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RESEARCH ARTICLE **BIOLOGY**

The Most Prominent Manifestations of Illness in COVID-19 Patients and Their Relationship to the Severity of Disease and Mortality in one of Isolation and Intensive Care Centers in North Western of Libya

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ABSTRACT

As SARS-CoV-2 spread rapidly across continents giving rise to the COVID-19 pandemic; scientists have worked intensively to understand the virus built, behavior and Response to vaccination and treatment. This descriptive-analytical study **aimed**: to assess the impact of predisposing risk factors, specifically age and chronic diseases, on predicting the extent of health deterioration and increased likelihood of mortality in COVID-19 patients. **Methods:** In this study, data from 100 treated patients were examined at one of Isolation and Intensive Care Centers in north western of Libya "Surman ".data were extracted from medical records using a data collection form, and patients were classified according to the WHO's clinical assessment criteria, reported risk factors and laboratory indicators. Most patients were men 66% with an average age of 68 years. Common conditions included diabetes 34%, hypertension 28%, and other comorbidities 24%. 11% of cases were classified as mild, 40% as moderate, and nearly 49% as severe. Significantly, many patients 89%, required intensive care with a survival rate of 69% and a mortality rate of 31%. **Results:** Disease severity was significantly associated with specific biomarker profiles at admission, characterized by decreased oxygen saturation 85.47% and elevated levels of CRP (118.5 mg/L) and D-dimer (1.86 µg/mL). Moreover, CRP and D-dimer levels showed a direct positive correlation with infection severity. **Recommendations:** the need to strengthen community compliance with preventive measures and activate early medical intervention mechanisms as soon as clinical symptoms appear to reduce the risk of morbidity.

أبرز المظاهر المرضية للمصابين بكوفيد 19 وعلاقتها بشدة المرض والوفاة بأحد مراكز العزل والإيواء بليبيا

نجوى المبروك الناجح[1،*]، رشاء محمد الكرشودي[1]

الكلمات المفتاحية
كوفيد 19
دي دايمر
بروتين سي التفاعلي
السكري
ارتفاع ضغط الدم
ليبيا

الملخص

عبر القارات وأدى إلى جائحة كوفيد-19، وعمل العلماء بكثافة لفهم بنية الفيروس وسلوكه واستجابته للتطعيم والعلاج. هدفت هذه الدراسة الوصفية التحليلية إلى تقييم تأثير عوامل الخطر المؤهبة، وتحديدًا العمر والأمراض المزمنة، على التنبؤ بمدى تدهور الحالة الصحية وزيادة احتمالية الوفاة لدى مرضى كوفيد-19. المنهجية: في هذه الدراسة، تم فحص بيانات 100 مريض تلقوا العلاج في أحد مراكز العزل والعناية المركزة في شمال غرب ليبيا (صرمان). استُخرجت البيانات من السجلات الطبية باستخدام استمارة جمع البيانات، وصُنِّف المرضى وفقًا لمعايير التقييم السريري لمنظمة الصحة العالمية، وعوامل الخطر المُبلغ عنها، والمؤشرات المختبرية. كان معظم المرضى من الرجال (66%) بمتوسط عمر 68 عامًا. شملت الحالات الشائعة داء السكري (34%)، وارتفاع ضغط الدم (28%)، وأمراض مصاحبة أخرى (24%). صُنِّفت 11% من الحالات على أنها خفيفة، و40% على أنها متوسطة، ونحو 49% على أنها شديدة. تجدر الإشارة إلى أن 89% من المرضى احتاجوا إلى رعاية مركزية، حيث بلغت نسبة النجاة 69% ونسبة الوفيات 31%. النتائج: ارتبطت شدة المرض ارتباطًا وثيقًا بملامح محددة للعلامات الحيوية عند دخول المستشفى، والتي تميزت بانخفاض تشبع الأكسجين (85.47%) وارتفاع مستويات البروتين التفاعلي (C) 118.5 ملغم/لتر و(D-DIMER) 1.86 ميكروغرام/مل. علاوة على ذلك، أظهرت مستويات البروتين التفاعلي C و D-DIMER ارتباطًا إيجابيًا مباشرًا بشدة العدوى. التوصيات: ضرورة تعزيز التزام المجتمع بالتدابير الوقائية وتفعيل آليات التدخل الطبي المبكر فور ظهور الأعراض السريرية للحد من خطر الإصابة بالأمراض.

