Early predictors of mortality for moderate to severely ill patients with Covid-19 in Erbil city

Taha Khudhur Ahmed*
Halgurd Fathulla Ahmed**
Haval Faris Mohammed***

Abstract

Background & Objectives: COVID-19 disease represents a major burden on national health institutes. The aim of study is to figure out the parameters that can predict the mortality in moderate to severely ill Covid-19patients. That enable us to predict the course of the disease and reduce the mortality of Covid-19 patients.

Methods: A prospective cross-sectional study carried out in West Emergency Hospital in Erbil city-Kurdistan region/Iraq from February to August 2021onsample of one hundred patients with positive real-time polymerase chain reaction.The patients were followed up from their admission to hospital until their discharge alive or dead.Their data were collected by direct interview with them or from their relatives or saved records in hospital and fulfilled in a prepared questionnaire.

Results: The mortality rate of hospitalized patients with moderate to severe Corona infections diseasewas (44%). The older age of patients was significantly related to higher mortality rate. The patients presented with dyspnea (51.4%), hypertension (57.1%) and renal failure were significantly associated with higher mortality rates. High respiratory rate (>25 bpm), low oxygen saturation (<88%), and high C-reactive protein level (>59) were accompanied with higher mortality rates. These results were statistically significant.

Conclusion: The early predictors of mortality in patients with moderate to severe Corona infections disease were elderly age, dyspnea, co-morbidity with hypertension and renal failure, high respiratory rate, low oxygen saturation and elevated levels of C-reactive protein.

Key words: Corona infections disease, Dyspnea, Hypoxia, Mortality, Severity of COVID-19.

Introduction

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) was firstly recorded in Wuhan/China at December, 2019 with unknown etiology and declared as a pandemic coronavirus disease 2019 (COVID-19) by World Health Organization (WHO) at March 2020, leading to hundreds of millions patients and about six million deaths globally[1,2].The first confirmed COVID-19 patient in Kurdistan region/Iraq was reported at first of March 2020 followed by outbreak leading nearly to four hundred thousand cases and seven thousands deaths in the region[3]. Incubation period of COVID-19 disease is ranged from 4- 14 days, and it could be asymptomatic or symptomatic disease to critical illness with death.[4,5]Assessment of COVID-19 disease severity is essential in planning for preventive and management strategies all over the world. Severity categorization for COVID-19 patients is required in emergency department of the hospital in

* M.B.Ch.B., trainee at Kurdistan higher council for medical specialties; West Emergency Hospital-Erbil-Kurdistan region/Iraq
** M.B.Ch.B., F.I.B.M.S; Assistant Professor in Internal Medicine-Director of training Kurdistan higher council for medical specialties-Erbil-Kurdistan region/Iraq
*** M.B.Ch.B, FKBMS_EM; Emergency Medicine Specialist; West Emergency Hospital-Erbil-Kurdistan region/Iraq
Contact: Taha Khudhur Ahmed. Email: tahakhidr@gmail.com

order to assess the general status of patients and allocate the management pathways that needs better distribution of medical staff, equipment's and financial resources in the hospital. [6-8]The WHO and many health committees.[9,10] developed a specific classification of COVID-19 severity depending on patients' clinical presentations, laboratory findings including arterial blood gas analyses and imaging results at their admission to emergency ward into mild, moderate, severe, and critical illness.[11] The COVID-19 disease severity classification is important in prediction of the disease progression regarding considerable variables. Many variables were reported to be linked with severe COVID-19 disease such as male gender.[12] elderly age.[13] urban residence.[14] and specific occupations[14]. Some authors documented that clinical features at presentation like cough.[15] and fever.[16]were related to severe to critical illness. The comorbidity factors such as cancer.[17] diabetes.[18] psychiatric disorders.[19] nephritis.[20] and obesity.[21] were found to be accompanied with severe COVID-19 disease and poor prognosis.Additionally, many literatures found that laboratory findings.[22,23]. imaging characteristics.[24] exposure risks,[21] management variables.[25] environmental hazards.[26] social variables.[27] and regional variables.[28] were related to severity of COVID-19 disease.Recently, many literatures reported that prognosis of COVID-19 disease was related to the co-morbidity with other chronic diseases and this clinical co-morbidity affected the severity and the clinical course of COVID-19 disease. Other literatures documented that death outcome of COVID-19 disease is attributed to the co-morbid disease.[29]The aim of current study was to figure out the parameters that can predict the mortality in moderate to severely ill Covid-19 patients that enable us to predict the course of the disease and be capable of finding the appropriate treatment algorithms and reduce the mortality of Covid-19 disease.

