DOI: https://doi.org/10.31351/vol31iss2pp39-49

Descriptive, Prospective Observational Study- Studying Possible Prediction Factors for Disease Severity and Progression among a Sample of COVD 19 Patients in Iraq

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Abstract

Coronavirus has affected many people around the world and caused an increase in the number of hospitalized patients and deaths. The prediction factors may assist the clinician in identifying patients who are at high risk of complications and require further medical attention. We aimed to study the possible relationship between C reactive protein level and the severity of symptoms and its effect on the prognosis of the disease. And determine patients who require closer respiratory monitoring and more aggressive supportive therapies to avoid poor prognosis. The data was gathered using medical record data, the patient's medical history, and the onset of symptoms, as well as a blood sample to test the C-reactive protein level. The patients were divided into three groups based on the severity of the disease. A descriptive, prospective observational study of 246 patients over the age of 18 years discovered that c-reactive protein levels were significantly higher in more severe cases than in mild cases, and that older patients with high levels of AST, TSB, Urea, Creatinine, and CRP were associated with the need for a high flow of oxygen, an intensive care unit, a longer length of hospitalization, and have a high mortality rate. The study concluded several predictor factors for the disease (COVID-19) severity, duration of hospitalization, ICU admission and need for oxygen therapy.
Key words- COVID-19, Prediction factors, severity of disease, Length of hospitalization, Intensive care unit, Death.

دراسة وصفيه مستقبليه المحتمله -دراسه عوامل التنبؤ المحتملة لشدة المرض وتطوره في عينة من مرضى كوفيد ١٩ في العراق

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الخلاصة

اصاب فايروس كورونا العديد من الاشخاص حول العالم وتسبب في زياده اعداد المرضى في المستشفيات وزياده الوفيات. من الممكن ان تساعد عوامل التنبؤ الطبيب لتصنيف المرضى الذين يحتاجون عنايه طبيه اكثر لتقليل الوفيات وتدهور حاله المريض. الهدف من الدراسه هو معرفة العلاقه المحتمله بين مستوى البروتين التفاعلي سي وشده الاعراض وتاثيره على تدهور الاعراض ، وتحديد المرضى الذين يحتاجون الى اوكسجين وعلاجات داعمه اكثر للتقليل من تدهور الاعراض. تم جمع البيانات بالاعتماد على السجلات الطبيه ،التاريخ المرضي وبدايه الاعراضوتم اخدعينه دم لاجراء فحص البروتين التفاعلي سي قسم المرضى حسب شده المرض الى ثلاثه مجاميع. دراسه وصفيه مستقبليه المحتمله ل ٢٤٦ مريض اعمارهم اكثر من ١٨ عاما وجدت ان مستوى البروتين التفاعلي سي يكون اعلى بشكل كبير في الحالات الشديده منه في الخفيفه،كما وجدت ان كبار السن والذين لديهم مستوى عالي من انزيم ناقلة الأمين أسبارتات ،تحليل البليروبين الكلي، اليوريا، الكرياتنين، ومستوى البروتين التفاعلي سي كان لها علاقه كبيرة بالاحتياج لمستوى عالي من الاوكسجين ، وحده العنايه المركزه، مده بقاء اكثر في المستشفى ، ومعدل وفيات اعلى .استنتجت الدراسه وجود العديد من العوامل التنبؤيه لشده مرض كوفيد ١٩ ، مده البقاء في المستشفى، الدخول الى وحده العنايه المركزه والحاجه الى الاوكسجين.
الكلمات المفتاحيه- كوفيد ١٩ عوامل التنبؤ ، شده المرض ، مده البقاء في المستشفى ، وحده العنايه المركزه ، والوفاة.

Introduction

Since December 2019, the Coronavirus disease, sever acute respiratory syndrome coronavirus-2 (SARS-CoV-2) has had a very negative effect on humans [(1)]. The pathogen that triggers COVID-19 is a novel coronavirus (nCoV) called sever acute respiratory syndrome coronavirus-2 (SARS-CoV-2) SARS-CoV-2 also known as Novel corona virus disease-2019 [COVID-19-nCoV] that was first identified in late January 2020 [(2)].Coronaviruses belong to the subfamily Coronavirinae, one of the two members of the family Coronaviridae [(3)]. The World Health Organization (WHO) announced COVID-19 a worldwide pandemic on11 March 2020 [(4)].