Introduction

Over the past two decades, viral diseases have repeatedly threatened public health worldwide, with outbreaks such as SARS-CoV-1 in 2002–2003, H1N1 swine flu in 2009, and MERS-CoV in 2012 highlighting the ongoing risks. [1] In March 2020, the World Health Organization (WHO) officially declared the novel coronavirus (SARS-CoV-2) a global pandemic, signaling the start of a worldwide health emergency. First identified in Wuhan, China, in December 2019 the virus rapidly spread across the globe causing more

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than 281 million reported cases and 5.4 million deaths all over the world. [2] Libya confirmed its first COVID-19 case on March 24, 2020, and by April 2022 the virus had claimed 6,430 lives out of nearly 502,000 reported cases. Globally WHO reported SARS-CoV-2 variants in more than 200 countries with the heaviest toll in the U.S., Brazil, and India. In 2020, COVID-19 was the third leading cause of death in the United States with nearly 375,000 lives lost to the virus. [3] By January 2023, over 6.69 million lives lost to COVID-19 and more than 660 million people infected worldwide reflecting an estimated global mortality rate of 22%. [4] Age, severity of COVID-19 and chronic conditions such as diabetes and hypertension played a key role in determining a patient's risk of severe outcomes and mortality. Biomarkers such as CRP and D-dimer were used to indicate disease severity help guide decisions about patient isolation and treatment. In the past three years, the world has been on high alert as the coronavirus spread quickly and caused severe illness and death in many infected individuals. This has made the coronavirus a source of widespread concern and panic. [5,6,7] Older adults and individuals with chronic illnesses face a greater risk of severe infection and as a result increases their chances of mortality. Laboratory markers, including high CRP or D-dimer levels further mounting a severe and potentially dangerous response to the infection, significantly raising their risk. [8] Since the pandemic outbreak, medical professionals have consistently advised people at higher risk including older adults, those with chronic illnesses, and individuals with elevated CRP or D-dimer levels to closely monitor their health. Following recommended guidance and precautions is essential to protect oneself from COVID-19 given the potentially life-threatening consequences including the need for intensive care or isolation. [9] This study aimed "to assess the impact of predisposing risk factors, specifically advanced age and chronic diseases, on predicting the extent of health deterioration and increased likelihood of death in COVID-19 patients."COVID-19 patients. Moreover, the study further investigates how important laboratory measurements, including high D-dimer and CRP levels relate to the severity of COVID-19 as well as the risk of death. To identify the most severe stages of COVID-19 that affect the largest number of patients.

Materials and methods

This descriptive-analytical study took place at the Surman Isolation and Intensive Care Center over the period from August 2021 to February 2022. In accordance to research and study ethics, the study was conducted after obtaining permission to obtain sufficient information for the study from the management of the isolation and intensive care center in Surman, on the condition that the names of the patients be kept confidential. Pathological data were collected from patients' medical records using a standardized data collection form. PCR testing confirmed viral infection in all patients, with every result testing positive. Oxygen levels, as well as D-dimer and CRP measurements, were also recorded. A structured data collection form was developed to capture patient demographics, including age and sex. Information on chronic conditions such as diabetes, hypertension, and other medical ailments was recorded. In addition, key clinical measurements including oxygen saturation, CRP, and D-dimer levels were documented at the time of admission. Cases were classified as mild, moderate, or severe according to the World Health Organization's clinical criteria, based on the level of oxygen support required, such as low-flow or high-flow methods. Data were collected from 100 patients at the Surman Isolation and Intensive Care Center. Patients were categorized into two groups: survivors and those who died, and each group was analyzed separately to better understand the factors influencing outcomes.

Statistical analysis

Descriptive statistics were calculated using SPSS and Excel. The results were presented in tables, showing measures such as the mean, standard deviation, variance, range, standard error, and confidence limits. the correlation coefficient to illustrate the strength of the relationship between the variables, and Percentages in graphical formats to illustrate the data were also used.