Materials and methods

The present study was a prospective cross-sectional study carried out in West Emergency Hospital in Erbil city-Kurdistan region/Iraq through period of seven months from 1st of February to 31[st]of August, 2021. It is the time of third wave of COVID19 at Erbil city. Patients with positive RT-PCR test for COVID-19 admitted to West Emergency Hospital were the study population. At which; medical treatment and assisted ventilatory machines were used (including C-pap, Bipap, Noninvasive ventilator,and invasive ventilator but unfortunately ECMO was not available). The PCR test used did not detect which strain.The inclusion criteria were adult (age ≥18 years) patients with COVID-19 disease (positive RT-PCR) and moderate or severe Covid-19 disease was classified according to the diagnosis and treatment protocol for novel coronavirus pneumonia (Version 7). [30] Moderate cases presented with fever, respiratory symptoms and radiological abnormalities, while severe cases were presented with respiratory distress, low oxygen saturation and low arterial partial pressure of oxygen/fraction of inspired oxygen .[30] All these cases they were not vaccinated.Exclusion criteria were younger age patients, negative RT-PCR, mild COVID-19 disease, and patients refused to participate. The ethical considerations were implementedaccording to Helsinki Declaration regarding ethical approval of Health authorities;an ethical approval was taken from Kurdistan Board Ethical Committee, oral informed consent of patients, agreement of hospital authorities and management of patients. A convenient sample of one hundredpatients with COVID-19 diseasewas selected after eligibility to inclusion and exclusion

criteria. The data of enrolled patients were collected by direct interview with patients or from their relatives or saved records in hospitaland fulfilled in a prepared questionnaire. The diagnosis of COVID-19 disease was done regarding National Guidelines by RT-PCR, imaging, and laboratory tests. The RT-PCR was done through oropharyngeal and nasopharyngeal swapping. The patients were followed up from their admission to hospital until their discharge alive or dead.

The data collected were analyzed statistically by Statistical Package of Social Sciences software version 22. The chi-square and Fishers exact tests wereapplied for analyzing categorical variables. Level of significance p value was regarded statistically significant if it was 0.05 or less.Ethical approval was taken from ethical committee from Kurdistan Higher council for Medical Specialties. Verbal consent was taken from all patients.

Results

This study involved one hundred COVID-19 cases in our study. According to Table 1;most of them (56) were male, majority having severe disease (76), shortness of breath (86), non-smoker (74), with no loss of taste (74), no loss of smell (82). Majority of them had cough (62), dyspnea (74), myalgia (68) but only minority of them felt being fatigue (18).

Table (1): Gender and presenting sign and symptoms of the participants.

Variables	Categories	No.
Gender	Male	56
	Female	44
Severity	Moderate	24
	Severe	76
Complaint at admission	SOB	86
	Cough	4
	SOB and cough	8
	Fatigability	2
Smoking	Current smoker	6
	Ex-smoker	20
	Non-smoker	74
Loss of taste	Yes	26
	No	74
Loss of smell	Yes	18
	No	82
Cough	Yes	62
	No	38
Dyspnea	Yes	74
	No	26
Myalgia	Yes	68
	No	32
Fatigue	Yes	18

	No	82
Total		100

The results of Table (2) show that 42% of them had hypertension, 30% diagnosed with diabetes mellitus, 16% had coronary artery disease, only six patients had heart failure, 10% with history of asthma and four cases with renal failure. Among the total cases 44% of them died finally.

Table (2): Outcome and chronic diseases of the study sample.