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Received: 26 / 8 /2021
Accepted: 15 / 11 /2021

Coronavirus first appeared in Iraq on 24 February 2020, in Al-Najaf city, south of Baghdad. Two weeks later, the Iraqi Ministry of Health (MOH) revealed that 101 instances of COVID-19 had been tested positive in 14 provinces, with 9 deaths. Baghdad city accounted for nearly 40% of those cases [5]. Infected individuals are thought to be the most important source of SARS-CoV-2 infection. Droplets and close contact with COVID-19 patients appear to be the most prevalent method of transmission, SARS-CoV-2 is mostly transferred from symptomatic patients by coughing or sneezing [6].Globally, as of 3 June 2021, there have been 171,292,827 confirmed cases of COVID-19, including 3,687,589 deaths, reported to WHO , as of 2 June 2021, a total of 1,581,509,628 vaccine doses have been administered. The reported cases in Iraq, from 3 January 2020 to, 3 June 2021, was 1,210,105 with 16,436 deaths, as of 25 May 2021, a total of 442,234 vaccine doses have been administered [7].

The incubation period ranges from 0 to 24 days, with an average of 5–7 days. Individuals of any age are susceptible to infection, including neonates and pregnant women. The majority of patients present with mild to moderate symptoms [8]. Acute respiratory distress syndrome, septic shock, metabolic acidosis, coagulation malfunction, and multiple organ dysfunction syndromes can all occur in severe instances and the death rate for patients with severe COVID-19 is rather significant [9]. Patients with concomitant conditions may be more likely to develop severe COVID-19 [10]. Liver damage has been known to occur during the course of the disease in severe condition [11]. Acute kidney damage (AKI) has been documented in severely ill SARS-CoV-2 patients, particularly those with underlying medical conditions [12].

C-reactive protein (CRP) is a widely used diagnostic marker for determining the severity of chronic inflammation. It is an acute phase response protein that appears in the blood 6–10 hours after tissue injury, has a plasma half-life of 19 hours, and doesn't require a memory response to be produced[13]. C-reactive protein is produced predominantly by hepatocytes in the liver, but also by smooth muscle cells, macrophages, endothelial cells, lymphocytes, and adipocytes in the body [14].

The study aimed to find the possible relationship between C reactive protein (CRP) level and the severity of symptoms and its effect on the prognosis of the disease among a sample of COVID-19 patients in Iraq and to identify patients who require closer respiratory monitoring and more aggressive supportive therapies to avoid poor prognosis. During the study, we searched for additional predictors, such as another laboratory parameter, chronic disease, and schedule medication use, to see whether they might be utilized as predictors.

Methods

Study design and patients

This is a descriptive, prospective observational study which was conducted between November-13th- 2020 and March-21st -2021. The data was collected from 246 Iraqi patients aged 18 years or older who were admitted to al Shefaa center and Al-Hayat hospital in Baghdad and were confirmed to have COVID-19 infection by using real-time polymerase chain reaction (PCR) and chest computed tomography (CT).

Inclusion criteria

- Inpatient Positive for COVID-19.
- Agree to participate in the study.
- Aged ≥ 18 years

Exclusion criteria

- The patient who voluntarily left the hospital before his health condition improved.
- Patient admitted after the onset of symptoms for more than two weeks.
- Immunocompromised patient.
- Patients who died within a few days after being discharged from the hospital.(Discharge or death was the end point of patient follow-up; some patients were needed to return to the hospital, and a few died just days after being discharged.
- Cancer patient.

Data collection

Within 24 hours of the patient being admitted to the ward, the data was based on the medical records, the patient's medical history and the onset of symptoms recorded by the patients, and a blood sample was taken to test the C-reactive protein level by using the Genrui and Beckman device in the laboratory department.

Follow up the progression of symptom

Within three weeks of hospitalization, the patients were placed into groups based on the severity of the disease, the recovery group were discharged patients and there was no need to be admitted to an intensive care unit, the worsening group were patients who need an intensive care unit (ICU) and a high flow of oxygen supply, and the mortality group include died patients.

Clinical classification

Clinical classification was carried out according to the Ministry of health guidelines, with following standards-

1. Mild type- mild clinical symptoms without pneumonia in chest imaging performance.
2. Moderate type- fever, respiratory tract and other symptoms with pneumonia in imaging performance.
3. Severe type- any one condition of the followings- respiratory distress, respiratory rate ≥ 30 times/min; fingertip oxygen saturation ≤ 93% in resting state; arterial oxygen partial pressure/fraction of inspired oxygen ≤300 mmHg.

