival so that equality should occur for those with similar prognoses using a random allocation, similar to a lottery; being sensitive to evidence; recognizing participation in research; and applying the same principles to all patients with COVID-19 or not[2,21].

Some countries have tried to estimate the impact of mortality[4, 29, 30]. In Brazil, the number of residents in long-term care facilities and the extent to which the disease affected their mortality are unknown[4].

Violence against older adults is a complex and multi-causal phenomenon. Therefore, the ecological model proposed by the WHO was used to comprehend the processes involved in the genesis of violence and to understand the possible determinants of the increase in this type of violence during the pandemic[5,36].

This model proposes that violence, especially interpersonal, is the result of macro-structural, community, relational, and individual factors that interact and give feedback to each other, promoting scenarios that could facilitate or hinder violence. These factors were impacted by the health and economic crisis caused by the pandemic and prolonged social distancing[5].

In Brazil, as in other parts of the world, exists a culture of contempt and discrimination based on age, identified as “ageism” or “agism”, more evident in crisis scenarios. Older adults are more vulnerable to developing severe forms of the disease and require ICU admissions[5,37], demanding higher health care. As a result, discriminatory and prejudiced attitudes towards this population increased at the beginning of the COVID-19 pandemic.

Among the aspects of physical health, we highlight “immunosenescence” (decreased immune system function), which predisposes older adults to adverse outcomes concerning infectious diseases, such as COVID-19 [5,38].

Social distancing may also cause mental health problems, such as loneliness, insomnia, anxiety, loss of appetite, and depression, which further debilitate the well-being of this population[5,37,39].

The intentional spread of fake news has become part of the daily routine of older adults. Sharing this information, even if it is untrue, influences public opinion, leads to treatment abandonment, and may lead to drug interactions and aggravate pre-existing diseases, putting at risk their health and their families[6, 46, 47].

## CONCLUSION

The COVID-19 pandemic has caused and exacerbated various problems among older adults. The studies evidenced that older adults are part of the risk group and the increased risk of complications associated with age and comorbidities. The studies also highlighted the increase in various aspects of violence against older adults and inappropriate communication,

such as cyber and television fake news. The pandemic has led to important reflections on implementing public social and health policies to ensure that the rights of older adults are protected.

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# HEALTH MEASUREMENT SCALES- A PRACTICAL GUIDE TO THEIR DEVELOPMENT AND USE. OXFORD PRESS. 5A.

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In the 5th edition of the book "Health Measurement Scales - A Practical Guide to Their Development and Use", David L. Streiner, Geofrey R. Norman, and John Cairney update the main work that guides studies focused on constructing and validating instruments used in epidemiological studies worldwide. Their academic efforts coincide with the exponential increase in the publication of specific studies in instrument development and validation in the same period.

One of the main aspects to be considered when analyzing epidemiological studies is the data accuracy. Assuming that epidemiology involves a measurement exercise, the use of valid instruments for data collection becomes challenging, especially when constructs are considered, which are characteristics of human life that cannot be directly evaluated, such as intelligence, pain, quality of life, and others.

In the first edition (1989), David and Steiner highlighted important aspects of this study. In the first situation, evaluating the validity of a scale or instrument for data collection consists of developing a new scale when other tools assessing the same or similar attributes are already available. In a second situation, some references are built to evaluate attributes that were not previously measured.

Therefore, the validation process consists of applying the experimental instrument (or under analysis) along with an already valid instrument (i.e., the gold standard) to a sample to correlate them. The gold standard means the measurement is a reference for certain attributes, such as measuring blood pressure with a mercury column tensiometer. This process is described in the literature as convergent validation, criterion validation, and concurrent validity. However, this method has two limitations. The first concerns justifying the need for a new scale when others already exist, and the second refers to the difficulty of identifying flaws when the correlation between the scales is not perfect.

In the second situation, the validation involves measuring attributes that are not yet measurable, which better justifies the construction of a new scale. This process is described in the literature as construct validity. Although the validation of a scale that has no previous valid instruments may seem impossible, a validation strategy consists of applying the instrument under analysis to two or more groups in which different levels of the attributes are expected.

If the correct differentiation of admittedly different conditions can be identified using the proposed scale, the validity hypothesis can be reinforced. However, given the need to build this type of validity, a single study is not enough to validate the new scale, even if it was well -planned and robust; thus, other convergent studies are needed. A universally recognized methodology must be consistently followed for this purpose, and this is the main contribution of Streiner and Norman.

By including John Carrey in the 5th Edition, David Streiner and Geoffrey Norman point out that its updating will be permanent, with the expansion regarding the chapter on Item Response Theory (IRT), the most discussed technique today with the epistemic density and considerations that the topic requires, being absolutely crucial. Similar broadening and deepening can be seen in the chapter on "Methods of Instrument Administration" and the inclusion of a chapter on reporting results in validation studies. Therefore, for those interested in this area of knowledge, this book can be considered essential reading for those interested in this area.

