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Pneumology

Predictors of Severity in COVID-19 patients in Pneumology Department Marrakesh, Morocco

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Abstract

Original Research Article

Background: The SARS-CoV-2 coronavirus, has been identified since 2019, as the causative agent of a new respiratory disease called the COVID-19 (Coronavirus Disease 2019). Numerous risk factors for COVID-19 severity have been described, but data on infected patients in North Africa are limited. We aimed to explore the predictive factors of disease severity in COVID-19 patients in the pneumology department of the Mohammed VI Hospital in Marrakech. Methods: A descriptive and analytical cross-sectional study conducted among patients hospitalized for COVID- 19 during the period from October 2020 to December 2020 in intensive care unit CHU Mohammed VI of Marrakech confirmed and presenting acute respiratory distress. The variables retained in the final model were selected using a stepwise forward method with an entry threshold at 0.2 and an exit threshold at 0.05. The significance threshold was retained for p <0.05. The descriptive analysis consisted of the calculation of absolute and relative frequencies for the qualitative variables, and of the positioning and dispersion parameters for the quantitative variables (mean, standard deviation). For the comparison of percentages in bivariate analysis, Pearson's Chi2 statistical test and Fisher's test if necessary were used. Results: 125 cases of COVID-19 were collected (40.8 women and 59.2 men). The average age was 59.6 years (26-90). 86.4% were exposed to tobacco. 66.7% were active smokers and 33.3% were passive smokers. The presence of comorbidities was noted in 77.6% of cases. These were arterial hypertension (28.4%), diabetes (32.6%), heart disease (7.1%), neoplasia (5.7%), dysthyroidism (5.7%) and bronchial asthma (6.4%). Confirmatory examinations included suggestive imaging in 76.9%, 47.9% a positive pcr. The predominant respiratory symptoms were cough in 84% of cases, followed by dyspnea in 70.9% of cases. The predominant extra-respiratory signs were asthenia in 79% of cases, followed by myalgia in 46% of cases, anosmia in 29.4% of cases and agueusia in 21% of cases. Fever was found in 68% of patients. 35% were tachycardic at >90 beats/min and 43.2% of patients had a saturation <90 beats/min, 16% a sa02 between 90-95%. 71 patients with saturation >90% had a mean age of 57.3 years while 54 patients with sao2 <90% had a mean age of 62.7 with one (p=0.027). 42 patients with sao2 <90% had a mean lymphocyte count of 1123 with one (p=0.003). Chest CT revealed a ground glass appearance in 83.2%, alveolar condensations in 40%. Lesions were critical in 12.8%, severe in 30.8%, moderate in 30.8%, and mild in 25.6%. Radiological images in favor of pulmonary superinfections were noted in 77% of cases. Radiological extension correlated with saturation: 76.1% of patients with sa02 >90% had mild to moderate pulmonary extension with a (p= 0.0001). Biological disturbances were also noted. These included elevated D-dimer levels in (31%), lymphopenia (47.4%), leukopenia (8%), thrombocytopenia (13%), PNN hyperleukocytosis (34.2%), liver cytolysis (10%), elevated CRP (54%), elevated fibrinogen (59%), and impaired renal function (36%). The evolution was marked by admission to the intensive care unit for all patients with the implementation of ventilatory assistance in 91% of patients. 84% of patients had an O2 flow rate <10 l/min with mild to moderate pulmonary extension with one (p= 0.011) and an OR of 3,94. Only one case of death was noted. The factors that conditioned the prognosis were: age, lymphocyte count, d-dimer, respiratory rate, saturation and o2 flow.92 patients with a mean age of 57.9 years +/- 13.03 had a good prognosis versus 33 patients with a mean age of 64.52 years +/- 13.97 had a poor prognosis with a (p=0.016). Lymphocyte count was also a factor that conditioned prognosis: 44 patients with a mean lymphocyte count of 1514 had a good prognosis versus 21 poor prognosis patients with a mean lymphocyte count of 1120 with a (p= 0.037). D-dimer assay: 37 patients with a mean d-dimer level of 1265 had a good prognosis versus 18 patients with a mean D-dimer level of 9193 with one (p=0.023). 02 saturation: 83.1% (59) of patients with a saturation >90% had a good prognosis compared to 61.1% (33) of patients with a saturation <90% with a (p=0.08). Discharge with an oxygen extractor was considered a poor prognostic element in 71% of patients with a (p=0.0001) and an OR of 9. Conclusion : The progression of patients with COVID-19 to worsening appears to be associated with age, cardiovascular and metabolic history, severity of radiological involvement, and observed biological disturbances. This study therefore shows the importance of predictive factors such as age, lymphocyte and d-dimer levels, respiratory rate and oxygen saturation as prognostic factors for the evolution of Covid-19 infection with rapid worsening synonymous with the severity of the evolution.