4. Critical type- any one condition of the followings- respiratory failure need mechanical ventilation; shock; other organs failure need intensive care unit (ICU) monitoring and treatment [15].

Statistical analyses

Descriptive statistics (means, standard deviation, frequencies and percentages) were conducted for all study items. Data was analyzed using the Statistical Package for the Social Sciences (SPSS) software, version 25. For association of continuous variables, we used correlation while for categorical variable, we used Chi-square. Additionally, Kruskual Wallis test and Mann Whitney test are applied to investigate differences among means for continuous (not normally distributed variables)The Kruskal Wallis Test was used to determine if there are statistically significant differences between the severity of the disease and many biomedical parameters, use this test instead of ANOVA as that when we checked the normality test we found that the data was not normally distributed, ANOVA was incorrect to use because the parametric test need to assume normality. Depending on the assumptions we made that data's are not normally distributed, the non-parametric test Mann-Whitney Test used instead of independent t-test. K Wallis & M Whitney tests are non-parametric test and applied to investigate differences among means .P-value of less than 0.05 was considered statistically significant.

Results

The study included 246 patients with COVID-19. Their average age was 58.28 ± 14.824. The majority were men (54.5%). Patients were admitted with severe condition (38.6 %) and 70.7% recovered. Approximately half (49.6%) of the patients were taking one or more chronic medication(s) before admission as illustrated in Table-1.

Table-1. Descriptive characteristics of the patients.

Character	**Subcategory**		**N**	**%**
Gender	female		112	45.5
	male		134	54.5
Smoker	Former smoker		89	36.5%
Disease Severity	Mild- moderate		71	28.9
	Severe		95	38.6
	Critical		80	32.5
	Total		246	100.0
Patient outcome	Recovered		174	70.7
	Died		72	29.3
Number of chronic diseases	1.00		62	39.0
	2.00		48	30.2
	3.00		28	17.6
	4.00		16	10.1
	5.00		5	3.1
	Total		159	100.0
Number of chronic medications	1.00		36	29.5
	2.00		33	27.0
	3.00		23	18.9
	4.00		15	12.3
	≥5.00		15	12.3
	Total		122	100.0
	Minimum	**Maximum**	**Mean**	**Std. Deviation**
BMI	17.3	٥٨.6	31.0324	6.88222
Age	18	93	58.28	14.824

BMI=body mass index (N=237) Age (N=244)

There were no differences in the severity of disease among the patients related to smoking and gender as shown in Table-2.

Table 2. The difference in the disease severity according to the gender and smoking.

			COVID-19 Severity			
			Critical	Mild- moderate	Sever	P-value
Smoking	No	Count	48	46	61	.825
		% within	31.0%	29.7%	39.4%	
	Yes	Count	31	25	33	
		% within	34.8%	28.1%	37.1%	
Gender	Female	Count	37	36	39	.460
		% within	33.0%	32.1%	34.8%	
	Male	Count	43	35	56	
		% within	32.1%	26.1%	41.8%	

Pearson Chi-Square

With the p-value of (0.001) age was related to disease severity, need of intensive care unit admission and the use of high flow of oxygen supply. It is the mean that as the age increase disease severity, the need of intensive care unit admission and the use of high flow of oxygen supply was also increase as illustrated in Table-3.

Table 3. The differences in need for oxygen (CPAP and NRM), ICU admission and disease severity according to patient age.

		N	Mean Rank for age	P-value
CPAP&	No need to use CPAP	182	111.53	.001*
	Need to use CPAP	62	154.70	
NRM&	No need to use NRM	56	90.91	.001*
	Need to use NRM	188	131.91	
ICU admission&	No need ICU admission	181	110.43	.001*
	Need ICU admission	63	157.17	
Severity⁑	Mild-moderate	71	77.92	.001*
	Severe	94	122.94	
	Critical	79	162.04	

&Mann-Whitney Test and
⁑Kruskal Wallis Test.
* The mean difference is significant at the 0.05 level.
CPAP= Continuous positive airway pressure. NRM=non rebreather mask.

The severity of disease was related to high Level of C-reactive protein as demonstrated in Table-4.

Table 4. The difference in C-reactive protein according to the disease severity.