Variables	Categories	No.
Hypertension	Yes	42
	No	58
Diabetes mellitus	Yes	30
	No	70
Coronary artery disease	Yes	16
	No	84
Heart failure	Yes	6
	No	94
Asthma	Yes	10
	No	90
Renal failure	Yes	4
	No	96
Outcome	Alive	56
	Dead	44
Total		100

The results of Table (3) show that there was non-significant statistical association between outcome and signs, symptoms and chronic diseases except for dyspnea, hypertension, and renal failure. Pearson Chi square test was done and p–values were more than 0.05. In contrary there was a significant statistical relationship between outcome and dyspnea, hypertension, and renal failure. Most of patients with dyspnea (54.1%), hypertension (57.1%) and the four renal failure cases had died due to COVID-19 complications. Pearson Chi square test was done and p–values were less than 0.05.

Table (3): Association between outcome and signs, symptoms, and chronic diseases.

Variable	Outcome		p-value
	Alive	Dead	
Loss of smell	14 (53.8%)	12 (46.2%)	0.797
Loss of state	8 (44.4%)	10 (55.6%)	0.275
Cough	34 (54.8%)	28 (45.2%)	0.765
Dyspnea	34 (45.9%)	40 (54.1%)	0.001
Myalgia	38 (55.9%)	30 (44.1%)	0.972
Fatigue	10 (55.6%)	8 (44.4%)	0.967
Hypertension	18 (42.9%)	24 (57.1%)	0.024

Diabetes mellitus	14 (46.7%)	16 (53.3%)	0.218
Coronary artery disease	6 (37.5%)	10 (62.5%)	0.104
Heart failure	2 (33.3%)	4 (66.7%)	0.249
Asthma	4 (40%)	6 (60%)	0.328
Renal failure	0 (0%)	4 (100%)	0.035

The results of Table (4) illustrate that there was a statistically significant difference in age, respiratory rate, pulse oximetry and C-reactive protein measures between alive and dead cases. On average, those who survived were younger (59.11 years) than who passed away (67.32 years), with lower respiratory rate (22 breaths per minute), and C-reactive protein measure (21.30) than dead cases who had higher respiratory rate (25.36 breaths per minute), and C-reactive protein measure (59.82). For their advantage, the mean pulse oximetry for the survivors was higher (90.61%) in comparison to dead COVID-19 cases (88.14%). t- test was performed to compare between the averages of the two groups and p-values were less than 0.05.In contrast, the difference between dead and alive cases regarding other numeric measures was not statistically significant, t- test was done and p-values were more than 0.05.

Table (4): Difference in parameters between dead and alive cases in numeric measures.

Variables	Outcome	N	Mean	S.D	p-value
Age (years)	alive	56	59.11	13.24	0.004
	dead	44	67.32	14.23	
SBP	alive	56	127.07	12.37	0.427
	dead	44	129.55	17.38	
DBP	alive	56	78.21	6.77	0.305
	dead	44	80.00	9.76	
pulse rate in bpm	alive	56	94.25	14.98	0.934
	dead	44	93.95	20.54	
respiratory rate	alive	56	22.00	5.30	0.006
	dead	44	25.36	6.67	
pulse oximetry %	alive	56	90.61	5.71	0.029
	dead	44	88.14	5.36	
WBC count	alive	56	13.21	6.72	0.568
	dead	44	12.52	4.88	
Neutrophil count	alive	56	9.26	4.07	0.334
	dead	44	8.51	3.48	
C-reactive protein	alive	56	21.30	46.36	0.001
	dead	44	59.82	52.45	
patient weight in kg	alive	56	86.46	17.12	0.119
	dead	44	81.02	17.23	

