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Hemogram Abnormalities Associated with the Severity of COVID 19 in Patients at the University Clinics of Kinshasa

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Abstract: ***Context: COVID 19 is a pathology related to SARS Cov 2. Affected patients may present with blood count abnormalities, including lymphopenia and neutrophilia. Object: To identify blood count abnormalities associated with the severity of COVID 19. Methods: This is a cross - sectional study conducted in the clinical biology department at University Hospital of Kinshasa (UHK). It covers the period from June to September 2020. All COVID 19 patients tested positive by PCR were included. The parameters of interest were the clinical characteristics of the patients, the hemogram parameters and the neutrophils lymphocytes ratio (NLR). Results: Sixty - two patients were included of whom 40 were men (64.5%). The M/F sex ratio was 2. Their average age was 53.3±16.3 years. The main complaints were cough (67.7%), fever (51.6%) and asthenia (30.6%). The average SaO2 was 83.2±14.7%; and 77.4% of patients had SaO2<95%. Compared to survivors, deceased patients had a significantly lower average SaO2 (p<0.001). The majority of patients were in the severe stage (61.3%). Twenty - one patients (33.9%) died. Patients with severe Covid 19 represented 90.5% of deaths and 46.3% of survivors (p=0.00). Deceased patients had significantly lower hemoglobin averages (p=0.023), higher median WBC and NLR. Anemia, NLR ≥7 and SaO2<95% were significantly associated with the risk of death in COVID - 19 patients. Conclusion: This study showed that certain hematological parameters are predictors of poor prognosis in patients with a severe form of Covid19. Physicians should seek them for a better care of our patients.***

Keywords: Covid - 19, hemogram abnormalities, Kinshasa

1. Introduction

The COVID - 19 pandemic is the largest health crisis the world has known in over a century. Virtually all countries have been affected and their health systems seriously challenged. SARS Cov - 2, the virus responsible for Covid - 19, has, since its discovery in Wuhan in December 2019, infected more than 3, 3 million people worldwide and caused more than two thousands deaths [1, 2]. Although the majority of patients develop a mild or moderate form of COVID - 19, characterized by fever, myalgia, cough, fatigue and moderate respiratory impairment [3, 4], a minority develop a more severe or critical form, resulting in bilateral pneumopathy, and even acute respiratory distress syndrome (ARDS) [4, 5]. Significant abnormalities in the blood count, as well as the production of pro - inflammatory cytokines reflect the impact of the virus on the immune system of patients.

Biological abnormalities associated with the severity of the disease have been described, notably elevated levels of creatine kinase, lactate dehydrogenase, antihemophilic factor A, Von Willebrand factor, and D - dimer [6, 7]. The hypercoagulable state, for example, is associated with the occurrence of cardiac damage in Covid - 19 patients and is therefore associated with mortality from this condition [6, 7, 8].

However, researchers have not paid much attention to the prognostic value of blood count abnormalities during covid - 19. Thus, in this article, we propose to study these abnormalities that can predict poor prognosis in Congolese patients with covid - 19 and to identify the associated factors.

2. Methods

Study design: This is a cross - sectional study that was conducted in the hematology laboratory of the UHK, in the period from June to September 2020. All COVID 19 patients tested positive by PCR at the National Institute for Biomedical Research, were eligible. The PCR analysis was performed. The Sampling was of convenience. Patients were included consecutively. The data was collected on a pre - established survey form.

Variables. Variables included the socio - demographic characteristics of the patients (age and sex), the clinical symptoms (cough, dyspnoea, physical asthenia, oxygen saturation, clinical signs), the level of disease severity (severe, moderate or mild), the vital outcome (survival or death) and blood count results.

The severity criteria were those used at the UHK including respiratory distress, oxygen saturation below 90% in open air, an average blood pressure below 65mmHg, coma, renal

failure, more than 40% of lung involvement on chest CT or extensive opacities on standard radiography.

Data collection
Demographic and clinical data were found in the medical records of patients. Hematological analysis were performed in the hematological laboratory of the UHK.

A 2ml blood sample was taken from each patient and put in a tube with EDTA. The hemogram was carried out using a five - subpopulation automated system from the firm mindray. Oxygen saturation was determined using a pulse oximeter. The Neutrophils/Lymphocytes ratio was calculated and a threshold of 7 was selected. The blood count results were interpreted according to the reference values used in the UHK hematology laboratory. Anemia was defined by a hemoglobin level below 10.5 mg/dl in women and below 12mg/dl in men, normal white blood cell values were 3300 to 8400/mm3 in women, 3300 to 9900/mm3 in men. Platelet baseline values were 150, 000 to 450, 000/mm3.

Sample constitution
All patients whose data were available were included in the study.

Data analysis
Data were entered and coded using Excel 2010 software. Data analyzes were performed using SPSS version 23 software.
Descriptive statistics were presented as average with standard deviation, percentages and confidence intervals (95% CI). To compare average between two and more than two groups we used the Student' t - test and Anova test respectively. Man Whitney's Wilcoxon U - test was used to compare medians between two groups and Kruskal Wallis K - test to compare medians between more than two groups. The chi - square test or Fisher's exact test for comparison between categorical (qualitative) variables.