Obstacles: Despite having obtained prior approval, certain isolation centers were hesitant to cooperate and share essential data, making it difficult to assemble and compare results across the study area.

Results

Focusing on established risk factors and key laboratory measurements linked to mortality, this study examined data from 100 patients treated at Surman's Isolation and Intensive Care Center. A total of 100 COVID-19 cases were analyzed, comprising 66% men and 34% women, with patients averaging 68 years of age. The study focused on describing the main clinical features of patients admitted to the intensive care unit at the Surman Isolation Center, while assessing key risk factors and laboratory measurements. The findings showed a survival rate of 69% and a mortality rate of 31%. Among the patients, 34% had diabetes, 28% had hypertension, and 24% had other underlying conditions, including heart disease, respiratory disorders, kidney complications, or tumors.

Based on disease severity, 11% of cases were classified as mild, 40% as moderate, and nearly half (49%) as severe. At admission, patients showed markedly low oxygen levels, averaging 85.47%, alongside elevated inflammatory and coagulation markers, with mean CRP levels of 118.5 mg/L and D-dimer levels of 1.86 µg/mL. Disease severity was closely associated with patient outcomes, showing a clear relationship with both survival and mortality.

Figure 3 demonstrates that individuals with chronic conditions were more susceptible to COVID-19, with diabetes emerging as the most prevalent comorbidity (34%). Hypertension was present in 28% of cases, while other conditions including heart, respiratory, and kidney diseases accounted for 24%. These trends were further explored by comparing outcomes between the survival and death groups. Regarding disease severity, Table 1 shows that females tended to have less severe disease. In mild cases, females accounted for a slightly higher proportion (55%) compared with males (45%). In contrast, males predominated in the more severe categories, representing 57% of moderate cases and 70% of severe cases. Overall, deaths were more common among males, who accounted for 59% of total fatalities,

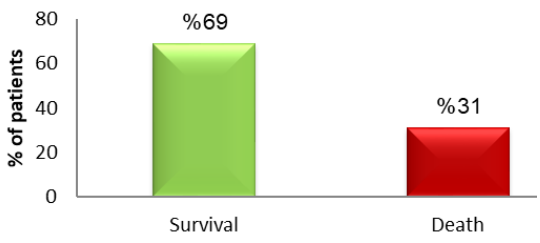

Figure 1: depicted the percentage between survival and death.

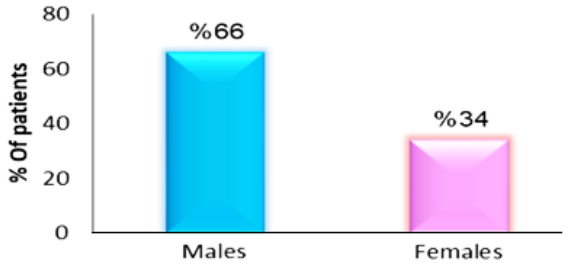

Figure 2: depicted % of males and females who entered isolation center during the study period

compared with 41% among females. The table also presents age distributions, showing average ages of 62 years for mild cases, 63 years for moderate cases, and 70 years for severe cases. The overall mean age among survivors was 65 years. The table also shows the prevalence of hypertension, affecting 9% of mild cases, 30% of moderate cases, and 26% of severe cases. Diabetes affected 32% of all patients, with the condition observed in 45% of mild cases, 26% of moderate cases, and 35% of severe cases.

Furthermore, Figure 5 shows a markedly elevated mean C-reactive protein (CRP) level among deceased patients reaching 139.19 mg/L. In contrast to the deceased group, the average CRP level among survivors was lower at 109.15 mg/L.