		N	Mean Rank for CRP mg\l	P-value
Severity	Mild-moderate	58	30.59	.000*
	Sever	80	117.27	
	critical	62	144.27	
	Total	200		

* Significant (P-value <0.05) according to Kruskal Wallis Test;
CRP = C-reactive protein. From 246 patients, CRP was tested for 200 patients only.

The differences among the three groups of severity were significant according to post-hoc (pairwise analysis) Mild-moderate vs severe, mild-moderate vs critical and severe vs critical as shown in Figure -1

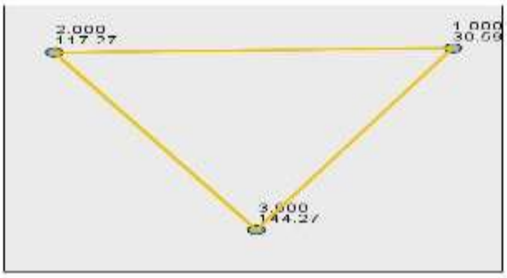

Figure 1. Pairwise Comparisons of Severity.
Each node shows the sample average rank of severity _ numeric

There is asymptomatic significant between mild-moderate vs severe, mild-moderate vs critical and severe vs critical as shown in Table-5

Table 5. The sample average rank of severity.

Sample 1-sample2	Sig.	Adj. Sig
1.000-2.000	.000	0.000
1.000-3.000	.000	0.000
2.000-3.000	.006	0.017

1-mild-moderate ,2-sever,3-critical.

Each row tests the null hypothesis that the sample1 and sample2 distributions are the same.
Asymptomatic significances (2-sided tests) are displayed.
The significance level is .05.
With a p-value of (0.001), 62 patients with chronic illness (39.0%) have severe symptoms, and around 67 (42.1%) have critical symptoms. And Schedule medication usage is evident in 51 (41.8%) and 49 (40.2%) of those with severe and critical symptoms, respectively as illustrated in Table-6.

Table 6. The association between patient severity of COVID-19 and having chronic disease/medication

Parameter			**Severity**			
			Mild-moderate	**Severe**	**Critical**	**P-value**
Chronic disease	No	Count %	41	33	13	.001*
			47.1%	37.9%	14.9%	
	Yes	Count %	30	62	67	
Chronic medication			18.9%	39.0%	42.1%	0.001*
	No	Count %	49	44	31	
			39.5%	35.5%	25.0%	
	Yes	Count %	22	51	49	

Each row tests the null hypothesis that the sample 1 and sample 2 distribution are the same
* Significant (P-value <0.05) according to the Pearson Chi-Square.

Three antidiabetic medications had significant association with the COVID-19 severity included metformin, insulin, dipeptidyl peptidase-4 inhibitor (DPP4), and Angiotensinogen II receptor blocker (ARBs) were also significantly associated, while others were not as shown in Table-7.

Table 7. The association between the individual chronic medication and the severity of COVID-19 disease.

			Disease Severity			**P-value**
			1.00	2.00	3.00	
Metformin	No	Count	65	73	69	.030*
		% within	31.4%	35.3%	33.3%	
	Yes	Count	6	22	11	
		% within	15.4%	56.4%	28.2%	
Insulin	No	Count	70	86	69	.023*
		% within	31.1%	38.2%	30.7%	
	Yes	Count	1	9	11	
		% within	4.8%	42.9%	52.4%	
Sulfonylurea	No	Count	61	75	71	.186
		% within	29.5%	36.2%	34.3%	
	Yes	Count	10	20	9	
		% within	25.6%	51.3%	23.1%	
DPP4	No	Count	68	80	74	.032*

		% within	30.6%	36.0%	33.3%	
	Yes	Count	3	15	6	
		% within	12.5%	62.5%	25.0%	
SGLE2 §	No	Count	71	93	80	.335
		% within	29.1%	38.1%	32.8%	
	Yes	Count	0	2	0	
		% within	0.0%	100.0%	0.0%	
ACEI §	No	Count	68	89	74	.709
		% within	29.4%	38.5%	32.0%	
	Yes	Count	3	6	6	
		% within	20.0%	40.0%	40.0%	
B-Blocker	No	Count	64	78	66	.303
		% within	30.8%	37.5%	31.7%	
	Yes	Count	7	17	14	
		% within	18.4%	44.7%	36.8%	
Statin	No	Count	69	85	72	.150
		% within	30.5%	37.6%	31.9%	
	Yes	Count	2	10	8	
		% within	10.0%	50.0%	40.0%	
Antiplatelet	No	Count	63	80	68	.691
		% within	29.9%	37.9%	32.2%	
	Yes	Count	8	15	12	
		% within	22.9%	42.9%	34.3%	
			Disease Severity			**P-Value**
			1.00	2.00	3.00	
ARBs	No	Count	62	73	56	.038*
		% within	32.5%	38.2%	29.3%	
	Yes	Count	9	22	24	
		% within	16.4%	40.0%	43.6%	
CCBs	No	Count	68	83	69	.116
		% within	30.9%	37.7%	31.4%	
	Yes	Count	3	12	11	
		% within	11.5%	46.2%	42.3%	