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# AUTHOR GUIDELINES

Journal title: **Annals of Olinda Medical School Acronym: afmo**

Abbreviation: **Annals FMO**

Publisher: **Faculdade de Medicina de Olinda Electronic**

ISSN: **2674-8487**

Print ISSN: **2595-1734**

## SCOPE

The Journal Annals of Olinda Medical School reflects the thinking and commitment to the production of knowledge based on the social responsibility that we assume as protagonists, and as part of the Institutional Development Project of the Faculdade de Medicina de Olinda (FMO). Aiming to strengthen the inseparability of teaching, research and extension, in addition to consolidating quality education, anchored in scientific bases and ethical values, the journal was created in light of an editorial line committed to a sustainable world and focused on medicine as a profession with a strong social and humanized component.

**The Journal Annals of Olinda Medical School - Health Social Responsibility**, was created in 2018. Since then, it has been the official vehicle of the Olinda School of Medicine to support its principles, especially those related to encouraging research, teaching, and professional medical practices. It is an important instrument for disseminating knowledge, allowing exchange with other areas that favor medicine and the community, and enabling improvement of the standard care provided to the population. Since its inception, Anais FMO has faithfully complied with the requirements for biannual online and printed periodicity for scientific publication, following the recommendations of the International Committee of Medical Journal Editors (www.icmje.org) , which are commonly used in the areas of medicine and related sciences. Currently, Anais FMO is duly registered as a journal in the ISSN system. Articles are published in a continuous flow and all are free and open access, offered through the link https://afmo.emnuvens.com.br. By publishing their article in Anais FMO, authors transfer copyright to the journal and grant it the right of first publication. Manuscripts are submitted online through the platform, available at https://afmo.emnuvens.com.br/afmo/about/submissions.

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Manuscripts must be sent in Word, dou- ble-spaced, and Arial font size 12. Do not use line breaks. Do not use force manual hyphenations. The full term must follow abbreviations cited for the first time in the document. Title and abstract must not contain abbreviations.

## Title page

**Title of the manuscript in Portuguese and English** (up to 25 words for each title);

**Author information** (full name, email, ORCID, affiliation, city, state, and country — do not include title and position);

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**Conflicts of interest**, in accordance with the Resolution of the Federal Council of Medicine (CFM) no. 1595/2000, which prohibits the publication of works for advertisement purposes of medical products and equipment, available at https://sistemas.cfm.org.br/normas/visualizar/resolucoes/BR/2000/1595. Conflicts of interest must be presented as follows: “The author(s) (name them) received financial support from the private company (mention its name) to conduct this study”. If there are no conflicts of interest, the authors must declare: “The authors have no conflicts of interest to declare”.

**Source of financing**, stating whether public or private; if there is none, mention that the study was not funded;

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**Authors contribution to the manuscript.**

On the following pages, always starting on a new page, the following sections must be presented:

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Authors must include a minimum of four and a

maximum of six keywords in both English and Portuguese regardless of the language in which the manuscript was submitted.The key- words must be standardized according to the Health Sciences Descriptors (DeCS), available at http://decs.bvs.br/.

### References

References must be numbered consecutively according to the first mention in the manuscript and using superscript Arabic numerals in accordance with Vancouver style (www.icmje.org). The reference list must follow the numerical order of the manuscript, ignoring the alphabetical order of authors. Journal titles must follow the Index Medicus/Medline. The name of the first six authors must appear, followed by the expression et al. when this number is exceeded. Whenever available, the Digital Object Identifier (DOI) must be provided (see examples below). Personal communications, unpublished or ongoing work, citations from books, thesis, and dissertations should be avoided. The accuracy of references is the responsibility of the authors.

### EXAMPLES

#### Reference to a journal publication:

Ng OT, Marimuthu K, Koh V, Pang J, Linn KZ, Sun J, et al. SARS-CoV-2 seroprevalence and transmission risk factors among high-risk close contacts: a retrospective cohort study. Lancet Infect Dis. 2021 Mar; 21(3):333-343. doi: 10.1016/S1473-3099(20)30833-1

Jardim BC, Migowski A, Corrêa FM, Azevedo e Silva G. Covid-19 no Brasil em 2020: impacto nas mortes por câncer e doenças cardiovasculares. Rev Saude Publica. 2022; 56:22. https://doi.org/10.11606/s1518-8787.2022056004040.

#### Reference to a World Health Organization Report

World Health Organization. Clinical Care for Severe Acute Respiratory Infection—Toolkit—Update 2022. Genebra: World Health Organization; 2022.

#### Reference to electronic documents

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### Figures and tables

Figures and tables must be inserted at the end of the manuscript, followed by their respective captions. Submission in separate files is not permitted. There must be page breaks between each one, respecting the maximum number of three pages for tables and figures combined. Do not format tables using the TAB key.

Figures must be up to 15 cm wide in Portrait orientation and 24 cm wide in landscape orientation and be presented within the requested margin (Normal Word setting). Colored figures are accepted. Figures must be provided in high resolution, plots in editable format, and tables, equations, charts, and flowcharts must be sent in an editable file (Word or Excel), never as an image.

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