



Aggregation of cardiovascular risk factors as a predictor of negative outcome in individuals affected by Covid-19

Agregação de fatores de risco cardiovascular como preditor para desfecho negativo em indivíduos acometidos por Covid-19

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ABSTRACT | OBJECTIVE: To verify whether the aggregation of cardiovascular risk factors (CVRF) is a predictor for negative outcomes in individuals affected by COVID-19. **METHODS:** Epidemiological study with secondary data on COVID-19 in Salvador/Bahia, from March to December 2020. There were 10,077 records obtained from the database made available by the Centro de Informações Estratégicas de Vigilância em Saúde (Center for Strategic Information on Health Surveillance) in the municipality of Salvador. **RESULTS:** The mean age of the individuals was 60.40 years (sd ± 19.30), most of them male (53.88%), mixed race/color (71.83%) and attended high school (43.53 %). Diabetes mellitus was present in 48.83% of people, chronic heart disease in 60.58%, and a mean BMI of 34.79 (SD ± 8.48). Most hospitalizations (52.79%) progressed to ICU admission after 1.20 days (sd ± 4.03). The mean ICU stay was 8.76 days (SD ± 11.17). Most of these individuals were cured (61.88%), but 37.97% died. In the association of outcomes, 54.83% (p<0.01) of people with heart disease and 54.71% (p<0.01) with diabetes were cured of COVID-19. Among the individuals who did not go to the ICU, 85.43% (p<0.01) were cured and 55.90% (p<0.01) of those who were, died. Descriptive analysis of CVRF accumulation did not point to differences in the outcome when one or more associated factors are present. **CONCLUSION:** the presence of one or more CVRF was not a predictor for a serious outcome in individuals with COVID-19 in the city of Salvador in 2020.

KEYWORDS: COVID-19 Virus Infection. Heart Disease Risk Factors. Cardiovascular Diseases.

RESUMO | OBJETIVO: Verificar se a agregação de fatores de risco cardiovascular (FRCV) é preditora para desfechos negativos em indivíduos acometidos por COVID-19. **MÉTODOS:** Estudo epidemiológico com dados secundários sobre COVID-19 em Salvador/Bahia, de março a dezembro de 2020. Houve 10.077 registros obtidos através do banco de dados disponibilizado pelo Centro de Informações Estratégicas de Vigilância em Saúde do município de Salvador. **RESULTADOS:** A média de idade dos indivíduos foi 60,40 anos (dp ± 19,30), a maioria sexo masculino (53,88%), raça/cor parda (71,83%) e cursou ensino médio (43,53%). Diabetes mellitus estava presente em 48,83% das pessoas, cardiopatia crônica em 60,58%, e IMC médio de 34,79 (dp ± 8,48). A maioria das internações (52,79%) evoluiu para admissão em UTI, após 1,20 dias (dp ± 4,03). A média de permanência na UTI foi 8,76 dias (dp ± 11,17). A maioria desses indivíduos evoluiu para a cura (61,88%), porém 37,97% foram à óbito. Na associação dos desfechos 54,83% (p<0,01) das pessoas com cardiopatias e 54,71% (p<0,01) com diabetes ficaram curadas da COVID-19. Dentre os indivíduos que não foram para UTI 85,43% (p<0,01) ficaram curados e 55,90% (p<0,01) dos que foram evoluíram à óbito. Análise descritiva do acúmulo de FRCV não apontou diferenças no desfecho quando se tem um ou mais fatores associados. **CONCLUSÃO:** A presença de um ou mais FRCV não foi preditor para desfecho grave nos indivíduos com COVID-19 no município de Salvador em 2020.

PALAVRAS-CHAVE: Infecção por Vírus COVID-19. Fatores de Risco de Doenças Cardíacas. Doenças Cardiovasculares.