*Significant (P-value < 0.05) according to Pearson Chi-Square. § Fisher's Exact Test.
ARB=Angiotensinogen II receptor blocker; DPP4=Dipeptidyl peptidase-4 inhibitor (anti hyperglycemic); SGLE-2=Sodium–glucose co-transporter-2; ACEI=Angiotensin converting enzyme inhibitor. CCBs=Calcium Channel blockers. Severity- 1=Mild-moderate; 2=severe; 3=critical

Age with the (p-value0.001), AST (P-value0.002), TSB (P-value0.002), Urea (P-value0. .001), Creatinine (P-value0. .001), CRP (P-value0. .001) were related to higher mortality rate as shown in Figure-2.

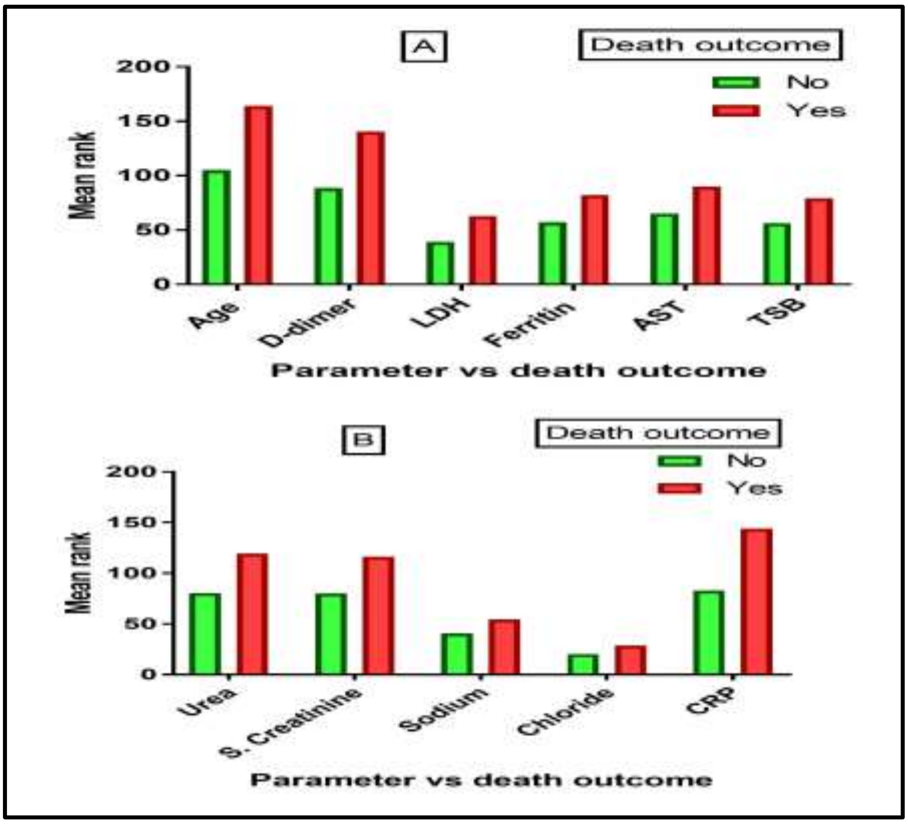

Figure 2.The significant (P-value < 0.05) associations between the levels of 11 biomedical parameters and the patient death probability.

LDH=lactate dehydrogenase; AST=aspartate aminotransferase; TSB=total serum bilirubin; CRP=C - reactive protein. The numbers in the y-axis (mean rank) mean as these parameter increase the death outcome increase and it's not limited value.

These results may help clinicians to identify on admission which patients with COVID-19 are at high risk of deterioration.