Keywords: Predictors, Severity, Pneumology.

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INTRODUCTION

Since December 2019, the emergence of a new coronavirus strain called SARS-CoV-2 coronavirus, which is highly pathogenic, has been identified as the

causative agent of a new respiratory disease: the COVID-19 (Coronavirus Disease 2019).

First appearing in Wuhan in China's Hubei province, this strain then spread to the rest of the world in the following months. On March 11, 2020, the WHO

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qualified the situation as a true pandemic, and containment was adopted everywhere.

At the time of this work, this health crisis has already claimed more than 3.5 million lives worldwide. This daily death toll is increasing with the appearance of new variants and mutants and despite a promising vaccine campaign, which started at the beginning of the year.

If the symptoms can go from a simple flu-like syndrome made of cough, fever or arthralgias, they can be atypical and translate the attack of all the systems. For example, some patients may present with moderate or severe respiratory involvement, ranging from pneumonia to acute respiratory distress syndrome (ARDS). High flow oxygen therapy or respiratory assistance is then necessary to improve the vital prognosis.

In addition, there is a disturbed biological balance, reflecting an excessive inflammatory response, described as a real cytokine storm. This storm is the consequence of an unbalanced innate and adaptive immune response, responsible for irreversible tissue damage leading to multivisceral failure.

In addition to the clinical picture, biological markers or biomarkers reflect the excessive inflammatory response but also the immune status of the host. They are used to guide therapy but also to predict the severity of COVID-19 pneumonia.

Our study was motivated by the reappearance of COVID-19 positive cases in our country in the period following mid-July 2020. Because this time, and contrary to the beginning of the crisis, more severe and therefore fatal forms were observed.

The development of predictive models for severe forms of COVID19 would be a way to rationalize patient management and to relieve the care facilities receiving these patients, whose capacities, including those in intensive care, are very quickly exceeded during a COVID pandemic.

The present study reports the data of 125 patients with laboratory-confirmed SARS-CoV-2 infection admitted to intensive care.

The objective of our study is to analyze all these clinical, biological and radiological parameters and to determine the most sensitive and specific ones to predict the severity of the COVID-19 disease and those that contributed to the prognostic evolution in the Mohammed VI hospital of Marrakesh.

MATERIALS AND METHODS

A retrospective descriptive and analytical cross-sectional study conducted among patients

hospitalized for COVID-19 during the period from October 2020 to December 2020 in the intensive care unit of the Marrakech University Hospital with acute respiratory distress.

Inclusion criteria

Patients with positive sars-cov 2 CRP or suggestive imaging. Statistical analysis was performed using SPSS version 19.0 software.

The descriptive analysis consisted of the calculation of absolute and relative frequencies for the qualitative variables, and of the positioning and dispersion parameters for the quantitative variables (mean, standard deviation).

Thus, the variables whose association was significant at the 20% threshold in bivariate analysis were included in a multivariate model. The threshold of significance was retained for a p < 0.05.

The variables retained in the final model were selected using a stepwise forward method with an entry threshold of 0.2 and an exit threshold of 0.05.

For the comparison of percentages in bivariate analysis, Pearson's Chi2 statistical test and Fisher's test if necessary were used. This method is used when the prognosis of the patients is to be predicted according to certain values or a set of explanatory variables. It suitable for models in which the variables are dichotomous (good/poor prognosis).