Introduction

The new coronavirus (Sars-Cov-2) was discovered in December 2019, in the city of Wuhan, China.¹ The increase in the number of cases of COVID-10 caused by the new coronavirus and its rapid global dissemination resulted in the decision of the World Health Organization (WHO) to declare a pandemic on March 11, 2020.²

By April 6, 2020, there were already 9,056 confirmed cases of the disease in Brazil and 359 deaths.³ In Bahia, the first case was confirmed in Feira de Santana, on March 6, 2020, and in the state capital, Salvador, the first case was notified on March 11, 2020. Since the first notification, the state of Bahia still presents an increase in the number of cases of COVID-19, however with oscillations in the measure of the intensity of notifications and varied incidence of periods of decline and stability.

The number of cases in Salvador between March and December of 2020 was already of 103,262. In this period, the population most affected by the disease in the city was of the male gender, age group ≥ 80 years, and cases of lower incidence in adults were of women in the age groups of 40 to 49 years. The number of deaths reached 4,237, with an average of 13 deaths per day.⁴

Pathophysiology and the clinical aspects of COVID-19 continue to be intensively researched and its main characteristics have already been elucidated for an improved understanding of the replication and infection process of the virus. It was initially believed that the Sars-Cov-2 was substantially transmitted through direct contact and mainly through the airways (respiratory droplets or aerosols), possible blood and fecal samples of patients, or fomites contaminated by the virus (surface contamination).⁵ Nevertheless, some recent studies contest contamination through surfaces as being low or often improbable. Under normal conditions, the quantity of viral particles deposited on surfaces would not be capable of infecting solely through contact.^{2,6,7} The Sars-Cov-2 incubation period lasts around 5.1 days⁸ and its main entry point to the body is through the receptor of the angiotensin- converting enzyme 2 (ECA-2). This enzyme can be found in the endothelial cells of the lungs, kidneys, heart and other organs.⁹

It is known that the course of this disease varies for each individual, and the main symptoms presented are fever, nasal congestion, anosmia, ageusia, dry cough, throat ache, fatigue, myalgia, dyspnea, nausea and anorexia.⁵ However, WHO data indicates that people over 60 years of age, with cardiovascular risk factors, are among the most vulnerable groups for complications, with higher risks for evolving into serious clinical outcomes.¹⁰

Cardiovascular risk factors are advanced age, diabetes mellitus (DM), systemic arterial hypertension (SAH), dyslipidemia and obesity, among others. Aggregation of such factors may be considered a concerning condition for these patients who, in the case of an infection by the Sars-Cov-2, increase the risk of evolving to an ICU, longer period of hospitalization and consequent death. The combination of all of these factors is a widely discussed reality when dealing with COVID-19.¹¹

People with cardiovascular diseases are among the groups that are more prone to COVID-19 complications and, accordingly, more likely to die than those without any comorbidities.⁵ Such information corroborates the preliminary results of Chinese studies that point out these individuals as the main groups of risk for complications from the disease. For patients with coronary artery diseases, there is greater severity, and mortality can reach 10.5% when the overall average is of 2.3%.¹² Among the guarded prognosis are patients presenting any prior comorbidity and/or associated cardiovascular risk factors (CVRF), such as advanced age, SAH, obesity, type 2 DM, or previous history of cardiovascular diseases.¹³

Contributions from this research are indirect once the study performed a situational diagnosis, extending local information on COVID-19 and aimed to verify whether the aggregation of cardiovascular risk factors (CVRF) in an individual results in negative outcomes of the disease. It is, therefore, considered that this study can contribute towards the development of strategies in the healthcare of individuals who contracted COVID-19 in relation to the aggregation of cardiovascular risk factors, which could minimize failures of healthcare teams towards this population and at-risk groups. It could also favor the definition and implementation of effective care in the field practice of nurses, as well as favoring the prevention

and control of the disease in the capital of Bahia and, consequently, improve the quality of the Sistema Único de Saúde - SUS (Unified Health System).

Considering that local data on the epidemiological behavior of COVID-19 are still scarce and that the effects of the disease in Brazil and in their different regions could present a different scenario, the present study aims to verify whether the aggregation of cardiovascular risk factors is a predictor for negative outcomes in individuals affected by COVID-19 in the municipality of Salvador/Bahia.

