

Risk Factors Linked to Infection with SARS-Cov2

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Abstract:- Infection with the SARS- CoV -2 (Severe Acute Respiratory Syndrome) is characterized by a wide spectrum of clinical syndromes ranging from disease asymptomatic, mild flu-like symptoms to severe pneumonia and acute respiratory distress syndrome Our goal is to study the risk factors in patients infected with COVID 19 (Coronavirus disease 2019).

➤ **Methods :**

This is a retrospective descriptive study of 54 patients hospitalized in unit B- COVID-19 at the Ibn Sina University Hospital Center in Rabat from 15 October 2020 to 1 November 2020.

➤ **Results:**

Fifty-four cases of COVID-19 confirmed by PCR (Polymerase chain reaction) were hospitalized including 30 women (55,56%) and 24 men (44,44%), divided into 27 cases with a non-severe form and 27 cases with a moderate to severe form requiring oxygen therapy. The overall median age was 55,13 years. Fever (18,52%), dyspnea (38,89 %), cough (22,22%) and fatigue (11,11%) were the most common clinical manifestations, while diabetes (40,74%), arterial hypertension (27,78%) and obesity (14,81%) were the most common comorbidities . Chronic smokers (12,96%) patients with the bronchopulmonary disease chronic obstructive pulmonary disease (COPD, 1,54 %) and asthma (1,54%) were rare. Bilateral frosted glass or uneven opacity (66.71%) was the most common sign on the chest CT scan. Lymphopenia (37,04 %) and eosinopenia (29,36 %) were observed in our patients. Significantly higher values of D-dimer, C-reactive protein (CRP) and LDH were observed especially in patients with moderate to severe form.

➤ **Conclusion:**

Advanced age, diabetes and high blood pressure remain the most frequent risk factors for developing moderate to severe forms of viral infection with SARS-CoV-2, hence the importance of taking in this category of patients. Lymphopenia, eosinopenia and inflammatory syndrome could be potential indicators of diagnosis and severity.

Keywords:- SARS- CoV-2, Comorbidities, Risk Actors.

I. INTRODUCTION

SARS- CoV -2 belongs to the coronaviridae , a family of large RNA viruses that infect many animal species. Six other coronaviruses are known and can infect humans. Four of them are endemically transmitted and cause the common cold (oc43, hku1, 229e and nl63), while SARS- CoV and the Middle East respiratory syndrome coronavirus (MERS - CoV) have caused epidemics of severe pneumonia [1,2]. In December 2019, the first epidemic appeared in Wuhan and quickly spread across China and various other countries [3]. In addition, projections from the World Health Organization estimate that the death rate worldwide will be 5,7% [4].

The first studies carried out in China reporting the demographic data and co-morbidities of patients suffering from severe respiratory disease, made it possible to suggest certain risk factors. Age and certain comorbidities such as cardiovascular disease, chronic respiratory disease, arterial hypertension and diabetes seem to be associated with severe damage [5].

This research aims to study comorbidity, clinical and laboratory characteristics regarding Covid 19 patients who were hospitalized , and to determine the differences between severe and not severe patients.

II. METHODS

The clinical features (including medical history, exposure history, comorbidities, surgical history, and symptoms), the results of chest computed tomography (CT), the date of occurrence of the disease as well as the date of admission to the hospital were recorded. The onset date was defined as the day the symptoms were first noticed by the patients. Severe COVID-19 has been designated when patients presented one of the following criteria : respiratory distress with respiratory rate ≥ 30 c / min; pulse oximeter oxygen saturation $\leq 93\%$ at rest; requiring oxygen therapy (low flow $\leq 5l$, high flow from 10 to 15l under high concentration mask) All patients were positive (the diagnosis of COVID -19 was retained by a positive RT-PCR) .

III. RESULTS

1. Epidemiological data and clinical characteristics

A total of 54 patients diagnosed with COVID-19 were included in this study, with 27 patients classified as non-severe and 27 moderate to severe cases on admission. The median age was 55.56, ranging from 22 to 82, and the majority (68.51 %) were over 50. Approximately 50% of patients were in contact with a positive Covid case whether it was an intra hospital link or within the family .