RESULTS

Demographic and clinical characteristics

In this study, we reported 125 patients with confirmed SARS-CoV-2 infection. The median age was 59.6+/- 13.53 (26-90) years with a median of 61 years and 75 (60%) were men. 66.7% were active smokers and 33.3% were passive smokers . 92 (73.6%) non-severe patients were discharged from the ICU after completing treatment, 11 (8.8%) were admitted to single rooms, and 21 (16.8%) were placed in the resuscitation unit, with only one death, due to the development of organ dysfunction.

Of the 125 patients, 61 (77.6%) had comorbidities, such as hypertension (n = 35; 28%), diabetes (n = 41; 32.6%) and heart disease (n = 8; 7.1%), neoplasia (n = 7; 5.7%), dysthyroidism (n = 6; 5.7%), bronchial asthma 6.4%. The confirmatory examinations included in 76.9% an evocative imaging, 47.9% a positive pcr.

The predominant respiratory symptoms were cough in 84,6% of cases, followed by dyspnea in 70.9% of cases. The predominant extra-respiratory signs were asthenia in 79% of cases, followed by myalgia in 46% of cases, anosmia in 29.4% of cases and agueusia in 21% of cases. Fever was found in 68% of patients. 35%

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were tachycardic at >90 beats/min and 43.2% of patients had a saturation <90 beats/min, 16% a sa02

between 90-95%.



Graph-1: The predominant respiratory symptoms

Regarding the clinical examination parameters, there was a significant difference, 71 patients with a saturation >90% had a mean age of 57.3 years while 54

patients with a sao2 <90% had a mean age of 62.7 with one (p=0.027). This difference was significant.

	Saturation	n	Average	Standard deviation	р
ACE	<mark><90</mark>	<mark>54</mark>	<mark>62,7</mark>	<mark>13,2</mark>	0.027
AGE	>=90	<mark>71</mark>	<mark>57,3</mark>	<mark>13,4</mark>	<mark>0,027</mark>

Clinical and laboratory findings

Biological disturbances were also noted. These included elevated D dimers in (31%) of cases, lymphopenia (47.4%), leukopenia (8%), thrombocytopenia (13%), PNN hyperleukocytosis (34, 2%), liver cytolysis (10%), elevated CRP (54%), elevated fibrinogen (59%), and impaired renal function (36%).

With regard to biological parameters, there was a significant difference, 42 patients with a saturation < 90% had a mean lymphocyte count of 1123, compared with 59 patients with a saturation >

90% with a (p=0.003). 24 patients with saturation < 90% had a mean platelet count at 234541, versus 27 patients with saturation > 90% with a mean platelet count at 320259 with one (p= 0.032). 24 patients with saturation < 90% had a mean NPC count at 8354 with one (p= 0.031). The initial crp level also conditioned the prognosis. 48 patients with an initial saturation < 90 had a mean crp level at 185.5 with one (p=0.0001). Regarding the initial D-dimer level, 23 patients had an initial saturation <90 with a mean of 7209 (p=0.037).

Correlations between clinical and laboratory parameters

	Saturation	n	Average	Standard deviation	p	
I ama ha anta a	<mark><90</mark>	<mark>42</mark>	<mark>1123,6</mark>	<mark>642,8</mark>	0.002	
Lymphocytes	<mark>>=90</mark>	<mark>59</mark>	<mark>1514,3</mark>	<mark>627,6</mark>	<mark>0,005</mark>	
Distan	<90	24	234541,7	109631,0	0.032	
Plates	>=90	27	320259,3	159338,2	0,032	
DNINI	<mark><90</mark>	<mark>24</mark>	<mark>8354,7</mark>	<mark>3357,4</mark>	0.021	
PININ	<mark>>=90</mark>	<mark>34</mark>	<mark>6451,5</mark>	<mark>3139,4</mark>	0,031	
Initial CRP	<mark><90</mark>	<mark>48</mark>	<mark>185,5</mark>	<mark>122,6</mark>	0.0001	
	<mark>>=90</mark>	<mark>63</mark>	<mark>95,4</mark>	<mark>87,6</mark>	<mark>0,0001</mark>	
D-Dimer	<90	23	7209,7	12377,8	0.027	
	>=90	32	1452,2	1372,5	0,037	