Discussion

The present study showed predominance of male patients with hospitalized COVID-19 disease. This finding is similar to results of Naguyen et al. [31] study in USA which reported predominant male gender for COVID-19 patients admitted to hospital and revealed that male gender was a predictable of mortality in COVID-19 disease. Our study reported that severity of COVID-19 diseases in hospitalized patients was distributed into; moderate (24%) and severe (76%). These findings are different from results of results of Mohammed et al.[32] study in Iraq which reported that only 25.2% of hospitalized patients had moderate to severe COVID-19 disease. This difference might be due to discrepancy in study aims and inclusion criteria between two studies. Current study revealed mortality rate of (44%) for hospitalized patients with moderate to severe COVID-19 disease. This mortality rate is higher than rate of (14.4%) for mortality of hospitalized patients with moderate to severe COVID-19 disease reported by Mammen et al.[33]study in India. This difference might be due to differences in risk factors (elderly age and male gender) and clinical co-morbidities (hypertension, diabetes and coronary artery diseases) prevalence between study populations in addition to differences in study methodology. In current study the mortality was significantly higher among COVID-19 patients presented clinically with dyspnea (p=0.001). This finding coincides with results of Aksel et al [34] prospective observational study in Turkey which found that dyspnea, the clinical co-morbidity, high CRP levels and SPO_2 are early predictors of mortality in moderate to severely ill Covid-19 patients.Our study showed a significant association between COVID-19 patients with hypertensionand mortality (p=0.02). Similarly, Chen et al.[35] found that clinical co-morbidity with

hypertension was an independent risk factor for severity and mortality of COVID-19 disease. Our study also showed a significant association between COVID-19 patients with renal failure and mortality (p=0.03). This finding is consistent with results of Pya et al .[36] retrospective cohort study in Kazakhstan on 293 hospitalized patients with COVID-19 disease which showed a statistically significant association between COVID-19 patients with renal failure and mortality.In present study, older age patients with moderate to severe COVID-19 disease were significantly related to mortality. Consistently, Sepandi et al.[37] systematic review and meta-analysis study in Iran revealed that elderly, male gender and clinical co-morbidity were early predictors of mortality in COVID-19 disease. Our study revealed that a higher mean respiratory rate patient with moderate to severe COVID-19 disease was significantly related to mortality (p=0.006). This finding is in agreement with results of Nlandu et al.[38]retrospective study in Democratic Republic of the Congo which reported the respiratory rate of hospitalized COVID-19 patients as early predictor of mortality. Our study found that low SPO_2 of patients with moderate to severe COVID-19 disease was significantly related to mortality (p=0.02). This finding is similar to results of many literatures such as Mukhtar et al.[39] and Xie et al.[40] which all documented that low SPO_2 was an independent predictor of mortality in hospitalized patients with COVID-19 disease. Our study showed that high C-reactive protein level in patients with moderate to severe COVID-19 disease was significantly related to mortality (p=0.001). This finding is parallel with results of Timpau et al.[41] retrospective study in Romania which revealed that C-reactive protein and D-

dimer levels had better performance in prediction of mortality in patients with moderate to severe COVID-19 disease. In conclusion, the early predictors of mortality in patients with moderate to severe COVID-19 disease were elderly age, clinical presentation of dyspnea, clinical co-morbidity with hypertension and renal failure, high respiratory rate, low SPO₂ and elevated levels of C-reactive protein. This study recommendedphysicians in emergency department to implement the prediction model in assessment of patients with moderate to severe COVID-19 disease which help in triage and better in planning of management for COVID-19 disease.

Conclusion

The early predictors of mortality in patients with moderate to severe COVID-19 disease were elderly age, clinical presentation of dyspnea, clinical co-morbidity with hypertension and renal failure, high respiratory rate, low SPO₂ and elevated levels of C-reactive protein. This study recommended physicians in emergency department to implement the prediction model in assessment of with moderate to severe COVID-19 disease which help in triage and better in planning of management for COVID-19 disease.

Conflicts of interest
There were no conflicts of interest.