The Kaplan - Meier curve was used to describe survival from day 1 of hospitalization to death (complete data). Patients lost to follow - up or alive at the end of the study were censored. Log - rank test was used to compare survival curves. Cox regression looked for independent predictors of mortality. A value of $p < 0.05$ was the threshold of statistical significance.

Ethical consideration
The present study was approved by the ethical commitee of the public health department of the Democratic Republic of Congo.

3. Results

Of a total of 62 patients with COVID - 19 recruited in this cohort 40 (64, 5 %) were men (M/F sex ratio of 2).

Their average age was 53.3±16.3 years. Cough (67.7%), fever (51.6%) and physical asthenia (30.6%) were the most common reasons for admission. The SaO2 average was 83.2±14.7% and 77.4% of patients had a rate of SaO2<95%. Twenty - one (33.9%) patients died and 41 (66.1%) survived.

The table1 shows Clinical characteristics of patients according to the vital outcome

The table 2, shows that patients with severe Covid were the most affected by oxygen desaturation. ($p<0.001$).

Comparing deceased patients to survivors, we note that deceased patients had a significantly lower average of SaO2 ($p<0.001$) and a higher proportion of people with SaO2 above 95% ($p=0.003$)

The figure1 shows that the majority of patients were in the severe stage (61.3%). Patients with severe covid represented 90.5% of the deceased ($p=0.001$). No patient with light stage died.

The probability of survival of patients admitted for COVID - 19 at the treatment initiation was, respectively, 87.1%, 71.0%, 67.7%, 66.1% and 66.1% at two, five, ten, fifteen and thirty days (figure2). The median overall survival time is 10.0 (IQR=9.0 - 11.0), 11 in survivors (IQR= 11.0 - 12.0) and 3 in deceased (IQR=2.0 - 3.0)

Depending on Survival according to the severity (EIQ=2, 0 - 3, 0).

Patients in the mild stage of COVID - 19 had better survival compared to patients with moderate and severe stages, and a statistically significant difference ($p=0.006$) (figure3).

Biological characteristics of patients
The mean and median values of biological characteristics of patients with COVID - 19 are shown in Table 3. Comparing to the survivors, the deceased had significantly lower mean hemoglobin (Hb) ($p=0.023$), lower median white blood cells (WBC) and higher neutrophil/lymphocyte ratio (RNLs). This shows a higher frequency of anemia, high white blood cells and RNL ≥7 in deceased patients.

In figure 4, Anemia reduced the survival of patients admitted with COVID - 19, Compared to patients with a WBC count <8.4/9.9 ($x10^3$/mm3) H/F, those with WBCs ≥ 8.4/9.9 ($x10^3$/mm3) H/F had significantly improved weaker survival (figure 5).
In univariate analysis, the SaO2<95%, the Hb rate <12/10 g M/F, the WBC rate≥8.4/9.9 x103 /mm3 (M/F), the NLR≥7, and the severe stage of the disease had emerged as the main predictors of mortality in patients admitted for COVID - 19. (table 4). After multivariate adjustment, SaO2<95%, Hb rate <12/10 g M/F, the NLR≥7 and the severe disease stage were significantly associated with the risk of death in COVID - 19 patients The risk of death was multiplied by 3 (adjusted HR 3.31; 95% CI (1.22 - 7.79) for SaO2<95%, by 2 (adjusted HR 2.44; 95% CI (1.69 - 8.62)) for Hb <12/10 g M/F, by 2 (adjusted HR 2.39; 95% CI (1.68 - 8.38)) for NLR≥ 7 and by 5 (adjusted HR 5.36; CI to 95% (1.12 - 25.65)) for the severe stage of the disease. (Table 5)

4. Discussion

Of the 62 patients included in the study, 64.5% were men. The average age of the patients was 53.3±16.3 years. Helmy El Rais [4], in France, observed that men represented 54% of hospitalized covid patients between September and November 2020. In the same study men represented 64% of patients admitted to critical care in September 2020. In China, some authors found that, compared to women, men were more likely to develop severe disease or to die [9].

Some researchers report that female sex hormones may protect against severe forms of covid 19 as they may have an anti - inflammatory and protective function against severe forms of the disease [10, 11, 12]. Indeed, these hormones would influence immune cells by stimulating the production of antibodies and would promote the repair of certain respiratory cells and inhibit the ACE2 receptor. This would be justified by the fact that women would have a more effective, intense and prolonged immune response to both humoral and cellular immunity [13]. On the other hand, Estradiol stimulates the humoral response in case of viral infection by inducing high levels of antibodies. promote the repair of certain respiratory cells and inhibit the ACE2 receptor [11]. Conversely, testosterone exerts effects of inhibition of certain parameters of immunity contributing to explain this gender difference in terms of severity and mortality gender related to Covid 19. [14]

In all countries, there are more men than women among COVID - 19 deaths, but the extent of the male disadvantage differs from country to country. These differences could also be explained by the high frequency of COVID - 19 severity risk factors in the male population [5]. While these data do not fully explain the sex ratio, they certainly call for special monitoring of older men with comorbidities.

