**Comorbidities and associated factors with death in patients hospitalized for COVID-19 at the Infectious Diseases Department of the El Hadji Ibrahima Niasse Regional Hospital of Kaolack, Senegal.**

**Abstract**

**Introduction**: COVID-19 is a systemic zoonosis with predominant respiratory tropism caused by coronavirus. It was declared a public health emergency and a pandemic in March 2020. Following the opening of the first CTE at Fann in Dakar, an Outbreak Care Center was established at Kaolack Hospital. This study aimed to evaluate comorbidities and risk factors in patients hospitalized for COVID-19 in this center. **Methodology**: This is a retrospective, descriptive, and analytical cross-sectional study conducted from February 4 to September 28, 2021, on 76 patients with COVID-19. **Results**: The median age of the patients was 61.5 (18 – 90) years. The dominant age group was 60 and Males (51.3%) with a sex ratio of 1.05. Hypertension was the main comorbidity (34.2%) followed by Diabetes (23.7%). The average length of hospital stay was 6.7 days (0 - 35 days). Symptomatic patients accounted for 94.7%. The most common functional signs were cough (90.8%) and dyspnea (77.6%). Anemia was present in 69.7% and CRP 100%. Age was a significant risk factor for severity and mortality (p-value<0.05). Thirteen (17.1%) patients died. **Conclusion**: COVID-19 disease is a serious infectious disease with high lethality in senior. Effective prevention is essential.

**Keywords**: COVID-19, comorbidities, risk factors, lethality, Senegal

1. **Introduction**

Corona Virus Disease 2019 (COVID-19) is a respiratory infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [1]. The virus was first identified in a group of patients presenting with atypical pneumonia in the city of Wuhan, China, in December 2019 [1]. This emerging disease became a pandemic following the announcement by the World Health Organization (WHO) on March 11, 2020 [2]. As of May 28, 2020, the number of patients contracting Covid-19 worldwide was 5,821,739, of whom 358,104 (6.15%) died and 2,522,202 (43.32%) recovered [3]. At the end of 2020, the number of confirmed cases was approximately 85 million and there were more than 1.8 million deaths worldwide [4]. One years after, it was estimated that 153 million people had been infected with the SARS-CoV-2 virus and that the coronavirus disease had caused 3.2 million deaths worldwide, of which 3% in Africa, 34% on the European continent and 19% in North America [5]. On March 2, 2020, Senegal reported its first case of COVID-19 [6] prompting the implementation of health measures by the Senegalese government. After the initial two waves of the pandemic, as of November 1, 2021, Senegal had recorded 73,920 confirmed cases, 72,025 recoveries, and 1,878 deaths. Dakar region has the highest number of cases (48,732), followed by Thies (7,849) and Diourbel (3,294) [7]. In Kaolack, a region of Senegal located in the groundnut basin, efforts to combat coronavirus disease were also underway, with a total of 2,570 cases as of November 1, 2021 [7]. Numerous studies have highlighted advanced age, male gender, and comorbidities such as diabetes, hypertension, and coronary heart disease as risk factors for mortality [3, 5, 8]. In light of this, we propose to describe the epidemiological, clinical, paraclinical, and evolutionary profile of the epidemic from February to September 2021 in the El Hadji Ibrahima Niass Regional Hospital in Kaolack (CHREINK) infectious diseases department, to describe the risk factors associated with Covid-19 and the comorbidities found in the Outbreak Care Center (OCC).

1. **Material and method**
	1. **Study setting**

The study was carried out in the Infectious Diseases Department, which was transformed into an Outbreak Care Center for COVID-19 purposes, of the El Hadji Ibrahima NIASS Regional Hospital located in the Kaolack region. The OCC had a capacity of twenty beds, including two intensive care beds. The staff consisted of 7 doctors, 1 senior nurse on duty, 12 nurses, 4 hygiene officers, and 1 surface technician trained in biocleaning. The Covid-19 resuscitation unit was managed by a resuscitator and a team of 8 nurses. Additionally, the Kaolack Regional Hospital houses several other departments such as Emergency, Internal Medicine, Cardiology, Infectious Diseases, Pediatrics, Pneumology, Otolaryngology, Ophthalmology, Gynecology, Nephrology, Anesthesia and Intensive Care, and a Diagnostic and Medical Imaging Center.