Method

This is an epidemiological analytical study. Secondary data of patients hospitalized with the diagnosis of COVID-19 in 2020 in Salvador/Bahia was used (between the months of March and December), obtained through the databank made available by Centro de Informações Estratégicas de Vigilância em Saúde "CIEVS" (Strategic Information on Health Surveillance Center) in the municipality of Salvador (CIEVS- SMS/SSA) consisting of information extracted from mandatory electronic notifications. Data collection was performed after authorization from the CIEVS - SMS/SSA in May 2021 and approval from the Research Ethics Committee (CAAE: 42994521.7.0000.5544).

The inclusion criteria considered were all confirmed cases of COVID-19 occurred in Salvador/Bahia, with hospitalization, during the period of March to December 2020. Variables used on the databank were: gender, age, race/color, schooling, comorbidities (cardiovascular disease and diabetes), body mass index (BMI), hospitalization (number of days and which unit: emergency, ward or intensive care) and outcome (cure or death). According to information from the literature, the CVRFs considered were advanced age (over 60 years), race/color black (black and brown), male gender, obesity, diabetes mellitus and prior history of heart disease. Negative outcomes considered were hospitalization in the ICU and/or death. The databank included a total of 10,077 patients.

Data was input on an Excel® file and after adjustment and clearing, migrated and processed on a software R® and presented in tables and graphs. These were analyzed in absolute frequency, and mean value and standard deviation calculated for age, body mass index (BMI) and days of hospitalization. To verify the association between sociodemographic variables and cardiovascular risk factors, the Pearson chi-square test or Fisher Exact tests were applied, and the statistical significance adopted was of 5% for all the tests.

Cases registered as "without information" were excluded for any of the selected variables. Underreported data (missing data) was described under results. A statistics professional verified the distribution, made tests and the proportional adjustment of cases to increase the power of the study.

The risk involved in performing this research with the use of secondary data refers to the breach of data confidentiality. Such risk was mitigated with the use of a safe platform for storing the information, as well as anonymizing the analyzed data and the ethical commitment of the researchers.

Results

The databank consisted of 10,077 registers of individuals with COVID-19 between the months of March and December 2020 in Salvador/Bahia. The lowest age was of 0 years and highest of 110 years, with an average of 60.40 years (sd ± 19.30 years), with 56.24% over the age of 60 years and a higher proportion of the male gender (53,88%). Regarding race/color (38.39%) and schooling (74.10%) the information was not input to the databank for lack of register. Thus, considering the loss of registers, most of the individuals were of race/color brown (71.83%) and secondary education (43.53%) (Table 1).

Table 1. Sociodemographic characteristics of individuals with Covid-19 in the period of March to December 2020 in Salvador, Bahia, Brazil

Sociodemographic characteristics	n	%
Gender (n=10,077)		
Female	4,648	46.12
Male	5,429	53.88
Age (n=10,077)		
<60	4,469	44.34
≥ 60	5,608	56.24
Race/Color (n=6,208)		
White	833	13.42
Yellow	55	0.89
Brown	4,459	71.83
Black	855	13.77
Indigenous	6	0.10
Schooling (n= 2,610)		
No schooling / Illiterate	162	6.20
Elementary education 1 st cycle (1 st to 5 th grade)	409	15.67
Elementary education 2 nd cycle (6 th to 9 th grade)	356	13.64
Secondary education (1 st to 3 rd year)	1,136	43.53
Higher education	547	20.96

Source: CIEVS- SMS/SSA - Strategic Information on Health Surveillance Center of the Municipality of Salvador.

According to the information in the databank, diabetes mellitus (DM) is present in 48.83% of individuals infected by the COVID-19, and heart disease in 60.58% of these patients. In relation to body mass index (BMI) it is possible to highlight a high percentage of individuals with BMI ≥ 30 (90.75%) with an average of 34.79 (sd ± 8.48) (Table 2).