More than three quarters (77,77%) of the patients had at least an underlying co-morbidity, which were the most common metabolic and cardiovascular diseases, such as diabetes (40, 74 %), hypertension blood (27.78%), obesity (14, 81%) and coronary heart disease (9, 25%). One patient suffering from COPD was identified and only seven patients were former smokers. There was only one case of asthma and no other allergic disease was declared (including rhinitis, dermatitis atopic , drug allergies o Food u). In addition, 27.77% of the patients were followed for a system disease or a malignant pathology (**Table 1**).

Table 1 : Epidemiological data and clinical characteristics of patients with COVID-19

	All patients (n = 54)	Severity of illnesses	
		Non-severe patients (n = 27)	Severe patients (n = 27)
Age : median (range)	55.13 (22-82)	51.96 (22-72)	58.29 (32-82)
Age group - Number (%)			
<30 years	4 (7.41)	4 (14.81)	0
30 to 49 years old	13 (24.07)	4 (14.81)	9 (33.33)
50 to 69 years old	30 (55.56)	18 (66.67)	12 (44.44)
≥70 years	7 (12.96)	1 (3.70)	6 (22.22)
Sex - Number (%)			
Women	30 (55.56)	15 (55.56)	15 (55.56)
Man	24 (44.44)	12 (44.44)	12 (44.44)
Without comorbidity	5 (9.26)	4 (14.81)	1 (3.70)
Comorbidity-Num ber (%)			
Diabetes	22 (40.74)	7 (25.93)	15 (55.56)
Hypertension	15 (27.78)	5 (18.52)	10 (37.04)
Coronary heart disease	5 (9.26)	2 (7.41)	3 (11.11)
Obesity	8 (14.81)	0	8 (29.63)
System Diseases-Number (%)			
Crohn's disease	1 (1.54)	1 (3.70)	0
Lupus	2 (3.70)	2 (7.41)	0
Rheumatoid arthritis	2 (3.70)	2 (7.41)	1 (3.70)
GougerotSjogren syndrome	1 (1.54)	0	1 (3.70)
Idiopathic Thrombocytopenic Purpura (ITP)	1 (1.54)	1 (3.70)	0
Bullous dermatoses	3 (5.56)	3 (11.11)	0
Malignancies -Name fiber (%)			
Digestive cancer	2 (3.70)	0	2 (7.41)
Non-Hodgkin lymphoma	1 (1.54)	1 (3.70)	0
Acute myeloid leukemia (AML)	1 (1.54)	0	1 (3.70)
Soft tissue B lymphoma	1 (1.54)	1 (3.70)	0
HIV	1 (1.54)	1 (3.70)	0
Sickle cell anemia	1 (1.54)	1 (3.70)	0
Smoking	7 (12.96)	7 (25.93)	0
COPD	1 (1.54)	0	1 (3.70)
Asthma	1 (1.54)	1 (3.70)	0

- HIV: Virus immunodeficiency fi ciency human.
- COPD: pulmonary chronic obstructive

The median interval between symptoms onset and hospitalization for all patients was 8 days (IQR: 2-10). The most frequent symptoms were dyspnoea (38,89%), cough (22, 22 %), fever (18,52%), fatigue (11.11%) and only 9, 25 % had astro-intestinal symptoms , including diarrhea and anorexia (**Table 2**). It was noted that despite low saturation, respiratory rate was normal (silent hypoxemia) in one third of severe cases. A low rate oxygen therapy was set up at 74,07% of patients, while 25, 92% of patients required an oxygen therapy under a high concentration mask.