* 1. **Type and Period of study**

This is a cross-sectional retrospective, descriptive and analytical study, conducted from February 4 to September 28, 2021.

* 1. **Study population**

All patients hospitalized in the Infectious Diseases Department for COVID-19 and whose COVID-19 PCR or RDT came back positive were included in the study. Patients with incomplete records were not included in the study.

* 1. **Data collection**: data were collected using a form based on the records of patients admitted to the CHREINK Infectious Diseases Department for COVID-19 during the study period.

The parameters studied included:

* Socio-demographic data: gender, age;
* Clinical data including:
* Time from onset of symptoms to hospitalization, functional and general signs,
* Physical signs: oxygen saturation, signs of severity, and case type according to WHO clinical criteria:
* Simple case: symptomatic, non-hypoxic patient with no apparent viral pneumonia;
* Moderate cases: symptomatic patients with oxygen saturation above 90% and signs of moderate pneumonia;
* Severe cases: symptomatic patients with one of the clinical signs of severity.
* Signs of severity include Dyspnea, Cyanosis, Thoracoabdominal rocking, Oxygen saturation below 94%, Tachycardia or bradycardia, Hypo or hypertension, and Neurological signs (agitation, confusion, obnubilation, and coma)
* Comorbidities: diabetes, hypertension, chronic kidney disease, cardiovascular disease, asthma, COPD, etc.
* Biological data: Hemogram, C-reactive protein (CRP), urea, creatinine, Blood crasis: prothrombin rate (PT), blood ionogram.

Data are interpreted as follows:

* Hemogram: normal hemoglobin levels are between 13-18g/dl in men and 12-16g/dl in women. In case of deficiency, anemia is classified as normocytic (normal MCV), microcytic (decreased MCV), or macrocytic (increased MCV).
* CRP is negative if less than or equal to 6mg/l and positive if less than or equal to 6mg/l.
* Blood urea levels and blood creatinine levels are elevated when greater than 0.5g/l and 13mg/l, respectively.
* Normal prothrombin rate is above 70%.
* The normal blood ionogram is as follows: sodium 135-145 mEq/l, potassium 3.5-5 mmol/l, and chlorine 90-100 mmol/l.
* Outcome: favorable, death, transfer to intensive care unit
	1. **Data entry and analysis**
* Data entry was performed using Excel, and data analysis was carried out using R software version 4.0.5. We performed descriptive analysis and analytical analysis.
* In the descriptive analysis, qualitative variables were described by numbers and percentages; and quantitative variables by mean, standard deviation, extremes, and median.
* The analytical study consisted of a comparison between the knowledge criteria with the other variables on the one hand, and examining correlations on the other. Pearson's Chi-square test, Fisher's two-tailed exact test, or Yates' exact test were used to compare proportions, depending on their applicability. The Student's t-test or Welch's t-test was used for comparisons of two means, and the ANOVA or Kruskal Wallis test for comparisons of several means. Statistical significance was determined when the p-value was strictly less than 0.05.
1. **Results**
	1. **Epidemiological aspects**

Out of a total of 124 cases, 76 were included, representing a retention rate of 61.3%. The median age of the patients was 61.5 years, with extremes of 18 and 90 years. The dominant age group was 60 and over. We noted a male predominance (51.3%) with a sex ratio of 1.05. In our study, the reported comorbidities were mainly hypertension (34.2%) and diabetes (23.7%). Other comorbidities were cardiovascular disease (7.8%), smoking (5.3%), asthma (2.6%), pre-eclampsia (2.6%), chronic renal failure (1.3%), and chronic obstructive pulmonary disease (COPD) (1.3%). Table I

* 1. **Clinical aspects**

The average hospital stay was 6.7 days, with extremes of 0 and 35 days. The majority of patients were symptomatic (94.7%). We recorded a total of 13 functional signs, the predominant ones being cough (90.8%) and dyspnea (77.6%). The main sign was asthenia (92.1%) Table II. Notably, over half the patients (53.9%) had an oxygen saturation of less than 90%. Oxygen saturation ranged from 40% to 99%, with an average of 85%. Half the patients experienced respiratory distress with saturations below 90% (Figure 1). Patients presenting with a severe Covid-19 course were more frequent 71.1%(n=54) followed by moderate cases 23.7% (n=18).