Cough, fever and physical asthenia were the most common complaints as in other studies [7, 8, 9]. However, the lower frequency of fever in our study could be explained by the practice of self - medication frequently encountered in our environments, which blunts the clinical manifestations of the disease, underestimates the cases, favors contamination and late consultations, at the severe stage of the disease.

The present study found lower hemoglobin average values in deceased patients than in survivors. Anemia would be the result of inflammation (cytokine cascade) with its deleterious effect on erythropoiesis [15] believes that this anemia, according to a conceptual model, is explained by the action of the Sarscov2 genome on hemoglobin [16]. Indeed, there are sequences coding for non - structural proteins of the virus which attack one of the beta chains of hemoglobin and extract the iron atom from the heme [15, 16]. In all cases, anemia is an independent risk factor that may be associated with the severity of COVID - 19 disease and has a multifactorial pathophysiological mechanism [16, 17, 18]. So, health care professionals and medical physician should be more sensitive to the hemoglobin levels of severe COVID - 19 patients at admission.

Our study reported high white blood cells rates in deceased patients. Other studies have similar results. Indeed, these results are in agreement with those of kazemi [19,] a study conducted in China showed that the number of leukocytes was higher in deceased patients than in cured patients [11]. The median rates of WBC in deceased patients were of 9, 8x109 /L against 5, 2 x109 /L in survivors. In addition, another study involving 140 patients hospitalized in Wuhan reported significantly higher leukocyte counts in patients with severe COVID - 19 than in other patients. Tao Chen and al. [17, 18, 20] found that hyperleukocytosis was present in 50% of deceased patients and in 4% of cured ones. Lymphopenia was present in 91% of deceased patients compared to 47% of cured patients; The proposed mechanism of lymphopenia involves the receptor for angiotensin - converting enzyme 2 (ACE2), which is expressed on the surface of lymphocytes, [19, 21]. SARS-CoV-2 can directly infect lymphocytes via this receptor. In critically ill patients, a systemic increase in cytokines and inflammatory mediators have been demonstrated, which can lead to marked lymphocyte apoptosis, suggesting that an immune deficiency would be involved in the occurrence of death. The present study showed that the NLR was associated with the severity of the disease, with a risk of death which was multiplied by 2 for an NLR ≥7. The higher NLR is explained by neutrophil proliferation and lymphocyte apoptosis. It is observed in cases of severe infection and systemic inflammation [21, 22, 23]. Since Covid 19 is a systemic inflammation, it, therefore, has harmful repercussions on the blood, hence the disturbance of hematological parameters that the doctor will have to look for. Furthermore, the immune disorder thus induced could promote an increased susceptibility to superimposed infections, which infections could play a role in mortality.

Patients in the mild stage of the disease had better survival compared to patients in the severe stage and the probability of survival decreases during the time of hospitalization. The present study show that anemia and and NLR greater than 7 were associated to a severe form of Covid - 19 and increases the risk of death. Leukocytosis and lymphopenia were associated to the risk of death. More than 70% of deceased patients were men, however men died 2.5 times more than women.

5. Conclusion

This study shows that in its severe form covid - 19 may present with hematological abnormalities. The later are associated to a poor prognosis. These abnormalities include hyperleukocytosis, anemia and a neutrophil/lymphocyte ratio greater than 7. These factors should be considered as determinants of the severity of the covid - 19. Clinicians should look for them systematically.

What is known about this topic

Severe covid - 19 may present with different clinical profiles and biological abnormalities such a d - dimere and creatine - kinase increase, coagulation troubles and other disorders that may cause death of patients.

What this study adds

- Anemia, hyperleukocytosis and a high Neutrophiles/lymphocytes ratio are observed in patients with severe covid - 19

- These hematological abnormalities participate to the poor prognosis of severe covid - 19

Competing interests
The authors declare no competing interests.

Authors' contributions
M Mbelu designed the study, collected the data and wrote the article; JJ Malemba, D Kaba, M Nganga, G Ilunga, B Longo participated in the drafting of the article. All authors have read and approved the final version of the manuscript.

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Table 1: Clinical characteristics of patients according to the vital outcome