Table 2 : Symptomatic and radiological characteristics of patients with COVID-19

	All patients (n = 54)	Severity of illnesses	
		Non-severe patients (n = 27)	Severe patients (n = 27)
Onset of symptoms at hospitalization median, days			
Symptoms - Number (%)			
Asymptomatic	17 (31.48)	0	17(62.96)
Fever	10 (18.52)	4 (14.81)	6 (22.22)
Cough	12 (22.22)	4 (14.81)	8 (29.63)
Tired	6 (11.11)	2 (7.41)	4 (14.81)
Chest tightness	5 (9.26)	1 (3.70)	4 (14.81)
Dyspnea	21 (38.89)	5 (18.52)	16 (59.26)
Anosmia	1 (1.85)	1 (3.70)	0
Diarrhea	1 (1.85)	1 (3.70)	0
Anorexia	4 (7.41)	1 (3.70)	3 (11.11)
Chest CT Scan- Number (%)			
Not done	18 (33.33)	18 (66.67)	0
Pulmonary embolism	1 (1.85)	1 (3.70)	0
Bilateral frosted glass	36 (66.67)	9 (33.33)	27 (100)
Extent			
10 to 25%	7 (12.96)	6 (22.22)	1 (3.70)
25 to 50%	11 (20.37)	1 (3.70)	10 (37.04)
50 to 75%	18 (33.33)	2 (7.41)	16 (59.26)

➤ IQR: interquartile range.

2. Radiological and biological results:

On the 54 affected patients, the thoracic scanner was performed on 36 patients, which made it possible to highlight typical images made of multiple bilateral opacities in peripheral frosted glass with an extent of lesions between 10% to 50% for simple cases vs. an extensive one exceeding 50% and going up to 75% in severe cases. The result of laboratory tests done on patients on the first day of hospitalization showed a normal white blood cell count in most patients (88, 89%), with an increase in 5,56% of cases . The lymphocyte level was normal in 62, 96% and low in 37,04 % of patients , this low level was more observed in severe patients. In 25, 92% of the patients, an eosinopenia was objectified . In addition, the value of other biological parameters increased particularly the C-reactive protein (44,44%), the D-dimer s (43,2%), the fibrinogen (34,7%) and LDH (43,2 %) (**Table 3**).

Table 3 : Laboratory results of patients with COVID-19

	All patients (n = 54)	Severity of illnesses	
		Non-severe patients (n = 27)	Severe patients (n = 27)
Leukocytes - Number (%)			
Normal (4000-10000 / mm ³)	48 (88.89)	26 (96.30)	22 (81.48)
Increased ($\geq 10,000$ / mm ³)	3 (5.56)	0	3 (11.11)
Reduced (≤ 4000 / mm ³)	3 (5.56)	1 (3.70)	2 (7.41)
Lymphocytes - Number (%)			
Normal (1000-4000 / mm ³)	34 (62.96)	23 (85.19)	11 (40.74)
Low <1000 (values between 220-960 / mm ³)	20 (37.04)	4 (14.81)	16 (59.26)
Eosinopenia (values between 0 and 60 / mm³)	16 (29.63)	7 (25.93)	9 (33.33)
Eosinopenia with normal lymphocytes	9 (16.67)	7 (25.93)	2 (7.41)
Eosinopenia with lymphopenia	7 (12.96)	0	7 (25.93)
Elevated CRP ≥ 4	24 (44.44)	3 (11.11)	21 (77.78)
D-Dimer ≥ 500 & Fibrinogen ≥ 4	24 (44.44)	3 (11.11)	21 (77.78)
Cytolysis (ALAT 2xN & ASAT 2xN)	3 (5.56)	0	3 (11.11)
Clearance (Cockroft & Gault at 34 ml / min / 1.72m²)	2 (3.70)	0	2 (7.41)

- ALAT: alanine aminotransferase .
- ASAT: aspartate aminotransferase

3. Characteristics of severe cases

The median age was 58,29 years in serious cases compared to 51, 92 years in non-severe cases. The metabolic and cardiovascular comorbid were more common in severe cases than in non-severe cases (68,51% vs 7%), and lymphopenia (59, 26% vs 14, 81%), eosinopenia (33, 33% vs 25,93%) and inflammatory syndrome (77,78% vs 11,11 %). The Hyperleukocytosis, insufficient kidney and Cy tolyse (ALT: 2N, AST: 2N) have been logged only in severe cases with extensive lung damage of over 50%.