In Table (2), Mortality findings were analyzed by gender and stratified according to disease severity. Importantly, no female deaths were recorded among moderate cases, whereas all fatalities in this group occurred in males. Furthermore, among severe cases, males accounted for 77% of deaths, while females represented 23%. Overall, males represented the majority, accounting for 81%, while females comprised19%. Table (2) presents the average age of fatalities, showing a mean age of 87 years for moderate cases, 73 years for severe cases, and an overall average age of 75 years. Disease severity is evident in the case distribution

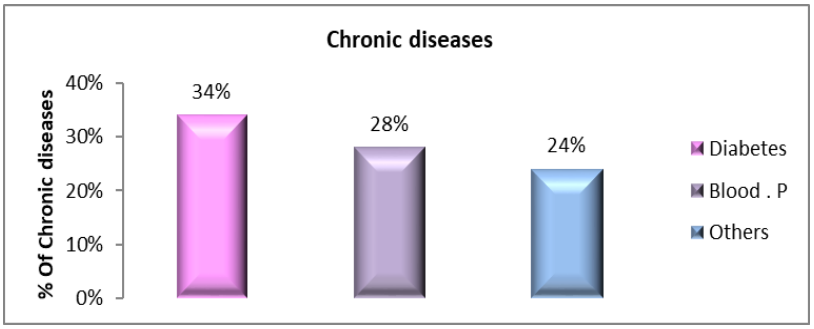

Figure 3: The % of major risk factors for all admitted cases.

Table 1: Illustrates survivor-specific risk factors

		Mild cases(11)		Moderate cases(35)		Sever cases(23)		Total cases(69)	
Sex	**Males**	5	45.4 %	20	57.1 %	16	69.6%	41	59.4 %
	Females	6	54.5%	15	42.9 %	7	30.4 %	28	40.6%
X̄ Age (years)		62		63		70		65	
Diabetes		5	45.4 %	9	25.7 %	8	34.8%	22	31.9%
Blood pressure		1	9.1 %	9	25.7%	7	30.4%	17	24.6%

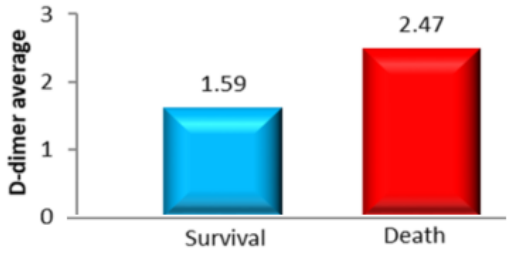

Figure 4: Average D-Dimer is shown in both fatalities and survivors

Figure 5: CRP average in survival and death

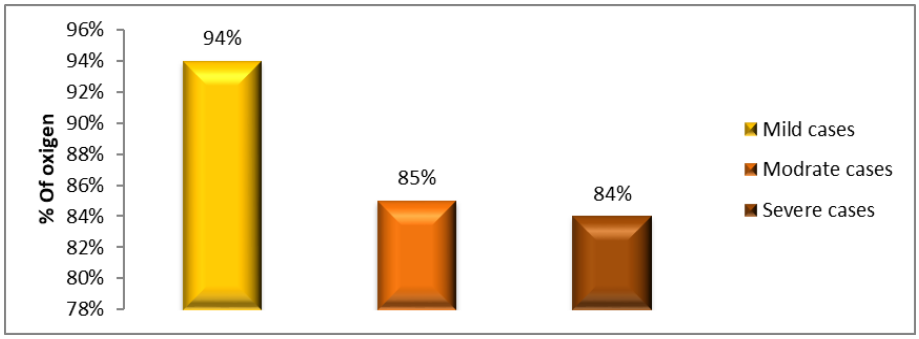

Figure 6: The average oxygen% in the three cases among the survivors

Table 2: Risk factors related to the mortality.

		Moderate cases(5)	Sever cases(26)	Total cases (31)
Sex	**Males**	5 100%	20 77% ~	25 81% ~
	Females	0 0%	6 ~ 23%	6 19% ~
X Age (years)		87	73	75
Diabetes		3 60% ~	9 ~35%	12 39% ~
Blood pressure		2 40% ~	9 35% ~	11 36% ~

with 60% classified as moderate and 35% as severe. The percentages point to a notable increase in disease severity especially among severe cases. Notably, the admission rate for individuals with comorbidities was six times higher than for those without, accounting for 86% of admissions compared with 14% for patients without underlying conditions.