References

1. Peeri NC, Shrestha N, Rahman MS, et al. The SARS, MERS and novel coronavirus (COVID-19) epidemics, the newest and biggest global health threats: What lessons have we learned? Int J Epidemiol 2020; 49(1): 717–26.
2. Worldometer Coronavirus Update: Cases and Deaths from COVID-19 Virus Pandemic. 2022. Available from: https://www.worldometers.info/coronavirus/
3. (COVID-19), What the KRG is doing 2020. Available from: https://gov.krd/coronavirus-en/situation-update/
4. Lauer SA, Grantz KH, Bi Q. The incubation period of coronavirus disease 2019 (COVID-19) from publicly reported confirmed cases: estimation and application. Ann Intern Med. 2020; 172(9):577-82.
5. Guan WJ, Ni ZY, Hu Y. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med. 2020; 382(18):1708-20.
6. Wu, JT, Leung K, et al. Estimating clinical severity of COVID-19 from the transmission dynamics in Wuhan, China. Nat Med. 2020; 26(1): 506–10.
7. Ng OT, Marimuthu K, Chia PY, et al. SARS-CoV-2 Infection among Travelers Returning from Wuhan, China. N Engl J Med. 2020; 382(1): 1476–8.
8. Bi Q, Wu Y, Mei S, et al. Epidemiology and transmission of COVID-19 in 391 cases and 1286 of their close contacts in Shenzhen, China: A retrospective cohort study. Lancet Infect Dis. 2020; 20(1): 911–9.
9. World Health Organization. Clinical management of severe acute respiratory infection when novel coronavirus (2019-nCoV) infection is suspected: interim guidance. 2020. https://apps.who.int/iris/handle/10665/330893
10. National Health and Health Commission of NPC Interim Guidance for Novel Coronavirus Pneumonia (Trial Implementation of Revised Eigthth Edition). 2020. Available

online:
http://www.gov.cn/zhengce/zhengceku/2020-08/19/content_5535757.htm

11. Zhang J, Wang X, Jia X, et al. Risk factors for disease severity, unimprovement, and mortality in COVID-19 patients in Wuhan, China. Clin Microbiol Infect. 2020; 26(1): 767–72.

12. Jin JM, Bai P, He W, et al. Gender Differences in Patients with COVID-19: Focus on Severity and Mortality. Front Public Health. 2020; 8(1): 152-3.

13. Verity R, Okell LC, Dorigatti I, et al. Estimates of the severity of coronavirus disease 2019: A model-based analysis. Lancet Infect Dis. 2020; 20(1): 669–77.

14. Pan A, Liu L, Wang C, et al. Association of Public Health Interventions with the Epidemiology of the COVID-19 Outbreak in Wuhan, China. JAMA. 2020; 323(1): 1915-6.

15. Sun Y, Dong Y, Wang L. Characteristics and prognostic factors of disease severity in patients with COVID-19: The Beijing experience. J Autoimmun. 2020; 112(1):102473-4.

16. Mo P, Xing Y, Xiao Y. Clinical Characteristics of Refractory Coronavirus Disease 2019 in Wuhan, China. Clin Infect Dis. 2021; 73(11): e4208-13.

17. Robilotti EV, Babady NE, Mead PA. Determinants of Severity in Cancer Patients with COVID-19 Illness. Preprint. MedRxiv. 2020;.20(1):863-4.

18. Bornstein SR, Rubino F, Khunti K. Practical recommendations for the management of diabetes in patients with COVID-19. Lancet Diabetes Endocrinol. 2020; 8(6):546-50.

19. Taquet M, Luciano S, Geddes JR, Harrison PJ. Bidirectional associations between COVID-19 and psychiatric disorder: Retrospective cohort studies of 62354 COVID-19 cases in the USA. Lancet Psychiatry. 2021; 8(1): 130–40.

20. Gross O, Moerer O, Weber M, Huber TB, Scheithauer S. COVID-19-associated nephritis: early warning for disease severity and complications? Lancet. 2020; 395(10236): e87-8.

21. Louapre C, Collongues N, Stankoff B. Clinical Characteristics and Outcomes in Patients with Coronavirus Disease 2019 and Multiple Sclerosis. JAMA Neurol. 2020; 77(9):1079-88.

22. Zhang X, Tan Y, Ling Y, et al. Viral and host factors related to the clinical outcome of COVID-19. Nat. Cell Biol. 2020; 583(1): 437–40.

23. Fajnzylber J, Regan J, Coxen K, et al. SARS-CoV-2 viral load is associated with increased disease severity and mortality. Nat Commun. 2020; 11(1): 1–9.