4. Thromboembolic complications:

A right distal pulmonary embolism occurred in a single 54-year-old patient without a history of thromboembolism or comorbidities , after 3 days of his hospitalization due to a non-severe infection with C OVID - 19. A stroke occurred in a single patient after 10 days from the onset of her symptoms. The patient was suffering from a severe form of COVID.

5. Therapeutic and evolutionary data

The azithromycin and hydroxchloroquine combination was initiated in all patients, except two : the first with an increased QT space of 500 ms before the initiation of treatment, and the second who presented a QT at 537 ms on the second day of treatment. . Anticoagulants based heparin of low molecular weight, type E noxaparine sodium protectant dose (4,000 / 24 h) in the majority of patients, and curative dose (100 IU / kg / 12h) in patients under high flow oxygen. Corticosteroid therapy was reserved for patients on oxygen, being based on M ethylprednisolone at a dose of 40 mg / 12 hours by injection for patients under high concentration mask or P rednisolone at a dose of 40 mg per day orally only for patients with low oxygen flow for an average period of 5 to 7 days. Antiviral therapy has not been administered to any patient.

The outcome was favorable in the majority of patients (92, 59%). 3 patients were transferred to the ICU and had a single death of a patient aged 82 years followed for digestive cancer who received chemotherapy recently (dating back less than one month).

IV. DISCUSSION

Three patient profiles seem to emerge: paucisymptomatic infection with initially high viral load, secondary respiratory worsening on the tenth day despite a decrease in viral load suggesting an inadequate immune response from the host , and a rapidly progressive infection with multiple failures visceral and persistent high viral load [6].

In our study, the median age was 55,13 years, which is close to the data reported by Wang et al [7] (56,0 years) and Chen et al [8] (55,5 years), but higher than that reported by Huang et al [3] (49,0 years). Severe patients were older than non-severe patients and associated with a higher frequency

of comorbidities. In our report, 88,89% of patients had comorbidities : the diabetes mellitus (40,74%) , the hypertension blood (27, 78%), and cardiovascular disease were the most common underlying diseases according to other recent reports [7-8] . The prevalence of hypertension and diabetes in China was 23,2% [9] and 10,9% [10] among adults. However , a study that compared the characteristics of 113 patients that died and 161 patients who were cured, all confirmed SARS-CoV-2 positive with an initial mod reached Eree to severe, has not shown any difference between the two groups in terms of autoimmune diseases (AID) [11] . Italian authors wondered about the risk of severe infection in patients with inflammatory bowel disease, they conclude due to a lack of data suggesting an increased risk, highlighting the absence of cases of Covid-19 in the specialized center for inflammatory bowel diseases of Wuhan [12] . Nonetheless, neither the May treatment nor the immunosuppressors have so far been reported as a poor prognostic factor in Covid-19 frame , which is consistent with the results of our study . Moreover , It has been suggested that obesity could be a risk factor for the development of severe COVID-19 in younger subjects, whereas in the absence of obesity, it is especially the very old patients who are the most at risk of presenting an unfavorable outcome [13-14-15] . It is therefore essential to systematically collect well-documented anthropometric data in patients hospitalized for COVID-19 [16] . The hypothesis of lipid microdeposits in the lungs, at the level of the interstitial alveolar spaces, has even been put forward [17] . This infiltration would worsen the inflammatory infiltrate linked to the viral infection, which could contribute to massive edema which would lead to acute respiratory distress syndrome (ARDS) and the need for ventilatory support [18] .

Only one patient with asthma was identified in our study. Allergic rhinitis, dermatitis atopic and food allergy have not been reported. Also given the prevalence of asthma among COVID-19 cases in China which was 4,2% [19] and allergic rhinitis in Wuhan which was 9,7% [20] among adults, we can conclude that asthma or allergy may not be a risk factor for infection with SARS-CoV-2.