In Table (3), Average C-reactive protein (CRP) levels increased with disease severity, measuring 72.56 mg/L in mild cases, 96.8 mg/L in moderate cases, and 145.45 mg/L in severe cases. Similarly, D-dimer levels increased with disease severity with averages of 0.88 µg/mL in mild cases, 1.32 µg/mL in moderate cases, and 2.34 µg/mL in severe cases. When examined by disease severity oxygen levels averaged 94% in mild cases, 85% in moderate cases, and 84% in severe cases, reflecting a decline with increasing disease severity.

Table 3: The average of CRP, D-Dimer and oxygen % in survivals

	Mild cases	Moderate cases	Sever cases
CRP (mg/l)	72.56	96.8	145.45
D-Dimer (ml/gµ)	0.88	1.32	2.34
Oxygen %	94.85	85	84

The results show an inverse relationship between D-dimer levels and disease severity in mild and moderate cases, whereas a positive correlation is observed in severe cases. Additionally, the table shows an inverse correlation between CRP levels and disease severity in both mild and moderate cases. In contrast, a positive correlation was observed between CRP levels and severe cases, indicating higher CRP with greater disease severity.

Table (4) presents the descriptive statistics for the most prominent laboratory measurements in the survival group (N=69). The results showed the following:

The mean oxygen saturation (SpO2) was 86.30% with a standard deviation of 9.27, ranging from a minimum of 60% to a maximum of 99%. This indicates a relative decrease in oxygenation levels in some patients, with moderate variation in values. As for the D-dimer coagulation index, its mean was 1.59688 with a standard deviation of 1.966111, with a relatively wide range (0.290–8.980). This reflects varying elevations in some cases, with significant variability among patients.

Regarding the C-reactive protein (CRP) inflammatory marker, the mean was 109.1559 with a relatively high standard deviation (88.82926) and a very wide range (6.90–396.60), indicating a clear variability in the severity of the inflammatory response among the survivors. The high variability values, particularly for CRP (7890.637), indicate significant dispersion in the readings, reflecting the varying severity of the clinical condition within the same group despite their survival.

Table (5) shows the laboratory measurements for the death group (N=31), where the results were as follows: The mean D-dimer was 2.4755 with a standard deviation of (2.40909), ranging from 0.32 to 8.05, which is higher than the mean of the survival group. The mean CRP was 139.1977 with a standard deviation of (77.21420), ranging from 34.4 to 316.3, indicating a higher level of inflammation compared to the survival group. The mean SpO2 was 83.61% with a standard deviation of (10.49), with values ranging from 50% to 97%, which is lower than the mean of the survival group, with greater variability in values. These results show a more pronounced increase in markers of inflammation and coagulation, with a greater decrease in oxygen saturation in patients ultimately died.

Table (6) shows the correlation coefficients between D-Dimer and CRP indices and disease severity stages in the survival group.

For D-Dimer: The correlation with mild cases was r = -0.158, a weak negative correlation. The correlation with severe cases was r = 0.27, a weak to moderate positive correlation. The correlation with mild cases was r = -0.139, a weak negative correlation.

Table 4: The most prominent laboratory measurements for the survival group.

	Descriptive Statistics							
					Mean			
	N	Range	Mini	Maxi	Statistic	Std. Error	Std. Deviation	Variance
SPo2	69	39	60	99	86.30	1.11647	9.27	86.00
D.dimer	69	8.690	0.29	8.980	1.59688	0.23669	1.966111	3.866
Crp	69	389.70	6.90	396.60	109.1559	10.69379	88.82926	7890.637

Table 5: The most prominent laboratory measurements for the death group

	Descriptive Statistics							
	N	Range			Mean		Std. Deviation	Variance
	Statistic	Statistic	Mini	Maxi	Statistic	Std. Error	Statistic	Statistic
D-Dimer	31	7.73	0.32	8.05	2.4755	0.43268	2.40909	5.804
CRP	31	284.33	34.4	316.3	139.1977	13.86808	77.21420	5962.032
SPo2	31	%47	%50	%97	%83.61	1.885	10.49	110.178

Table 6: Correlation value for the stages of disease severity in the survival group**.**

		correlation value		
Survival	D-Dimer	Mild cases	Sever cases	Moderate cases
		-0.158	0.27	-0.139
	CRP	Mild cases	Sever cases	Moderate cases
		-0.181	0.291	-0.142

Regarding CRP: The correlation with mild cases was r = -0.181 (a weak negative correlation). The correlation with severe cases was r = 0.291 (a weak positive correlation tending towards the moderate level). The correlation with moderate cases was r = -0.142 (a weak negative correlation). These values indicate that the relatively strongest relationship within the survivor group was between elevated D-Dimer and CRP levels and severe cases. However, the correlation coefficients remained within the statistically weak range, indicating that these indicators were not strongly associated with the severity gradient within the survivor group.