Discussion

The study reported numerous risk factors that may predict poor outcomes. The current study found that elderly patients experienced more severe COVID-19 symptoms and a higher intensive care unit (ICU) admission rate and needed more oxygen therapy and stayed longer in hospital compared to younger patients. Shengmei Niu and his colleagues (2020) in China studied clinical characteristics of old patients infected with COVID-19 and reported that COVID-19 infection in elderly individuals is associated with a high number of severe infections and a high mortality rate [16]. Another study of Aline Mendes, (2020) studied predictors of in-hospital mortality in older patients with COVID-19 and reported hospitalization for COVID-19 older individuals was an independent risk factor for death [17]. This may be related to his immune system that considered to weaken with age. Overproduction of cytokines furthermore, the activity of T-cells and B-cells decreases with age this might speed up virus replication and prolong pro-inflammatory reactions, causing serious health problems [18,19].

The current study resulted that gender had no influence on the severity of the disease, requirement for an ICU, or the length of hospitalization. In addition to that, there is no substantial difference in the need for oxygen treatment based on gender. Hongdou Li 1 (2020) in China studied on 5319 COVID-19 patients and reported that there isn't much of a distinction between males and females only in the age categories of 15 to 50 years old is there a variation in the incidence risk for different genders, where males have a slightly greater incidence risk than females after the age of 15, although the difference is insignificant in those over 50 [20]. The study does not support a previous one of Jonathan Kopel (2020) which studied Rasial and gender- based Difference in COVID-19 and reported that through an increase in the innate and humoral response, increased estrogen levels in female COVID-19 patients may lower the severity and fatality of COVID-19 fatalities (21). This difference may be related to 84.8% of females in the study aged over 45 years were defined as post-menopausal women and with last period menopause. Differences in susceptibility to viral infections are most likely attributable to intrinsic differences in male and female immune systems, as a result of more powerful humoral and cellular immune responses, females mount a greater immunological response to viral infections than males [(22)] .Most cells of the innate and adaptive immune systems, including T cells, B cells, neutrophils, macrophages, dendritic cells (DC), and natural killer (NK) cells, express estrogen receptors, during the menstrual cycle, when estrogen levels are high, more regulatory T cells are present, it is widely recognized that the aging process has an impact on sexual dimorphism in terms of immunocompetence and disproportionality [(23)].

In terms of smoking, the study found that smoking has no significant effect on the severity of the disease and the need for an ICU, and the length of hospitalization, and has no significant effect on the need for oxygen therapy. This may be related to the immune system of a current smoker is more tolerant and less reactive, compared to patients who have never smoked, whose immune system may be more suitable for triggering a cytokine release syndrome, that could be associated with COVID-19-related high mortality[(24)]. Meta-analysis of Roengrudee Patanavanich MD, LLM, (2020) in USA studied the association of smoking with COVID-19 progression, and found that smokers have 1.91 times the odds of progression in COVID-19 severity than never smokers [(25)].

The study found that C-reactive protein (CRP) has significant correlation with disease severity and mortality. Severe COVID19 individuals with high CRP levels may be related to the overproduction of inflammatory cytokines. Although cytokines combat germs, when the immune system becomes overactive, it can cause lung tissue damage. In individuals with COVID19, inflammatory cytokines and tissue damage cause CRP production [(26)]. This result agrees with a study done by Weifeng Shang1and his colleague in China (2020) who studied the value of clinical parameters in predicting the severity of COVID-19 and reported that CRP in the severe group was significantly higher than that in the non-severe group, and CRP was an independent risk factor for severe COVID-19[(27)]. And with AshaqAli1 (2021) studied Myoglobin and C reactive protein are efficient and reliable early predictors of COVID 19 associated mortality and reported that CRP was specific risk factors related to mortality and highly correlated to organ failure in COVID-19 disease [(28)].

Patients with chronic disease/medication experienced more severe symptoms with a percent of 42.1, 40.2 critical cases respectively reported in the study. Nancy Chow, (2020), studied preliminary estimates of the prevalence of selected underlying health conditions among patients with Coronavirus Disease 2019 — United States, February 12–March 28, 2020 and reported that people who have underlying health issues tend to have a higher risk of severe COVID-19–related disease than those who don't [(29)].