24. Li K, Wu J, Wu F, et al. The Clinical and Chest CT Features Associated with Severe and Critical COVID-19 Pneumonia. InvestigRadiol. 2020; 55(1): 327–31.

25. Wu J, Li W, Shi X, et al. Early antiviral treatment contributes to alleviate the severity and improve the prognosis of patients with novel coronavirus disease (COVID-19). J Intern Med. 2020; 288(1): 128–38.

26. Domingo JL, Rovira J. Effects of air pollutants on the transmission and severity of respiratory viral infections. Environ Res. 2020; 187(1): 109650-1.

27. Walker PG, Whittaker C, Watson O, et al. Report 12—The Global Impact of COVID-19 and Strategies for Mitigation and Suppression. 2020. Available from: https://www.imperial.ac.uk/mrc-global-infectious-diseaseanalysis/covid-19/report-12-global-impact-covid-19/

28. Leung K, Wu JT, Liu D, Leung GM. First-wave COVID-19 transmissibility and severity in China outside Hubei after control measures, and second-wave scenario planning: A modelling

impact assessment. Lancet. 2020; 395(1): 1382–93.

29. Choi YJ, Park JY, Lee HS, et al. Variable effects of underlying diseases on the prognosis of patients with COVID-19. PLoS ONE. 2021; 16(7): e0254258.

30. Srinivasan BS. Diagnosis and treatment protocol for novel coronavirus pneumonia (Version 7) Chin Med J. 2020; 133:1087–95.

31. Nguyen NT, Chinn J, De Ferrante M, et al. Male gender is a predictor of higher mortality in hospitalized adults with COVID-19. PLoS One. 2021; 16(7):e0254066.

32. Mohammed IA, Ali AH, Al-Shenaty JA. Clinical course and disease outcomes in hospitalized patients with 2019 novel corona virus disease at Ibn- Al Khateeb Hospital in Baghdad, Iraq. JFac Med Baghdad. 2020; 62 (3): 48-59.

33. Mammen JJ, Kumar S, Thomas L. Factors associated with mortality among moderate and severe patients with COVID-19 in India: a secondary analysis of a randomised controlled trial. BMJ Open. 2021; 11(1): e050571.

34. Aksel G, İslam MM, Algın A, et al. Early predictors of mortality for moderate to severely ill patients with Covid-19. Am J Emerg Med. 2021; 45(1):290-6.

35. Chen J, Liu Y, Qin J. Hypertension as an independent risk factor for severity and mortality in patients with COVID-19: a retrospective study. Postgrad Med J. 2021; 1(1):4067-14.

36. Pya Y, Bekbossynova M, Gaipov A, et al. Mortality predictors of hospitalized patients with COVID-19: Retrospective cohort study from Nur-Sultan, Kazakhstan. PLoS ONE. 2021; 16(12): e0261272. Available from: https://doi.org/10.1371/journal.pone.0261272

37. Sepandi M, Taghdir M, Alimohamadi Y, Afrashteh S, Hosamirudsari H. Factors Associated with Mortality in COVID-19 Patients: A Systematic Review and Meta-Analysis. Iran J Public Health. 2020; 49(7):1211-21.

38. Nlandu Y, Mafuta D, Sakaji J. Predictors of mortality in COVID-19 patients at Kinshasa Medical Center and a survival analysis: a retrospective cohort study. BMC Infect Dis. 2021; 21(1): 1272-3. Available from: https://doi.org/10.1186/s12879-021-06984-x

39. Mukhtar A, Rady A, Hasanin A. Admission SpO_2 and ROX index predict outcome in patients with COVID-19. Am J Emerg Med. 2021; 50(1):106-10.

40. Xie J, Covassin N, Fan Z. Association Between Hypoxemia and Mortality in Patients With COVID-19. Mayo Clin Proc. 2020; 95(6):1138-47.

41. Timpau AS, Miftode RS, Petris AO, et al. Mortality Predictors in Severe COVID-19 Patients from an East European Tertiary Center: A Never-Ending Challenge for a No Happy Ending Pandemic. J Clin Med. 2022; 11(1): 58-9. Available from: https://doi.org/10.3390/jcm11010058