It should be noted that some information was not registered in the databank. Out of the 10,077 registers, the absence of data reached 3,587 (35.59%) for diabetes, 3,378 (33.52%) for chronic heart disease and 9,714 (96.40%) for BMI.

Table 2. Clinical characteristics of individuals with Covid-19 in the period of March to December 2020, in Salvador, Bahia, Brazil

Clinical characteristics	n	%
Diabetes (n=6,490)		
Yes	3,169	48.83
No	3,321	51.17
Chronic heart disease (n=6,699)		
Yes	4,058	60.58
No	2,641	39.42
BMI (n=346)		
18.5 – 24.9	4	1.16
25 – 29.9	28	8.09
≥ 30	314	90.75

Source: CIEVS- SMS/SSA - Strategic Information on Health Surveillance Center of the Municipality of Salvador.

During hospitalization of individuals with COVID-19, emphasis is given to the fact that most of the cases evolved to admission in intensive care units (52.79%), after an average of 1.20 days (sd ± 4.03) in the ward and/or emergency. Average permanence in the ICU was of 8.76 days (sd ± 11.17). Among the outcomes, it was observed that the majority of these individuals evolved to a cure (61.88%), however 37.97% died due to COVID-19 (Table 3).

Table 3. Clinical evolution of individuals with COVID-19 in the period of March to December 2020, in Salvador, Bahia, Brazil

Clinical evolution	n	%
ICU (n=9,449)		
Yes	4.988	52,79
No	4.461	47,21
Outcome (n= 9,065)		
Cure	5.609	61,88
Death	3.442	37,97
Death through other causes	14	0,15

Source: CIEVS- SMS/SSA - Strategic Information on Health Surveillance Center of the Municipality of Salvador.

Table 4 presents the associations between sociodemographic data and cardiovascular risk factors and the outcome of individuals with COVID-19. With reference to the sociodemographic variables, it is possible to observe that both genders have similar values among both outcomes, with emphasis on the male gender with a higher number of deaths (53.6%) than the female gender (46.0%), followed by the race/color variable, with a higher number of deaths in the population with brown skin (70.0%).

It is important to note that patients presenting some form of heart disease had a high number of deaths (67,2%) in comparison to the population without any cardiopathy (32.8%). In the population with diabetes, 54.1% died. Among patients with some cardiovascular risk factor (CVRF) and were admitted to the ICU, 81.9% died.

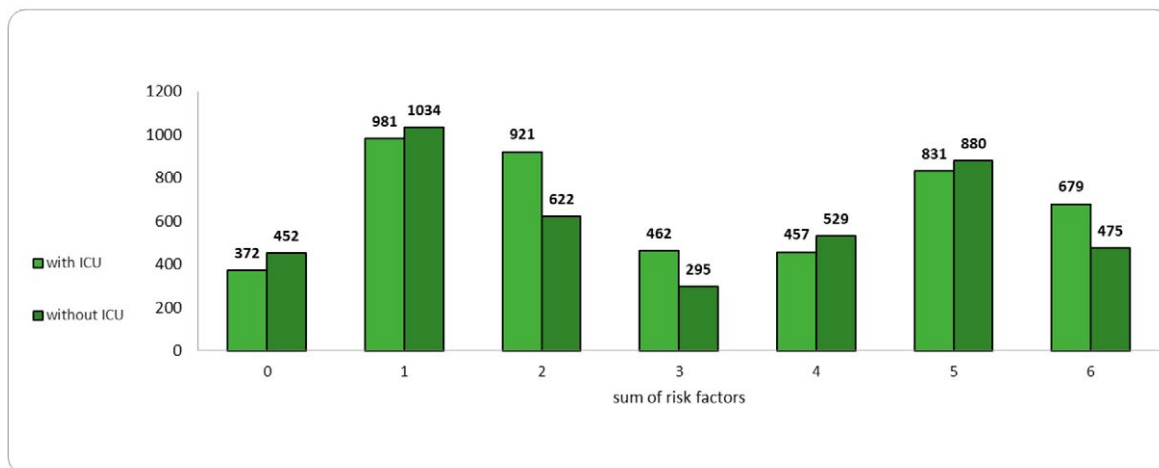
Table 4. Association between sociodemographic data and cardiovascular risk factors with outcomes of cure or death in individuals with COVID-19, in the period of march to December 2020, in Salvador, Bahia, Brazil