Variables	Total (n=62)	Deceased (n=21)	Alive (n=41)	p
Age (years)	53, 3±16, 3	51, 5±19, 8	54, 2±14, 4	0, 433
<40	15 (24, 2)	7 (33, 3)	8 (19, 5)	
40 - 59	20 (32, 3)	5 (23, 8)	15 (36, 6)	
≥60	27 (43, 5)	9 (42, 9)	18 (43, 9)	
Sex				0, 486
M	40 (64, 5)	13 (61, 9)	27 (65, 9)	
F	22 (35, 5)	8 (38, 1)	14 (34, 1)	
Fever	32 (51, 6)	11 (52, 4)	21 (51, 2)	0, 572
Cough	42 (67, 7)	14 (66, 7)	28 (68, 3)	0, 558
Asthenia	19 (30, 6)	7 (33, 3)	12 (29, 3)	0, 480
Rhinorrhea	19 (30, 6)	9 (42, 9)	10 (24, 4)	0, 115
Headache	10 (16, 1)	3 (14, 3)	7 (17, 1)	0, 544
Dyspnea	27 (43, 5)	8 (38, 1)	19 (46, 3)	0, 365
Dysphagia	6 (9, 8)	1 (4, 8)	5 (12, 5)	0, 318
Chest pain	13 (21, 0)	3 (14, 3)	10 (24, 4)	0, 281
Anuria	8 (12, 9)	2 (9, 5)	6 (14, 6)	0, 447
Diarrhea	7 (11, 3)	2 (9, 5)	5 (12, 2)	0, 558
Vomiting	5 (8, 1)	2 (9, 5)	3 (7, 3)	0, 556
Dialysis	8 (12, 9)	2 (9, 5)	6 (14, 6)	0, 447
SaO2	83, 2±14, 7	74, 1±18, 0	87, 9±10, 1	<0, 001
SaO2<95%	48 (77, 4)	19 (90, 5)	29 (70, 7)	0, 005

Table 2: Clinical characteristics and Severity of Disease

Variables	Light stage (n=10)	Moderate stage (n=14)	Severe stage (n=38)	P
Age	57, 0±14, 1	56, 3±17, 2	51, 2±16, 6	0, 883
<40 years	2 (20, 0)	2 (14, 3)	11 (28, 9)	
40 - 59 years	3 (30, 0)	5 (35, 7)	12 (31, 6)	
≥60 years	5 (50, 0)	7 (50, 0)	15 (39, 5)	
Sex				0, 750
M	6 (60, 0)	8 (57, 1)	26 (68, 4)	
F	4 (40, 0)	6 (42, 9)	12 (31, 6)	
Fever	9 (90, 0)	3 (21, 4)	20 (52, 6)	0, 004
Cough	5 (50, 0)	11 (78, 6)	26 (68, 4)	0, 371
Asthenia	3 (30, 0)	4 (28, 6)	12 (31, 6)	0, 519
Rhinorrhea	5 (50, 0)	1 (7, 1)	13 (34, 2)	0, 056
Headache	3 (30, 0)	1 (7, 1)	6 (15, 8)	0, 383
Dyspnea	1 (10, 0)	9 (64, 3)	17 (44, 7)	0, 026
Dysphagia	1 (10, 0)	1 (7, 1)	4 (10, 8)	0, 556
Chest pain	3 (30, 0)	3 (21, 4)	7 (18, 4)	0, 823
Anuria	1 (10, 0)	2 (14, 3)	5 (13, 2)	0, 949
Diarrhea	0 (0, 0)	2 (14, 3)	5 (13, 2)	0, 556
Vomiting	0 (0, 0)	3 (21, 4)	2 (5, 3)	0, 122
Dialysis	1 (10, 0)	2 (14, 3)	5 (13, 2)	0, 540
SaO2	97, 2±3, 1	93, 4±1, 7	75, 8±14, 4	<0, 001
SaO2<95%	1 (10, 0)	10 (71, 4)	37 (97, 4)	<0, 001

Table 3: Biological characteristics according to the vital outcome

Variables	Total (n=62)	Décédé (n=21)	Vivant (n=41)	p
Hb (avarage value)	10, 1±2, 9	8, 9±2, 9	10, 7±2, 7	0, 023
Hct (avarage value)	33, 7±8, 3	35, 3±6, 8	32, 8±8, 9	0, 264
GB (median value)	12, 2 (8, 9 - 13, 8)	13, 9 (11, 8 - 15, 8)	10, 0 (7, 5 - 12, 5)	0, 042
N (median value)	77, 6 (68, 9 - 81, 4)	77, 2 (60, 1 - 81, 2)	78, 3 (66, 8 - 83, 3)	0, 820
L (median value)	17, 8 (10, 8 - 26, 9)	18, 4 (40, 8 - 28, 8)	17, 1 (10, 5 - 29, 7)	0, 688
M (median value)	6, 1 (5, 5 - 6, 2)	6, 2 (5, 0 - 6, 5)	6, 1 (5, 2 - 6, 2)	0, 816
E (median value)	0, 2 (0, 2 - 0, 2)	0, 2 (0, 0 - 0, 9)	0, 2 (0, 2 - 0, 2)	0, 371
B (median value)	0, 2 (0, 2 - 0, 2)	0, 4 (0, 2 - 0, 5)	0, 2 (0, 2 - 0, 2)	0, 007
NLR (median)	6, 6 (3, 7 - 8, 2)	7, 4 (5, 8 - 10, 8)	4, 2 (2, 2 - 8, 2)	0, 010
Plaquette (median)	21±9	21±9	21±10	0, 963
GR ($Nx10^6$)	3, 9±0, 9	4, 1±0, 8	3, 9±1, 0	0, 322