Table 7: Correlation value for the stages of disease severity in the mortality group

		correlation value		
Mortality	D-Dimer	Mild cases	Sever cases	Moderate cases
		No correlation	0.057	-0.057
	CRP	Mild cases	Sever cases	Moderate cases
		No correlation	0.234	-0.234

Table (7) shows the correlation coefficients between D-Dimer, CRP, and severity stages in the mortality cohort. **For D-Dimer:** There is no significant correlation with mild cases. The correlation with severe cases was r = 0.057 (very weak positive correlation). The correlation with moderate cases was r = -0.057 (very weak negative correlation).

For CRP: No correlation was found with mild cases. The correlation with severe cases was r = 0.234 (weak positive correlation). The correlation with moderate cases was r = -.234 (weak negative correlation). These values indicate a clear weakness in the correlation between laboratory indicators and severity stages within the mortality group, despite the positive trend with severe cases.

Discussion

Taken together, the figures and tables highlight the increased susceptibility of older adults to COVID-19, driven reflecting the impact of health conditions and physiological factors. Several factors contribute to this heightened susceptibility in older adults including a weakened immune system, fewer white blood cells to combat infection, and reduced cellular ability to detect foreign pathogens and also chronic diseases as heart and lung conditions, diabetes, and hypertension as well as the loss of lung tissue elasticity which leads to an increased heartbeat to meet the tissues' oxygen requirements.

Figure (1) The data show a rise in the survival rate to 69%, alongside a drop in the mortality rate to 31%. These results are consistent with the findings of a study conducted by Ferrando et al. [9] which reported a similar death rate of 31However, these findings differ from those reported in a study conducted by Elhadi et al. [10] where the death rate was 60.4% and the survival rate was 39%.

The observed gender disparity with higher proportion of infected males compared to females, is likely due to greater workplace exposure, and longer periods of social interaction among men, the proportion of males is almost identical and the sample size is the same as what was reported by Younes et al. [11] however, this does not necessarily imply a direct link between infection risk and gender. Additionally, these findings highlight that people with diabetes not only have a higher risk of infection but also often face more severe illness particularly if they do not maintain careful disease management. By affecting the nervous system, diabetes weakens the lungs' natural defences allowing the virus to cause tissue damage, trigger inflammation and increase the risk of other infections. When examining disease severity, diabetic patients were distributed as follows: 45% in the mild category, 26% in moderate cases, and 35% in severe cases. The results support the conclusions reported in the study by Carlos et al. [12]

Table (1) shows that the average age of patients in moderate cases was 87 years, compared with 73 years in severe cases. The average age of all deaths is reported as 75 years. These findings are consistent with the results of the study conducted by Zheng et al. [13] as well as other earlier mentioned study.

Regarding disease severity about 60% of patients were classified as moderate cases while 35% were classified as severe. These percentages indicate a progression in disease severity especially with poor outcomes. Notably, patients with comorbidities were admitted at a rate six times higher than those without underlying conditions, accounting for 86% of admissions compared with 14%. This observation is supported by a study carried out by Stokes et al. [14] which found that COVID-19 patients with pre-existing medical conditions were six times more likely to require hospitalization than those without such conditions.

Elevated CRP and D-dimer levels reflect the body's response to acute infections not limited to viral infection but also observed in conditions such as tumours. COVID-19 patients may develop blood clots due to immobility or increased blood viscosity that often-requiring treatment with anticoagulants such as heparin. Low blood oxygen levels are commonly linked to pneumonia particularly when inflammation rates exceed 50%.