Variables	Cure n (%)	Death n (%)	P Value
Gender			0.7187
Female	2,579 (46.0%)	1,596 (46.4%)	
Male	3,030 (54.0%)	1,846 (53.6%)	
Race			<0.01*
White	490 (14.1%)	277 (13.1%)	
Black	442 (12.7%)	342 (16.2%)	
Yellow	30 (0.9%)	16 (0.8%)	
Brown	2,502 (72.2%)	1,481 (70.0%)	
Indigenous	3 (0.1%)	1 (0.0%)	
Heart disease			<0.01
Yes	2,037(57.0%)	1,678 (67.2%)	
No	1,538(43.0%)	818 (32.8%)	
Diabetes			<0.01
Yes	1,586 (45.6%)	1,313 (54.1%)	
No	1,895(54.4%)	1,113 (45.9%)	
BMI			0.0619
18.5 – 24.9	3 (1.26%)	1 (0.92%)	
25 – 29.9	14 (5.88%)	14 (12.97%)	
>= 30	221 (92.86%)	93 (86.11%)	
ICU			<0.01
Yes	2,045 (37.9%)	2,592 (81.9%)	
No	3,353 (62.1%)	572 (18.1%)	

Source: CIEVS- SMS/SSA - Strategic Information on Health Surveillance Center of the Municipality of Salvador.

Graph 1 represents the sum/aggregate of CVRFs in individuals with COVID-19 who evolved or not for hospitalization in intensive care units (ICU). According to data from the literature, the CVRFs considered were advanced age (over 60 years), race/color black (black and brown), male gender, obesity, diabetes mellitus and prior history of heart disease. It should be observed that considering two aggregate factors, the possibility of hospitalization in the ICU for COVID-19 patients increases. Nevertheless, it also stands out that the majority of individuals with four or five aggregated CVRFs were not hospitalized in ICUs.

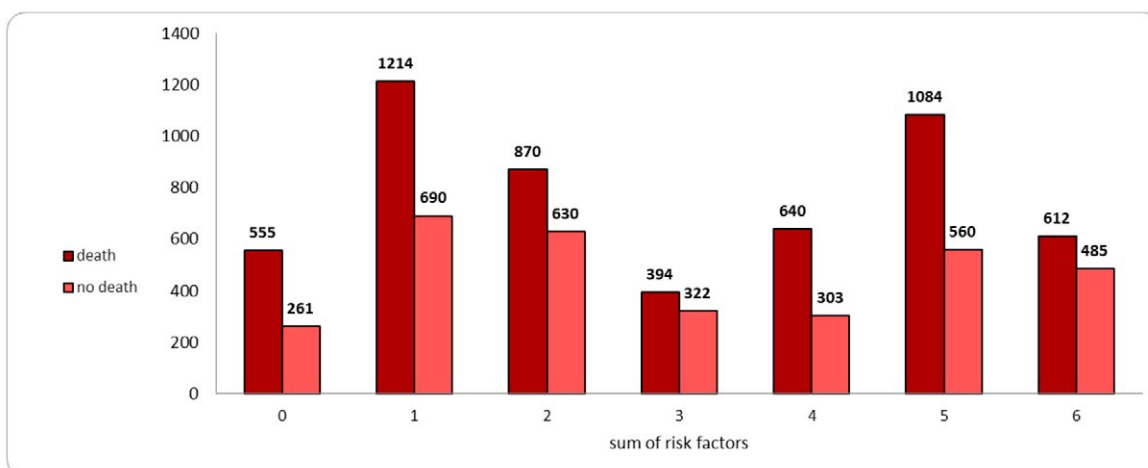
Graph 1. Aggregated CVRFs of participants according to the outcome of hospitalization in the ICU in the period of March to December 2020, in Salvador, Bahia, Brazil



Source: CIEVS- SMS/SSA - Strategic Information on Health Surveillance Center of the Municipality of Salvador.