VGM (	78, 7±8, 8	78, 4±9, 4	78, 8±8, 6	0, 841
TCMH	26, 6±5, 5	26, 5±6, 5	26, 8±4, 9	0, 922
CCMH	33, 5±3, 4	32, 9±4, 9	33, 8±2, 3	0, 287
Hb <12/10 g H/F	43 (69, 4)	18 (85, 7)	25 (61, 0)	0, 040
GB≥8, 4/9, 9 /mm3 H/F	36 (58, 1)	16 (76, 2)	20 (48, 8)	0, 035
Plaquette <1, 50/mm^3	15 (24, 2)	6 (28, 6)	9 (22, 0)	0, 390
VGM <80	28 (45, 2)	10 (47, 6)	18 (43, 9)	0, 495
TCMH ≥30	18 (29, 0)	8 (38, 1)	10 (24, 4)	0, 202
CCMH ≥35	22 (35, 5)	8 (38, 1)	14 (34, 1)	0, 486
NLR ≥7	41 (66, 1)	18 (85, 7)	23 (56, 1)	0, 018

Table 4: Biological characteristics and severity of the disease

Variables	Light stage (n=10)	Moderate stage (n=14)	Severe stage (n=37)	p
Hb	10, 6±2, 9	10, 6±2, 2	9, 8±3, 1	0, 545
Hct	31, 4±8, 6	34, 8±8, 2	33, 9±8, 4	0, 619
Platelet	1, 89±1, 17	2, 03±0, 5	2, 1±1, 1	0, 778
RBC	3, 9±1, 2	4, 2±0, 9	3, 9±0, 9	0, 583
MCV	82, 2±9, 4	79, 0±7, 9	77, 6±8, 9	0, 335
MCHC	28, 4±3, 4	26, 2±7, 0	26, 3±5, 4	0, 546
CCMH	32, 7±3, 6	34, 9±1, 7	33, 3±3, 7	0, 240
WBC	7, 1 (5, 3 - 11, 0)	13, 9 (9, 0 - 18, 9)	12, 5 (8, 0 - 13, 9)	0, 206
N	73, 7 (53, 8 - 84, 2)	75, 2 (55, 0 - 86, 8)	77, 6 (69, 3 - 81, 3)	0, 852
L	22, 9 (10, 0 - 50, 3)	17, 0 (8, 0 - 30, 8)	18, 9 (10, 8 - 28, 0)	0, 659
M	5, 7 (3, 0 - 6, 2)	6, 2 (5, 0 - 7, 4)	6, 2 (5, 5 - 6, 3)	0, 373
E	0, 3 (0, 1 - 0, 7)	0, 2 (0, 0 - 0, 2)	0, 2 (0, 2 - 0, 3)	0, 056
B	0, 2 (0, 1 - 0, 4)	0, 2 (0, 2 - 0, 2)	0, 2 (0, 2 - 0, 4)	0, 673
NLR	4, 6 (1, 6 - 8, 5)	4, 4 (1, 8 - 10, 6)	6, 9 (3, 8 - 8, 3)	0, 037
Hb <12/10 g% H/F	60 (60, 0)	9 (64, 3)	28 (73, 7)	0, 019
HCt <38/32% H/F	60 (60, 0)	7 (50, 0)	21 (55, 3)	0, 877
WBC ≥8, 4/9, 9 /mm3 H/F	3 (30, 0)	9 (64, 3)	24 (63, 2)	0, 166
Platelet<1, 50/mm3	3 (30, 0)	2 (14, 3)	10 (26, 3)	0, 698
RBC <4/3, 5 H/F	4 (40, 0)	4 (28, 6)	17 (44, 7)	0, 576
MCV < 80	2 (20, 0)	7 (50, 0)	19 (50, 0)	0, 245
MCHC ≥30	4 (40, 0)	4 (28, 6)	10 (26, 3)	0, 672
CCMH ≥35	3 (30, 0)	7 (50, 0)	12 (31, 6)	0, 453
NLR ≥7	5 (50, 0)	9 (64, 3)	27 (71, 1)	0, 041

Table 5: Determinants of mortality in Covid - 19 patients

Predictor factor	**Unadjusted HR (95%CI)**	**P**	**Adjusted HR (95%CI)**	**p**
SaO2<95%				
No				
Yes	3.49 (1.81 - 15.07)	0.019	3.31 (1.22 - 7.79)	0.013
Hb <12/10 g M/F				
No				
Yes	3.02 (1.89 - 10.28)	0.018	2.44 (1.69 - 8.62)	0.016
WBC≥8, 4/9, 9 x10^3 /mm3 (M/F)				
No				
Yes	2.52 (1.91 - 6.93)	0.017	1.44 (0.50 - 4.12)	0.496
NLR≥7				
No				
Yes	3.31 (1.97 - 11.29)	0.015	2.39 (1.68 - 8.38)	0.017
Severe stage				
No				
Yes	4.98 (1.38 - 17.93)	0.014	5.36 (1.12 - 25.65)	0.036