Only one (1.54%) patient had COPD in our report; this percentage was close to that reported by Guan et al (1,1%), whose study included 12 cases of COPD among the 1099 cases studied [5] . In addition, only 7 patients (12, 96%) had a history of smoking. Also, it has been reported that the prevalence of COPD in adults aged 40 and over was 13,7% [21] and that 27.3% of adults in China are smokers [22] . The relationship between smoking and coronavirus infection is unclear, and the exact underlying causes of the incidence of COVID-19 in current smokers are still unknown.

Two patients followed for digestive cancer under chemotherapy developed a severe form, which is consistent with two studies which show that cancer patients have a higher risk of COVID19 infection with an older age at diagnosis and prognosis possibly more unfavorable than in non-cancerous patients [23-24] .

The seric parameters inflammatory are highly increased in Covid-19 patients with severe impaired Breathing equipment in particular the significant elevation of cytokines proinflammatory, including interleukin-6 (IL-6), and the marked lymphopenia (reduction of CD4, CD8 and NK). However, there is no alteration of serum immunoglobulin values in these patients [3]. The hypothesis put forward in COVID-19 is linked to poor control of viral infection by the immune system which would lead to massive tissue destruction and an excessive inflammatory response. [25]. Lymphopenia and inflammatory syndrome were common in the patients in our study (75.4%), which is consistent with the data in the literature. Furthermore, a decrease in the number of eosinophils can be used as an indicator of SARS-CoV-2 infection in suspected patients with or without lymphopenia.

Radiologically, the most common findings on chest computed tomography were bi-lateral ground glass or uneven opacity [8-5]. Which is similar to what we observed in our report. The distribution of opacity was not different between severe and non-severe patients, however an extent of lesions of more than 50% is a factor of severity.

Indeed, a Chinese study [26] carried out between January 6 and February 6, 2020 showed that the sensitivity of CT is 97%, based on positive results by RT-PCR, and 75% on patients negative by RT-PCR. Thus, after the data analysis of a l'imagerie and s laboratory tests, it appears that the chest CT is greater than the biological test in the diagnosis of Covid-19. A sample during a bronchoalveolar enema to be able to find the viral RNA and to support the diagnosis can be interesting in this case.

The majority of our patients (96, 29%) were in combination hydroxychloroquine and azytromycine. In the context of the current pandemic, they arouse considerable interest because of their anti-inflammatory effect and their potential demonstrated antiviral effect in in vitro studies on SARS-CoV [27-28] and SARS-CoV-2 [29-30].

The antiviral effect of hydroxychloroquine be attributed firstly to the increased pH endosomal, disrupting the process of internalization and intracellular viral replication, and also to inhibition of e the glycosylation of 'ECA2, essential for virus penetration into the cell [31]. Moreover, by inhibiting the proinflammatory cytokine cascade triggered by viral infection, these molecules could attenuate the extent of tissue damage [32]. The most feared short-term side effect is the prolongation of the QT space, especially in the event of comedication with certain antiemetics, antiarrhythmics, psychotropics and antibiotics (macrolides, quinolones). This effect was identified in a cardiac patient with a QT at 530 ms on D2 of treatment. In COVID-19, data on the clinical efficacy of synthetic antimalarials is still incomplete.

Ischemic stroke and pulmonary embolism occurred in two of our patients. It seems plausible that patients with COVID-19 whose D-dimer levels increase, a sign of coagulopathy, may benefit from anticoagulant therapy [33].

V. CONCLUSION

A particular susceptibility of patients with cardio-metabolic comorbidities to contract the infection and to develop a severe form is evident. This could be explained by the immune dysfunction in these patients, most often elderly, diabetic and dyslipidemic, and by the existence of a mechanism of interaction with the cardiovascular system, specific to the coronavirus family. In addition, also as a preventive measure, any elderly patient with these comorbidities, presenting the first symptoms of the COVID-19 disease should be particularly monitored and hospitalized quickly in the event of a negative development to prevent or, at least, limit the risk of an unfavorable outcome.

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