In Graph 2 the sum/aggregate of CVRFs is presented for individuals with COVID-19 that evolve or not to death. This graph also considers as CVRFs advanced age (over 60 years), race/color black (black and brown), male gender, obesity, diabetes mellitus and history of heart disease. It can be observed that the number of deaths was always higher in patients with one or more CVRF, however, this increase was not linear, ascending. There were more deaths where there was only one CVRF or five aggregate factors.

Graph 2. Aggregation of the CVRFs in participants according to the outcome of death in the period of March to December 2020, in Salvador, Bahia, Brazil



Source: CIEVS- SMS/SSA - Strategic Information on Health Surveillance Center of the Municipality of Salvador.

Discussion

During the COVID-19 pandemic, the presence of risk factors and pre-existing cardiovascular conditions alarmed the scientific community once many studies observed the increase in morbimortality in patients presenting one or more comorbidities and who caught COVID-19, mainly in patients who evolved to more serious cases and had to be admitted to ICUs.^{9,14}

Researches worldwide demonstrated a high number of patients hospitalized with COVID-19 who presented some cardiovascular risk factor, or heart disease.¹⁵⁻¹⁷ In Wuhan, China, a research carried out at the beginning of the pandemic to identify clinical characteristics of patients, pointed out that over half of those infected were of the male gender (73%), with average ages of around 49 years, and 32% of the total number of infected patients presented some risk factor, such as hypertension (15%), diabetes (20%) and pre-existing cardiovascular diseases (15%).¹⁸

Studies indicate that hypertensive and diabetic individuals could have an increased risk for hospitalization and death in cases of COVID-19. This information favored greater care and protection of individuals with these pathologies and other cardiovascular diseases during the pandemic, and even the Brazilian National Immunization Program considered these individuals and priority for vaccination.^{19,20}

Another factor of emphasis is obesity. Increased body weight can also contribute towards worsening clinical conditions, having observed that these patients have a greater risk of developing severe acute respiratory syndrome (SARS), requiring the use of invasive mechanical ventilation when hospitalized in ICUs. These researches also observed that the prevalence of complications for these groups was identified mainly in individuals with BMI ≥ 35 , with a consequent increase in the mortality rate.²¹

The greater susceptibility of these individuals could be justified by the metabolic syndrome resulting from obesity, since a lot of these patients develop other pathologies such as dyslipidemia, hypertension and diabetes. The consequence is the increase of proinflammatory mediators, such as interleukin 6, as well as cytokines and adipokines, increasing type-

2 inflammation which can act mainly in pulmonary parenchyma.²²

Most of the findings in the present study corroborate with the data from the literature where it is possible to observe that the rate of individuals infected with the COVID-19 in the municipality of Salvador with high BMI ≥ 30 and cardiopathy corresponds to a higher number than when compared to individuals who do not present these factors. Furthermore, the number of individuals of the male gender affected by the disease was greater than for the female gender, as well as individuals of age group ≥ 60 years. However, the percentage of individuals affected by COVID-19 in patients with diabetes was lower than those without diabetes.

Nevertheless, from the analysis of associations, it was identified that there was a statistically significant relation between having heart disease or diabetes and dying because of COVID-19, both associations with $p=0.01$. It was observed that the number of patients with heart disease and diabetes is very high in the municipality and should be of importance in the creation of health measures for such population. In the same manner, it was evidenced that the negative outcome of death was high for patients with BMI ≥ 30 , however, no statistically significant proportional differences were identified between the type of outcome (cure or death) in relation to the BMI value. As expected, the higher proportion of individuals who died were hospitalized in ICUs, and it should be emphasized that the proportional differences found were statistically significant ($p=0.01$).