* 1. **Biological aspects**

Anemia was observed in 69.7% of patients, with normocytic predominance at 48.7%. Other blood count abnormalities were as follows: 43.4% hyperleukocytosis, 4% leukopenia, 10.5% thrombocytosis, and 9.2% thrombocytopenia. Blood ionograms were normal in 38.1% of patients. Ionic disorders were most marked by hypernatremia (31.6%), hyperchloremia (27.6%), and hypocalcemia (13.1%). CRP was positive for all patients. Renal assessment outlined elevated blood creatinine and urea levels in 27.6% and 18.4% of patients respectively (Table III).

* 1. **Outcome and risk factors of death**

Among the 76 patients in our study, 82.9% had a cogent outcome. Death occurred in 17.1% of cases. Patients admitted to intensive care accounted for 10.5%. In our analysis, we found that age was a risk factor for severity and mortality (p-value < 0.05). Men presented more severe forms and had more deaths than women.

The proportion of severe cases was 79.5% in men versus 62.2% in women. Severity was not related to gender (Fisher=4.15). The proportion of moderate and severe cases was higher among patients with comorbidities, at 25.6% and 69.8% respectively. There was no statistically significant relationship between case type and diabetes or hypertension.

1. **Discussion**

A total of 76 cases were collected during the period. This low number of cases may be attributable to the fact that during this period, which corresponded to the 4th wave, care was also provided at home. The median age of patients was 61.5 years, with extremes of 18 and 90 years. This age distribution is similar to studies carried out in other regions [9-13], suggesting that middle-aged and elderly people were more susceptible to infection, while healthy young adults were less susceptible. Male predominance has been observed in several other studies [13, 14]

In line with numerous studies [14-16], the main comorbidities found in our study were arterial hypertension (34.2%) and diabetes (23.7%). However, the prevalence of hypertension was higher in our study compared with the overall Senegalese population, as indicated by the results of the 2015 STEPS survey on non-communicable diseases [17]. Indeed, besides the pronounced epidemiological transition in urban areas (influenced by factors such as changes in lifestyle habits, stress, sedentary living...), our survey is performed in a hospital setting. These same comorbidities were also prominent in the studies by Zamparini et al. and Liu et al. [18-20]. While mortality was higher in patients with comorbidities in our study, the statistical association of these comorbidities with COVID-19 severity and mortality was not demonstrated. However, several reviews and meta-analyses have consistently shown the involvement of comorbidities such as diabetes and hypertension in severity and generally poorer prognosis for COVID-19 [3, 13, 21, 22]. Among the evaluated comorbidities, hypertension and diabetes were most commonly observed in severe presentations. Other comorbidities have also been reported, depending on the study. Nikpouraghdam et al identified chronic respiratory disease, hypertension, cardiovascular disease (CVD), chronic kidney disease (CKD), and cancer as the most common comorbidities among patients who died in their study [23]. The median duration of symptoms was 6.7 days, a result similar to other studies [6, 2].

The main functional signs reported were cough (90.8%) and dyspnea (77.6%). Asthenia (92.1%) was the major general sign. However, there was a wide difference in symptoms between studies [25-28], with dyspnea, cough, and fever being the most prominent symptoms compared with those of the digestive and nervous systems [13], and this could be attributed to differences in study populations such as race, ethnicity, gender and other host-related factors [29-30]. For example, a study involving 1420 European patients with mild-to-moderate COVID-19 disease reported headache (70.3%), loss of smell (70.2%), nasal obstruction (67.8%), cough (63.2%), myalgia (62.5%), rhinorrhea (60.1%), sore throat (52.9%), and fever (45.4%) [30]. In other studies, such as that carried out in Algeria, agueusia and anosmia were frequent reasons for consultation [3]. Apart from the above-mentioned clinical manifestations, additional symptoms were recorded, such as chest pain, vomiting, diarrhea and dizziness; this clearly shows the diversity of COVID-19 symptomatology, and aligns with findings reported in the literature [3, 16, 31-32].