 Table-2: Comparison of capillary blood saturation and biological findings

Clinical and radiological findings

Chest CT revealed a ground glass appearance in 83.2%, alveolar condensations in 40%. Lesions were

critical in 12.8%, severe in 30.8%, moderate in 30.8%, and mild in 25.6%. Radiological images in favor of pulmonary superinfections were noted in 77% of cases.

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Graph-2: Chest CT extension in COVID 19 disease



Graph-3: COVID 19 CORADS classification disease

Correlations between clinical and radiological parameters

Radiological extension correlated with saturation: 51 (76.1%) of patients with sa02 > 90% had

mild to moderate pulmonary extension, whereas 38 (65.5%) with saturation <90 had severe to critical involvement with one (p= 0.0001).

Table-3: Comparison of capillary blood saturation between patients who have mild, severe and critical lung involvement

			Saturatio	n	p
			<90	>=90	
	mild to	Workforce	<mark>16</mark>	<mark>51</mark>	
Pulmonary extension	moderate	<mark>%</mark>	<mark>23,9%</mark>	<mark>76,1%</mark>	0.0001
	severe to	Workforce	<mark>38</mark>	20	0,0001
	critical	<mark>%</mark>	<mark>65,5%</mark>	<mark>34,5%</mark>]

The evolution was marked by admission to the intensive care unit for all patients with the implementation of ventilatory assistance in 91% of

patients. 84% of patients had an O2 flow rate <10 l/min with mild to moderate pulmonary extension with one (p= 0.011). Only one case of death was noted.

Table-4: Correlation	s between O	2 flow rat	te and p	ulmonarv	extension
Lable II Collemation	s seen een o		ve ana p	annonal y	en cenoron

			O2 flow	rate	p
			<=10	<mark>>10</mark>	
		Workforce	<mark>42</mark>	8	
Pulmonary extension	mild to moderate	<mark>%</mark>	<mark>84,0%</mark>	<mark>16,0%</mark>	- <mark>0,011</mark>
	severe to critical	Workforce	<mark>34</mark>	21	
		<mark>%</mark>	<mark>61,8%</mark>	<mark>38,2%</mark>	

Correlations between laboratory and radiological parameters

The correlation between initial lymphocyte count and radiological extension was as follows: 31 patients with severe radiological extension and a mean lymphocyte count of 1201 (p = 0.005). The correlation

between the initial CRP level and radiological extension: 35 patients with severe extension and a mean CRP level of 157 (p=0.001). These results are statistically significant with respect to the D-dimer level.

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Table-5: Comparison of biological findings between patients who have mild, severe and critical lung involvement

		Ν	Average	Standard deviation	р	
	mild	27	1727,19	628,401		
Lymphoaytos	moderate	31	1192,39	627,752	005	
Lymphocytes	severe	31	1201,74	437,814	<mark>,005</mark>	
	critical	12	1306,67	971,300		
	mild	28	68,923	61,3269	0001	
CDD initial	moderate	33	125,233	88,8701		
	severe	35	157,458	111,7739	<mark>,0001</mark>	
	critical	15	222,800	161,5011		
	mild	11	926,182	1311,7044		
D-Dimer	moderate	20	1494,000	1244,9874	0.50	
	severe	16	6119,750	12455,8423	,038	
	critical	8	9288,375	11799,9263		

Prognosis

The cohort formed between October and December 2020 included 125 patients with Covid-19, classified into two groups according to severity. The median age of the participating patients was 59.6 years. 73.6% (92) of the patients left the ICU after completing treatment, 16.8% (21) were transferred to an intensive care unit, 8.8% (11) to an inpatient unit, and 0.8%(1) died. 73.6% (92) were considered to have a good prognosis (group A) and 26.4% (33) a poor prognosis (group B).