The justification for the correlation between the CVRFs and heart diseases with the seriousness of the COVID-19 can be explained with the connection between the Spike protein of the virus and the angiotensin- converting enzyme 2 (ECA-2), which is present in many tissues of the human body, among which the lungs, heart and blood vessels. The virus uses the enzyme active site to enter human cells. The renin-angiotensin-aldosterone system, of which the ECA2 is a part of, is one of the main systems responsible for the equilibrium of the cardiovascular and immunological systems. Accordingly, the expression and viral replication can affect the systems, increasing viral concentration in certain tissues, causing more serious damages, triggering a negative response to the body.¹⁴

Moreover, the increase in cytokines that can induce an inflammatory cardiac response can also be a justification for a higher risk of deterioration in this population, once patients with COVID-19 present a high level of troponin, d-dimer, C-reactive protein (CRP), among other markers. Thus, these patients could have even more heart complications, such as myocarditis and heart failure, with consequent death.¹²

Admission to an intensive care unit is another problem observed during the pandemic. Many patients presenting aggregated CVRFs or not, can quickly evolve to a UCI requiring mechanical ventilation and more intensive care.²³ The reality observed in the period of the study was an increase in the number of cases, with a high percentage of occupation of UCI beds and consequent running out of available hospital beds, mainly in large-sized hospitals in the municipalities of Brazil and in Salvador/BA.

Regarding the negative outcome of COVID-19, in the present study it was observed that the existence of one or more FCRVs did not have a direct relationship with the ICU hospitalization rates in the municipality of Salvador/BA, nor in the increase of deaths. This data differs from a research performed in Acre where all the cases of COVID-19 notified until September 1, 2020 (24,389), showed the presence of multi-morbidities such as obesity, arterial hypertension and diabetes as the main aggregated factors which summed to the respiratory infection, led the individuals to be hospitalized in ICUs, with the outcome of deaths.²⁴ In this case there is information bias such as the seriousness of the infection and the quality/resource of the healthcare provided that could have impacted the results.

Limitations of the present study refer to the fact that it was performed from secondary data extracted from the COVID/2020 Databank, some information having been underreported. However, statistical tests performed aim to maintain the power of the study.

Despite the limitations, this study presents relevant data on COVID-19 in Salvador/BA and its relationship with CVRFs. Results may instrumentalize healthcare professionals, mainly nurses, in conducting healthcare actions and healthcare education guided towards groups of risk; accordingly, contributing to the definition and implementation of effective

healthcare, prevention and control strategies of COVID-19 in the capital city of Bahia.

Conclusion

Individuals, mostly adults, over the age of 60 years, male gender, race/color brown, having secondary education, and hospitalized due to COVID-19 in the municipality of Salvador in 2020, did not have as a predictor for serious outcomes (hospitalization in ICU and/or death) the aggregation of cardiovascular risk factors (advanced age, race/color black, male gender, obesity, diabetes mellitus and history of heart disease). However, the isolated analysis of these factors point out statistically significant differences associated with the type of outcome.

Studies such as this can be considered as sources of information/guidance for the planning of interventions and favoring an effective healthcare by health professionals in individuals affected by the COVID-19 in this municipality.

Contributions of the authors

Santana GCS contributed with data collection. Oliveira LB performed statistical analysis. Mendes AS and Lordello GGG worked in the writing and/or critical review, as well as on the approval of the final version. Gama GGG performed the conception and planning of the project, writing and/or critical review, and approval of the final version. All of the authors participated in the data analysis and interpretation.

Conflicts of interest

No financial, legal or political conflicts involving third parties (government, private companies and foundations, etc.) were declared for any aspect of the work submitted (including but not limited to subventions and financing, participation in advisory boards, study design, preparation of the manuscript, statistical analysis, etc.).

Indexers

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