We observed anemia (69.7%) in its normocytic pattern in 48.7% of cases and increased CRP (100%) which was higher than reported in the literature (where anemia ranged from 0-15% and increased CRP from 35-85.6%) [3]. Hyponatremia (7.9%) and PT (3.9%) corroborate to those reported in the literature [3]. A comparison with a study carried out in India on 60 people in a type 3 hospital revealed anemia and hyperuricemia as abnormalities [3]. Biological abnormalities (hyperleukocytosis, hypercreatininemia, hypernatremia) found in the study by Ketfi A et al were comparable to the results of our study [3, 13].

Severe and moderate cases accounted for 71.1% and 23.7% respectively in our study. The predominance of severe cases, in our study, can by exemplify by the fact that patients of advanced age were more numerous, yet age is described as a factor in the severity of COVID-19 [33-34]. Some epidemiological reviews also support the same observation [35-36].In our series, the average hospital stay was 6.7 days, lower than that reported in the literature [3]. Case fatality was 17.1%. However, studies carried out in Africa [3, 16, 7, 20] and worldwide have reported a lower mortality rate than our study (17.1%). This situation is justified by the fact that our study is based on a hospital survey; and the hospital, as the last link in the health pyramid, is expected to manage moderate and especially severe cases. On the other hand, other studies have observed higher case-fatality rates [13].

The results obtained in our study showed that advanced age is a risk factor for the severity and mortality of the disease. Indeed, among 13 patients who died, 10 were over 60, with a p-value<0.05. Moreover, Jaspard M et al showed that mortality was 3 times higher in people over 60 [16]. Thus, several studies have reported that age is the most important predictor of severity and death in patients with Covid-19 [33-34]. This age-related variation in the severity of COVID-19 could be explained by a decrease in cell-mediated immune function, and a decrease in humoral immune function [34], but also by advanced age, which alone is a risk factor for the onset of chronic non-communicable diseases.

Moreover, in most studies, deaths were higher in people aged 60 and over or with comorbidities. Numerous studies [3, 14-15, 21-22] have shown the effect of comorbidities in the unfavorable evolution and occurrence of patient deaths. Our results showed that men were more exposed to mortality than women (23.1% vs. 10.8%); however, there was no statistical association. This may be explained by the small size of our sample. Moreover, some meta-analysis studies consider that the effect of gender was not statistically significant [37-39]. On the other hand, other studies have highlighted male gender as a risk factor for mortality [13, 16, 37].

1. **Conclusion**

COVID-19 disease is a significant public health concern, with a global impact due to the high number of reported cases, since it first appeared, and the substantial loss of life. Anyone, regardless of age or sex, can be infected by the coronavirus. However, elderly individuals and those risk factors and co-morbidities are particularly susceptible to severe outcomes. As the clinical signs are nonspecific and may be confused with other pathologies, it is vital to protect the population by disseminating information and raising awareness of the need to comply with preventive measures known as "barrier measures". To date, no curative treatment is available. Vaccination is currently the only alternative that appears as the primary preventive treatment, although its current efficacy is the subject of much controversy.

**Study limitations**

Our study encountered a number of problems. Firstly, the sample size was very small compared with many studies carried out on Covid-19. Indeed, the sample must be sufficiently representative of the population and large enough to obtain results that more closely resemble those of the general population. In addition, certain factors such as missing data and socio-economic factors render the search for biological and paraclinical data incomplete.

**Ethical considerations**: The head of the department approved the protocol and authorized the survey. As per international standards or university standards written ethical approval has been collected and preserved by the author(s). Confidentiality and anonymity were respected. Confidentiality was ensured by the identification numbers used to ensure anonymity. Patients will not be identified in scientific publications and/or in various presentations related to this study.

**Highlights**: COVID-19 disease is a serious infectious disease with high lethality in senior. Deaths were higher in people aged 60 and over or with comorbidities. Our results showed that men were more exposed to mortality than women, however, other studies have highlighted male gender as a risk factor for mortality. Effective prevention is essential.