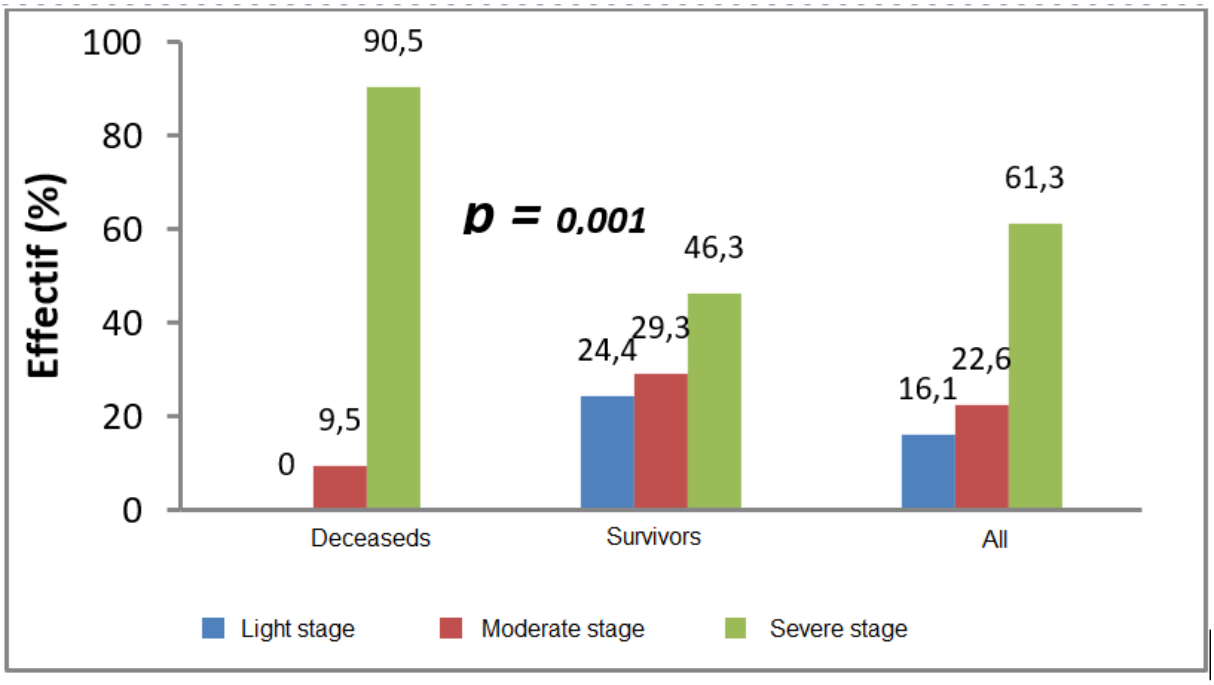

Figure 1: Severity of covid - 19 according to the vital outcome.

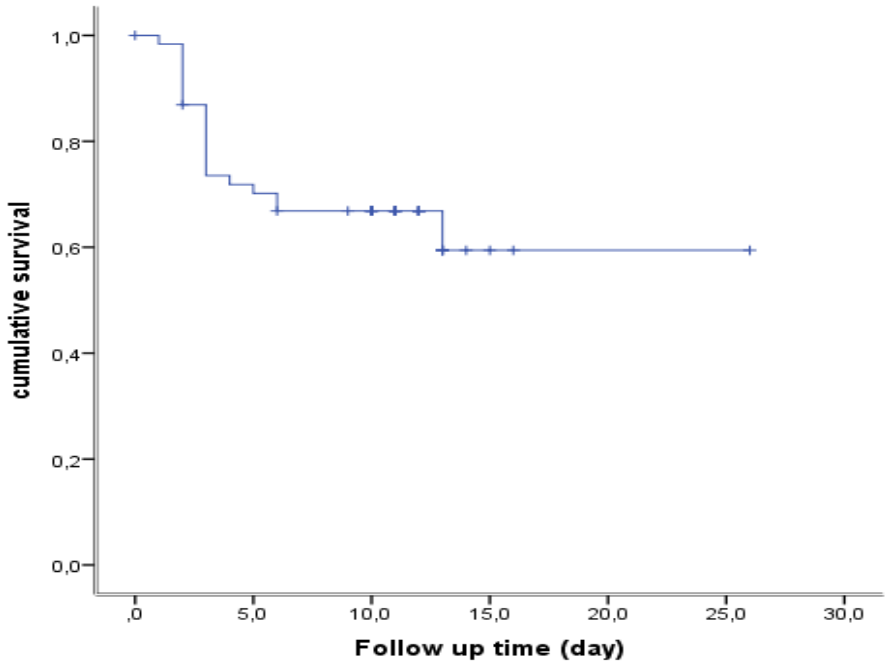

Figure 2: Survival curve (Kaplan - Meier) of patients admitted for covid - 19.