Table-6: Patient outcome						
	Workforce	Percentage				
Deaths	1	,8				
Discharge from the ICU (after completing treatment)	92	73,6				
Transfer to inpatient unit	11	8,8				
Transfer to intensive care unit	21	16,8				
Total	125	100,0				

Table-7: Prognostic evolution of the two groups

	Workforce	Percentage
Good prognosis (groupe A)	92	73,6
Poor prognosis (groupe B)	33	26,4
Total	125	100,0

The factors that conditioned the prognosis were: âge, lymphocyte count, D-dimer, respiratory rate, saturation and o2 flow.

Correlation between clinical parameters and prognostic evolution

92 patients with a mean age of 57.9 years +/-13.03 had a good prognosis against 33 patients with a mean age of 64.52 years +/- 13.97 had a poor prognosis with a (p=0.016).

Table-8	8: Association	i of age and	l prognosis

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	Evolution	n	Average	Standard deviation	р
ACE	Good prognosis	<mark>92</mark>	<mark>57,90</mark>	<mark>13,03</mark>	0.016
AGE	Poor prognosis	<mark>33</mark>	<mark>64,52</mark>	<mark>13,97</mark>	<mark>0,010</mark>

Respiratory rate: in patients with a respiratory rate <24 cycles/min: 85.7% (48) of them had a good

prognosis, 14.3% (8) a poor prognosis with a (p= 0.006).

Table-9: Association of respiratory rate and prognosis								
			Evolution		p			
			Good prognosis	POOR PROGNOSIS				
Respiratory rate	< 24 cycles/min	Workforce	<mark>48</mark>	8				
		<mark>%</mark>	<mark>85,7%</mark>	<mark>14,3%</mark>	006			
	241/	Workforce	<mark>44</mark>	<mark>25</mark>	<mark>,000</mark>			
	> 24 cycles/min	<mark>%</mark>	<mark>63,8%</mark>	<mark>36,2%</mark>				

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83.1% (59) of patients with >90% saturation progressed well compared to 61.1% (33) of patients with <90% saturation with a (p=0.08). 86.8% of patients with a good prognosis had an 02 flow <10L/min while 65.5% had a poor prognosis with an 02 flow >10L/min with a (p=0.0001).

Tuble 10. Hisboendich of Saturation and Prognostic evolution					
			Evolution		p
			Good	Poor	
			prognosis	prognosis	
Saturation	<mark><90</mark>	Workforce	<mark>33</mark>	<mark>21</mark>	
		<mark>%</mark>	<mark>61,1%</mark>	<mark>38,9%</mark>	
	> _00	Workforce	<mark>59</mark>	<mark>12</mark>	<mark>,008</mark>
	<mark>≥-90</mark>	<mark>%</mark>	<mark>83,1%</mark>	<mark>16,9%</mark>	

Table-10: Association of saturation and prognostic evolut	ution	
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Table-11: Association	between 02 fl	ow rate and	prognostic evolution

Evolution					p	OR OR
			Good prognosis	Poor prognosis		
O2 flow	<mark><10</mark>	Workforce	<mark>66</mark> 86,8%	10 13,2%	0001	
rate	<mark>>=10</mark>	Workforce <mark>%</mark>	<mark>10</mark> 34,5%	<mark>19</mark> 65,5%	,0001	<mark>3,944</mark>

Correlation between biological parameters and prognostic evolution

Lymphocyte count was also a factor that conditioned prognosis: 44 patients with a mean lymphocyte count of 1514 had a good prognosis versus 21 poor prognosis patients with a mean lymphocyte count of 1120 with one (p=0.037). D-dimer assay: 37 patients with a mean d-dimer level of 1265 had a good prognosis versus 18 patients with a mean d-dimer level of 9193 with a (p=0.023).