The current study found that metformin had significant association with the COVID-19 severity, this explained by metformin might theoretically enhance the availability of ACE2 in the respiratory tract via the AMPK–phospho-ACE2 axis, promoting SARSCoV-2 infection and worsening COVID-19 illness [(30)]. Xu Cheng, and his colleague (2020)in china agree with this by studied metformin is associated with higher incidence of acidosis, but not mortality, in individuals with COVID-19 and Pre-existing type 2 diabetes of 1,213 and reported that metformin usage was linked to an increased risk of acidosis, particularly in patients with severe COVID19[(31)].

For the use of insulin the study was found that insulin had a significant association with the COVID-19 severity. Insulin therapy was linked to an increase in systemic inflammation and a worsening of important organ damage [(32)]. Shayan Riahi (2020) in USA that studied Insulin Use, diabetes control, and outcomes in patients with COVID-19 showed home insulin treatment was linked to a higher risk of death [(33)].

This study found that, the Peptidase-4 inhibitor (DPP4) was also have a significant association with COVID-19 severity. DPP-4 regulates the immune system by activating T cells via the nuclear factor-B pathway, and therefore its suppression may have an unfavorable effect on the immunological response to viral infection, especially as lower numbers of T cells have been linked to COVID-19 severity [(34)]. Dr. Rinkoo Dalan, and his colleague (2020) in Singapore supported this by studying the association of hypertension and diabetes with COVID-19 severity and immune signatures found that Patients using DPP4 inhibitors were more likely needs to be admitted to the ICU [(35)].

The study found another drug that has a significant association with the disease severity, which is angiotensin receptor blockers (ARBs). One theory is that SARS-CoV-2 utilizes ACE2 receptors for cellular entrance, and that blocking the receptor with ACEI/ARBs prevents viral attachment, entry, and multiplication. Continuous use of these medicines, on the other hand, may result in overexpression of ACE2 receptors through a negative feedback mechanism, increasing coronavirus binding to target cells [(36)]. This agree with a study carried out by Murat Selçuk in Turkey (2020) that studied is the use of ACE inb/ARBs associated with higher in-hospital mortality in Covid-19 pneumonia patients? And found that the use of ARBs therapy might be associated with an increased in-hospital mortality in patients who were diagnosed with Covid-19 pneumonia [37].

The current study's mortality results are linked to high levels of urea and creatinine. The etiology of this might be complex, with direct effects of the coronavirus on renal parenchyma, such as ACE2 expression in urinary organs, being one possibility. Secondary, the kidney may be damaged by the deposition of immune complexes of viral antigen or virus-induced particular immunological effector mechanisms (specific T-cell lymphocyte or antibody). Third, virus-induced cytokines or mediators may have an effect on the immune system [38]. This was supported by, Lei Chen (2020) in London who studied risk factors for death in 1859 subjects with COVID-19 and confirmed that SCr (serum creatinine) on admission was shown to be more useful in predicting in-hospital death in patients with COVID-19 and AKI who had an increased baseline SCr [39]. Another study by Ye-Mao Liu (2021) in China who studied kidney function indicators to predict adverse outcomes of COVID-19 and found that blood urea nitrogen and SCr levels were shown to be related with a higher risk of death [40].

This study found that, aspartate aminotransferase (AST) and total serum bilirubin (TSB) were also linked to high mortality. Though the specific mechanism of COVID19-induced liver injury is unknown, several ideas have been presented, including direct viral cytotoxicity via ACE-2, drug-induced liver injury, immune-mediated damage, and passive congestion [41]. Ze-yang Dingand (2020) in china studied the association of liver abnormalities with in-hospital mortality in patient with COVID19 and reported that early start of increase AST and direct bilirubin patient treated with COVID19 was found to be an independent predictor of in-hospital mortality [42]. And a retrospective Cohort Study of Zeming Liu (2020) in china studied bilirubin levels as potential indicators of disease severity in Coronavirus disease patients and reported those with high STB levels showed a greater mortality risk [43].

Limitations of the study include- some information was obtained from relatives due to the patient's tiredness, which may not guarantee the accuracy of the information and not all laboratory parameters are performed on admission but rather according to the doctor's discretion.

Conclusion

The study found several predictors for the disease (COVID-19) severity, duration of hospitalization, ICU admission and needed for oxygen therapy including CRP, liver and renal function tests. Old age, having chronic disease and taking scheduled medications are also predictors for oxygen need, ICU admission or having more severe COVID-19 symptoms. Additionally, several biomedical parameters including age, CRP, AST, TSB, urea and creatinine had significant association with higher probability of patient death due to the disease (COVID-19).

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