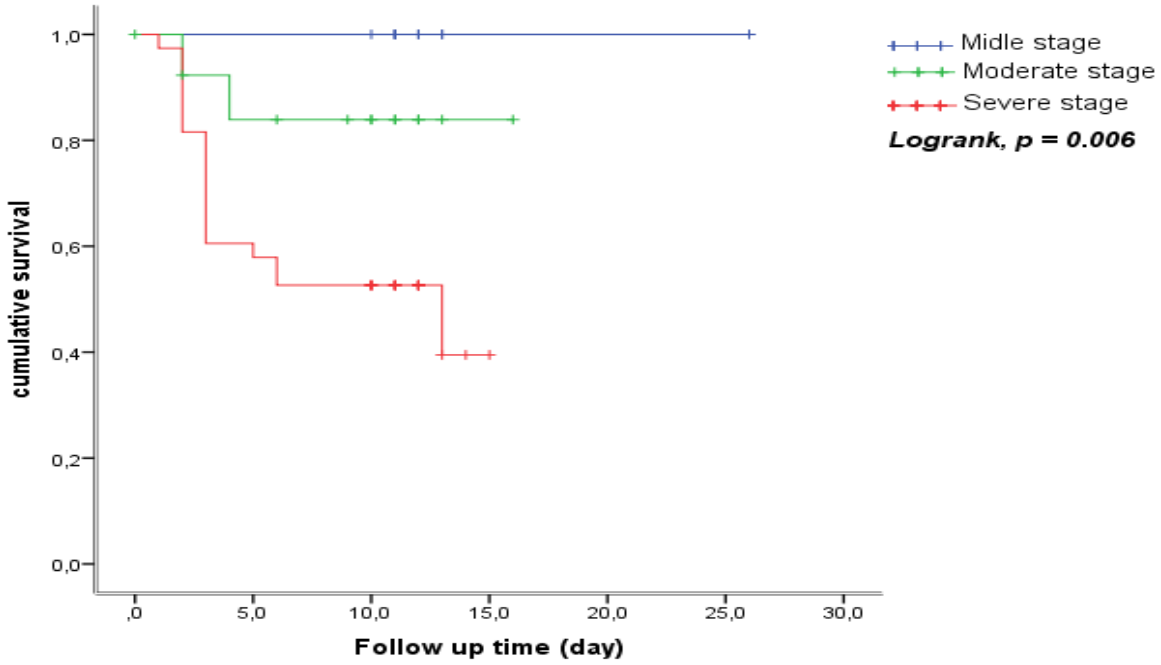

Figure 3: Survival curve (Kaplan - Meier) of patients admitted for covid - 19 according to severity.

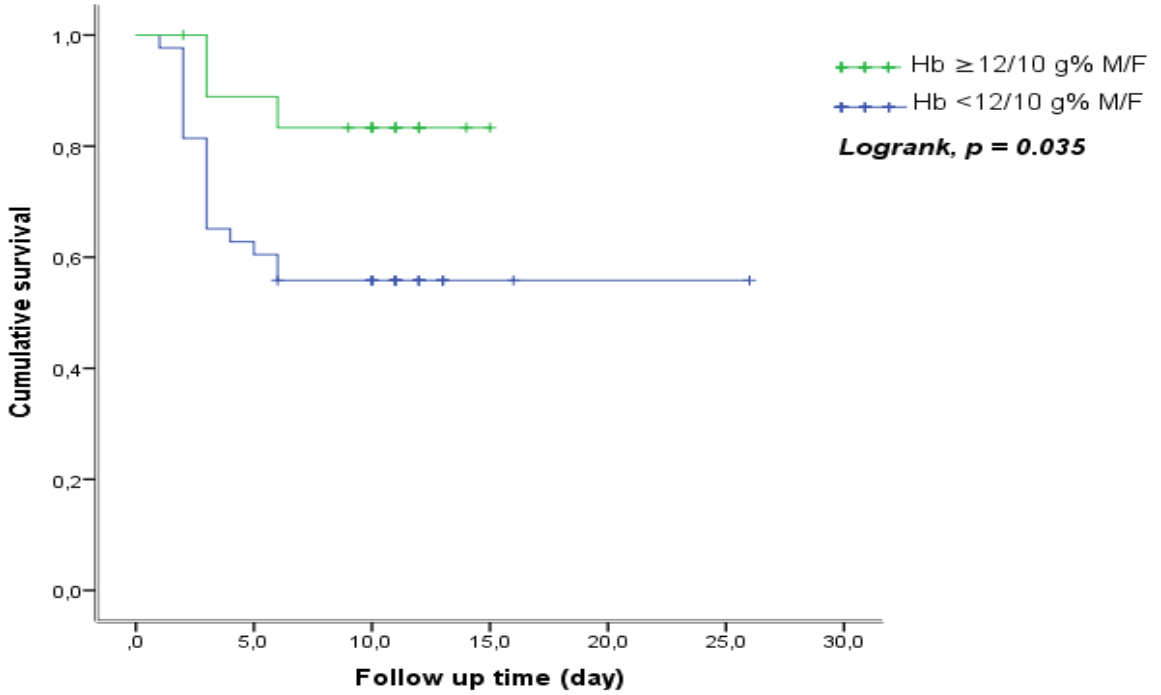

Figure 4: Cumulative proportions of surviving patients (Kaplan - Meier) according to hemoglobin.