Table-12: Association of biological	parameters and prognostic evolution
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	Evolution	n	Average	Standard deviation	p	
Lymphocytes	Good prognosis	<mark>44</mark>	<mark>1514,23</mark>	<mark>739,15</mark>	<mark>0,037</mark>	
	Poor prognosis	<mark>21</mark>	<mark>1120,95</mark>	<mark>597,19</mark>		
D-Dimer	Good prognosis	<mark>37</mark>	<mark>1265,29</mark>	<mark>1093,42</mark>	0.022	
	Poor prognosis	<mark>18</mark>	<mark>9193,05</mark>	<mark>13435,11</mark>	<mark>0,025</mark>	

Prognosis evolution of the two groups

Discharge with an oxygen extractor was considered a poor prognostic element in 71% of patients with one (p=0.0001).

			Evolution		p	
			Good	Poor		OR
			prognosis	prognosis		
Output	With 02 control at a r	Workforce	<mark>9</mark>	<mark>22</mark>	,0001	
	with 02 extractor	<mark>%</mark>	<mark>29,0%</mark>	<mark>71,0%</mark>		
	With ant O2 antes at a	Workforce	<mark>83</mark>	<mark>11</mark>		<mark>9,001</mark>
	without O2 extractor	0/0	88 3%	11 7%		

p: degré de signification du test de Wald, OR: Odds Ratio: rapport de côte, IC: intervalle de confiance ; * : p<0,05 ; *** : p <0,00



Fig-1: Enhanced thoracic CT: ground glass patch and foci of condensation with an estimated impairment of>75%, with no evident sign of pulmonary embolism

DISCUSSION

We report on 125 patients with confirmed SARS-CoV-2 infection, of whom 26,4 % (33) were characterized by severe hypoxemia and admitted to the ICU. This study adds supplementary data about specifics of COVID 19 in Morocco and North Africa. Overall, data from a few thousand analyzed patients show that severe illness can be expected in the elderly, although the younger patients are not protected either.

In most Chinese studies, the age range of severe patients is 52 to 66 years. In the Italian population, the mortality rate increases with age: 12% in patients over 70 years and 20% in those over 80 years [1].

In this study, we found that severe patients are aged approximatively 59.6+/- 13.53 years, which is similar to published data from China and Italy.

The study confirms the association between advanced age and increased severity rates in patients with COVID-19, consistent with a previous study. Advanced age is known to be associated with impaired immune function and more underlying comorbidities, which may lead to a poor outcome in these patients.

Severe patients had more diabetes, heart disease, neoplasia, bronchial asthma mellitus and hypertension, as published by Posso M *et al.* [2] in a spanish study.

The presence of comorbidities in patients hospitalized with COVID-19 is commun and may negatively affect their prognosis. [3] Previous studies have shown pre-existing diabetes, cardiovascular, or any other chronic diseases can increase the risk of developing severe covid 19 [4] whereas the increase in mortality was mostly associated with cardiovascular diseases.

Cough, and dyspnea were the most common repiratory symptoms in patients with severe COVID-19. A higher body temperature (>38°C) observed initially, and asthenia, myalgia also appeared to be predictive of worsening disease severity [5].

In a retrospective cohort study among 369 adult patients with COVID-19 admitted to Hospital Cayetano Heredia; a tertiary care hospital in Lima, Peru, Oxygen saturation below 90% on admission is a strong predictor of in-hospital mortality in patients with COVID-19 [6].

In our study, 71 patients with saturation >90% had a mean age of 57.3 years while 54 patients with sao2 <90% had a mean age of 62.7 with one (p=0.027). As published by Ana B Gómez-Belda , where the study showed that Oxygen saturation \leq 93% on room air on admission was a predictor of mortality (odds ratio 11.65, 95% confidence interval 3.26–41.66, *P* < 0.001) in patients aged >70 years [7].

Regarding radiological examinations, computed tomography (CT) imaging has a high sensitivity for the diagnosis of severe COVID-19 pneumonia. Chest CT revealed a ground glass appearance in 83.2%, alveolar condensations in 40%. Lesions were critical in 12.8%, severe in 30.8%. Radiological extension correlated with saturation: 76.1% of patients with sa02 > 90% had mild to moderate pulmonary extension with a (p= 0.0001).