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 Figure 1: Distribution of patients by oxygen saturation.

Table I: Distribution of patients by socio demographic characteristics

|  |  |  |
| --- | --- | --- |
| Variable | Effectifs N=76 | Pourcentages % |
| **Median age (years)** | **61.5 [18-90]** |
| **Age group (years)** | **n=76** |  |
| ≤44 | 17 | 22.3 |
| 45-59 | 17 | 22.3 |
| ≥60 | 42 | 55.2 |
| Male | 39 | 51.3 |
| **Comorbidities** | n= 60 | 78,9 |
|  Diabetes mellitus | 18 | 23,7 |
|  Hypertension | 26 | 34,2 |
|  Cardiovascular disease  | 6 | 7,8 |
|  Tobacco smoking | 4 | 5,3 |
|  Asthme and COPD | 3 | 3,9 |
|  Other comorbidities | 3 | 3,9 |

Table II: Distribution of patients by clinical aspects

|  |  |  |  |
| --- | --- | --- | --- |
| **Signs** | **Absolute frequency (n)** |  **Relative frequency *(%)*** | ***Cumulative frequency (%)*** |
| **Fever** | 40 | *52.6* | *52.6* |
|  |  |  |  |
| **Headaches** | 25 | *32.9* | *32.9* |
| **Cough** | 69 | *90.8* | *90.8* |
| **Dyspnea** | 59 | *77.6* | *77.6* |
| **Odynophagia** | 5 | *6.6* | *6.6* |
| **Congestion** | 5 | *6.6* | *6.6* |
| **Agueusia** | 47  | *61.8* | *61.8* |
| **Anosmia** | 15 | *19.7* | *19.7* |
| **Arthralgia** | *32,9* | *32.9* | 25 |
| **Myalgia** | 32 | *42.1* | *42.1* |
| **Asthenia** | 70 | *92.1* | *92.1* |
| **Other signs** | 7 | *7.8* | 7 |

**Table III: Results of biological aspects**

|  |  |  |
| --- | --- | --- |
| **Laboratory data** | **Mean (n)** | ***IC (95%)*** |
| **Hémoglobine (g/dl)** | 11.7 | *(11.2-12.1)* |
| **VGM (fl)** | 84,1 | *(82,1-86)* |
| **TCMH (pg)** | 28,1 | *(27,3-28,5)* |
| **Platelets (/mm3)** | 361200 |  |
| **Leukocytes (/mm3)** | 10730 | *(9450,4-12010)* |
| **Lymphocytes (%)** | 19.7 | *(17.1-22.3)* |
| **Neutrophiles (%)** | 70.2 |  |
| **Granulocytes (/mm3)** | 7926 | *(6814.1-9037.9)* |
| **C-Reactive Protein (mg/l)** | 84.6 | *(72.4-96.7)* |
| **Créatinine (mg/l)** | 12.7 | *(10.1-15.2)* |
| **Urea (mg/l)** | 0,4 | *(0.3-0.4)* |
| **TP (%)** | 91,6 | *(89,3-93,7)* |
| **INR** | 1,2 | *(1,1-1,2)* |

**Table IV: Death associated risk factors**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  |  | **Type of cases** | **Total** |  |  |
|  |  | **Simple** | **Moderate** | **Severe** | **P value** |  |
|  |  |  |  |  |  |  |  |
|  | **Comorbidities** | 2*(4,7)* | 11*(25,6)* | 30*(69,8)* | 43*(100,0)* | O,92 |  |
| **Diabetes mellitus** | 1*(5,6)* | 5*(27,8)* | 12*(66,7)* | 18*(100,0)* | 0,68 |  |
|  **Hypertension** | 2*(7,7)* | 3*(11,5)* | 21*(80,8)* | 26*(100,0)* | 0,97 |  |
|  **Age** | **Evolution** | **Means** | **Ecart-type** | **Test de Welch** | **Pvalue** |  |
|  | **Favorable** | 57,2 | 18 | 2,7 | 0,01 |  |
| **Death** | 66,3 | 8,8 |  |  |  |