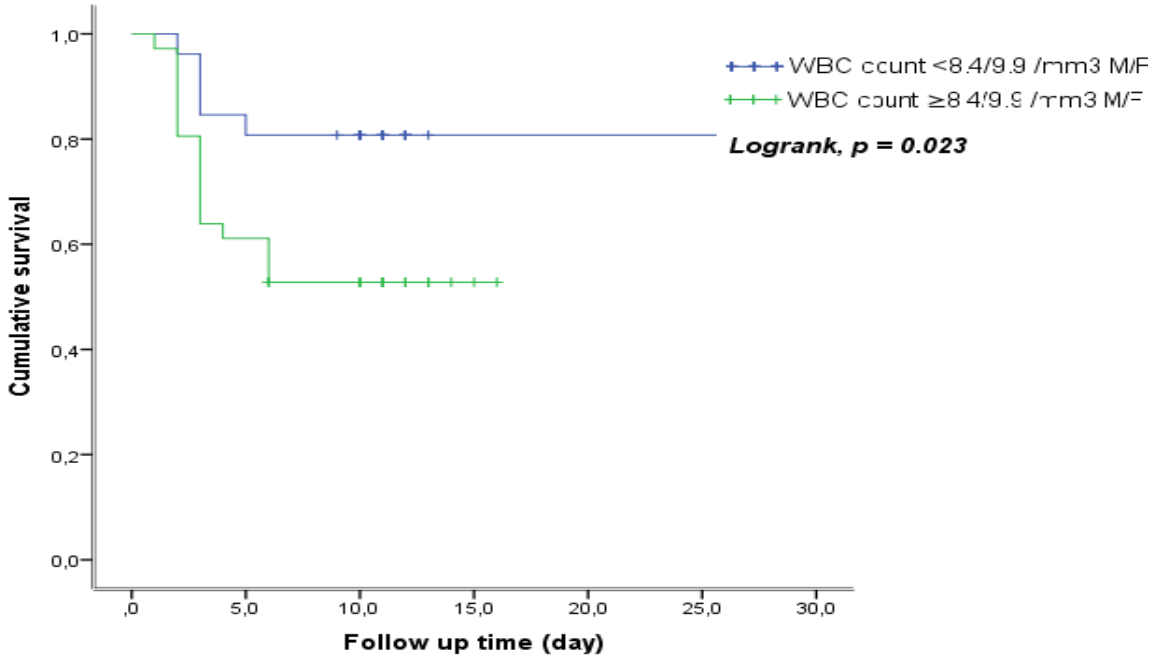

Figure 5: Cumulative proportion of covid - 19 patients who survived (Kaplan - Meier) according to White blood cells.

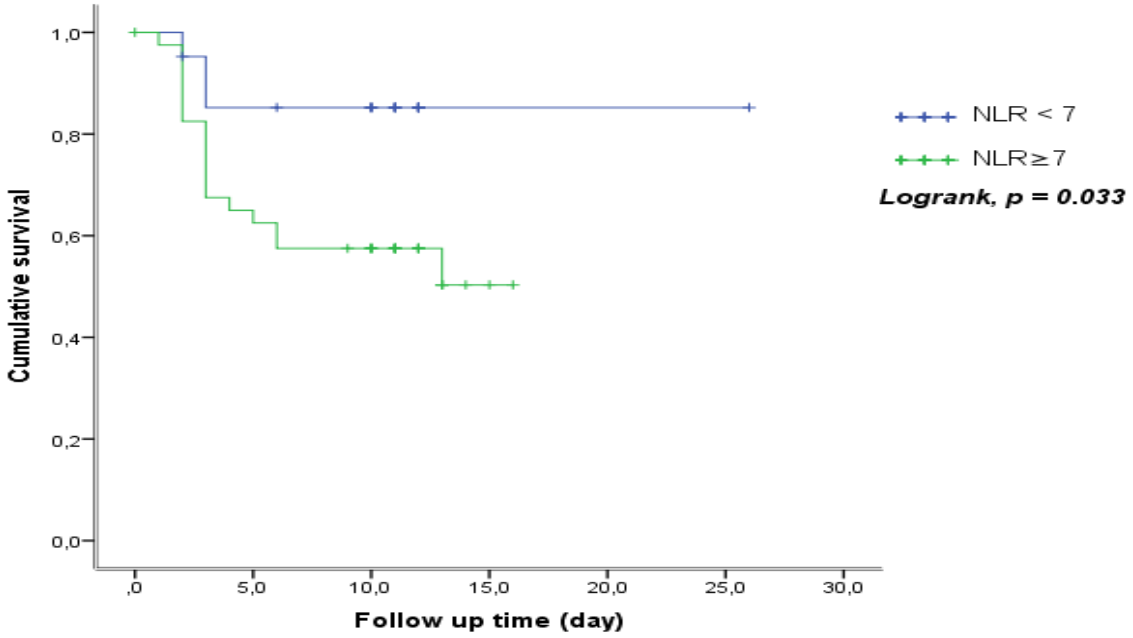

Figure 6: Cumulative proportions of patients who survived (Kaplan - Meier) according to the Neutrophil - lymphocyte ratio (NLR).