The French Society of Radiology in France has proposed a harmonization of the estimation of total lung extension, qualified as mild between 0 and 25%, moderate between 25 and 50%, severe between 50 and 75%, and critical beyond 75% (https://ebulletin.radiologie.fr/covid19). However, the association between the extent of radiological lesions thus estimated and the prognosis of the disease has not been established [8].

Some studies have also emphasized the relationship between CT scan findings and the clinical condition of patients explaining the possible role of lung CT scan in determining the severity and spread of the disease [9].

The aim of our study is to assess the severity of Covid - 19 disease based on its correlation with level of biomarker and radiological severity.

The correlation between initial lymphocyte count, initial crp and radiological extension showed that patients with severe to critical radiological extension had a mean lymphocyte count of 1306 with a significant p at 0.005. 50 patients with severe to critical radiological extension had a mean initial crp of 222. Several inflammatory markers have been identified as predictive of severe disease and/or death.C-reactive protein (CRP) is a well-known marker of inflammation. It is synthesized by hepatocytes under the control of IL 6. Several series have reported increased CRP as a predictive factor for COVID 19.

CRP is a non-specific acute-phase protein induced by IL-6 in liver and sensitive biomarker of inflammation, infection, and tissue damage.18 Studies showed that it increased significantly in severe Covid – 19 patients at the initial stage, which is a signal of lung deterioration and disease progression as in Prakhar and al study that demonstrated a significant association between levels of CRP and severity of lung involvement (p=0.0346, RR of 2.02, Odds Ratio of 2.37).11 Our study agrees and confirms that CRP levels can be an indicator for severe disease and progressive inflammation [10, 11].

The lymphocyte count, although statistically correlated with the occurrence of severity (p<0.001), is not a powerful biomarker in predicting the occurrence of severity (AUC= 0.222). Lymphopenia is the most constant and most observed element in COVID-19 infection, Guan *et al.* in their large series of 1099 patients, noted it in 83.2% of them.

It is present in all 3 phases of the infection. The meta-analysis of Huang and Pranata noted that the occurrence of lymphopenia is associated with

the occurrence of severity, mortality, ARDS, and admission to intensive care. The lymphocyte count, although statistically correlated with the occurrence of severity (p<0.001), is not a powerful biomarker in predicting the occurrence of severity (AUC= 0.222) [12].

In our study, CRP and lymphocytes are powerful biomarkers in the prediction of the occurrence of severity in COVID-19 patients. Several studies also demonstrated that a higher level of D-dimer was associated with in-hospital mortality [13, 14].

The most suggested mechanism was that the hypercoagulable state, which could be reflected by an elevated D-dimer level, might lead to thrombotic events, resulting in poor outcomes. However, the coagulopathy was thought to result from local and systemic inflammation caused by the coronavirus. Also, D-dimer is known as a biomarker of inflammation [15].

This study was limited by the relatively small number of patients, which may limit statistical power and the inclusion of hospitalized patients exclusively (non-hospitalized patients were not included in the analysis). These limitations may be the cause of statistical bias and therefore of the significant difference identified in demographic and symptomatic characteristics, as well as in laboratory results between groups. Missing data on some variables, such as CT image information and biochemical parameters, may lead to bias in identifying risk factors for mortality in severe patients.

The progression of patients with COVID-19 to worsening appears to be associated with age, cardiovascular and metabolic history, severity of radiological involvement, and observed biological disturbances. This study therefore shows the importance of predictive factors such as âge, lymphocyte and ddimer levels, respiratory rate and oxygen saturation as prognostic factors for the evolution of Covid-19 infection with rapid worsening synonymous with the severity of the evolution. Earlier medical intervention and support on these patients with high risk may reduce the fatality of this disease [16].

CONCLUSION

The progression of patients with COVID-19 to worsening appears to be associated with age, cardiovascular and metabolic history, severity of radiological involvement, and observed biological disturbances. This study therefore shows the importance of predictive factors such as age, lymphocyte and ddimer levels, respiratory rate and oxygen saturation as prognostic factors for the evolution of Covid-19 infection with rapid worsening synonymous with the severity of the evolution.

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