This study provided detailed results based on the severity of the disease revealing rates of 94% in mild cases, 85% in moderate cases and 84% in severe cases. These lower percentages may point to an increased inflammatory reaction in the lungs triggered by COVID-19. The findings of this study supported by previous research study conducted by Kim et al. [15] along with other mentioned studies.

The results of the laboratory measurements mentioned earlier align with most previously referenced studies including the study by Lippi et al ; Sanchis-Gomar et al. [16.17] In contrast, these findings differ from those reported in Saudi Arabia by Al Mutair et al. [18].

The results show that elevated D-Dimer and CRP levels tended to be associated with severe disease, even within the survival group. This aligns with Tjendra et al. [19] suggesting that these markers are associated with increasing disease severity but do not necessarily indicate a fatal outcome. Therefore, the results of Table (6) indicate that vital signs contribute to determining severity, but they do not act as a

decisive independent factor in patients whose condition ended in survival.

Despite the weak correlation coefficients, the positive trend between elevated CRP and severe cases (r = 0.234) is consistent with what Ali et al. [8] stated that increased in CRP is associated with increased inflammation severity and poor clinical prognosis. In addition, the systematic review by Zheng et al. [13] so confirmed that increased in D-Dimer is a significant risk factor to have severe illness and death. However, its effect is more pronounced when comparing survival and mortality groups, rather than necessarily within the same mortality group. Albitar et al. [5] found that risk factors for death are multiple and interconnected, and the biomarkers operate within a complex network of physiological changes, that may explain the weak correlation coefficients within the same outcome category (death). Therefore, the results in Table (7) support the literature indicating the importance of these biomarkers in predicting poor outcomes when comparing groups, but they are less able to explain the internal gradient of disease severity within the mortality group alone.

The link between the two tables: Comparing the results in Table (6) for the survival group with those in Table (7) for the mortality group reveals that the correlation coefficients between the (CRP and D-Dimer) and severity of disease were weak in the two groups. However, there are significant in the statistical trends. In the survival group, a weak positive correlation was observed between both D-Dimer (r = 0.27) and CRP (r = 0.291) and severe cases, indicating that higher levels of these markers are associated with increased disease severity, but the correlation is not strong enough to determine the clinical outcome. In the mortality group, the correlation coefficients were even weaker, with D-Dimer (r = 0.057) and CRP (r = 0.234) being associated with severe cases. This suggests that these markers, while important, do not alone explain the progression of disease severity Within the same outcome category. These findings are consistent with Zheng et al. [13] who indicated that elevated D-Dimer is associated with an increased risk of critical illness and death when comparing groups, more so than with an internal severity scale Ali et al. [8] also demonstrated that CRP is an important predictor of inflammation severity and poor prognosis. However, it operates within a complex system of clinical and biochemical factors. Albitar et al. [5] also indicated that the risk of death in COVID-19 patients is associated with the simultaneous interaction of several variables, rather than a single laboratory marker. Therefore, the weak correlation coefficients in both tables can be explained by the fact that while biomarkers contribute to determining disease severity, their effect is more pronounced when comparing the survival and mortality groups, rather than within each group individually. This underscores the multifactorial nature of disease progression and poor clinical outcome.

Conclusion

The study found a 31% mortality rate among patients admitted to the isolation center. Factors such as age, pre-existing health conditions, elevated CRP and D-dimer levels and low oxygen saturation in severe cases were identified as indicators of heightened inflammation and mortality risk. Notably, high CRP and D-dimer levels were strongly associated with severe outcomes in COVID-19 patients.

Recommendations

The study emphasizes the need to strengthen community compliance with preventive measures and activate early medical intervention mechanisms as soon as clinical symptoms appear to reduce the risk of morbidity. The findings also highlight the importance of targeted care for vulnerable groups, particularly the elderly and those with chronic conditions such as diabetes, through the application of strict precautionary protocols. Furthermore, the study recommends adopting regular monitoring of inflammatory and coagulation markers, specifically C-reactive protein (CRP) and D-dimer, as key predictive tools to prevent clinical deterioration and reduce the burden on isolation units.

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Conflicts of Interest: "The authors declare that they have no conflict of interest**."**

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