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Mortality Analysis of COVID Patients to Develop a Scoring System for Early Identification of Severe Cases: A Retrospective Cohort Study

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Abstract

Objectives

To develop a scoring system to identify patients at increased risk of mortality in COVID 19 cases at admission.

Methods

This retrospective cohort study involved analysis of data from hospital records of patients above 18 years in age admitted to ICU of a tertiary care hospital with RTPCR positive COVID-19.

Results

Age, gender, comorbidity, LDH, D Dimer, CRP, N:L ratio and S. Ferritin were included in the scoring. The mean severity score was 19.22 ± 3.69. More than 95% of them had severity score≥15.

Conclusion

We have derived an easy-to-use scoring system that suggests a cutoff value. 95% of those who expired scored above this cutoff value. Validation of the same on a different validation cohort and categorization into mild, moderate and severe categories is the next step to enable accurate stratification of patients with covid-19 admitted to hospital.

Keywords

COVID 19, Severity scoring system, risk factors.

Introduction

The novel Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) disease (COVID-19) emerged in Wuhan, China, and spread worldwide. The case fatality rate reported across countries, settings and age groups is highly variable, ranging from about 0.5% to 10% [1]. In hospitalized patients it has been reported to be higher than 20% [2].

Prognostic factors are important as they guide stratification of patients based on their risk of developing severe disease or death. Several studies have analyzed the factors affecting morbidity and mortality in patients hospitalized with COVID-19 [3 - 5]. Factors that have been correlated with a poor prognosis and increased mortality in COVID 19 infection include old age, male gender, comorbidities like morbid obesity, chronic pulmonary disease, coronary artery disease, chronic kidney disease, and malignancies.[6 - 8]. Laboratory parameters like lymphocytopenia and increased levels of inflammatory biomarkers such as C-reactive protein (CRP), lactate dehydrogenase (LDH), serum ferritin and interleukin-6 (IL-6) have been shown to be related to mortality in these patients[9 - 12]. Multiple prognostic factors have been proposed and some have been accepted as "established" but the predictive value of most of these potential prognostic factors has not been robustly evaluated and remains uncertain.[13] Hence, we conducted this study to assess the demographic and laboratory profile of the RTPCR positive Covid 19 cases who expired, to identify the risk factors associated with mortality of patients with COVID-19 disease and to develop a scoring system to identify patients with higher risk of mortality at admission.

Materials and Methods

This was a retrospective cohort study. It was carried out in April - May 31 2021 after obtaining approval from Institutional Ethics Committee. All adults > 18 years in age and admitted in our hospital with laboratory confirmed (RTPCR positive) COVID-19 who expired were included. The hospital records of these patients were accessed to collect the data. Data abstracted included age, gender, history of underlying comorbidities (e.g, diabetes mellitus, hypertension, cardiovascular disease, cerebrovascular disease, chronic pulmonary disease, chronic kidney disease, chronic

liver disease, and malignancy), laboratory parameters (CBC, N:L ratio, blood glucose level, RFT, SGPT, serum electrolytes, CRP, Serum Ferritin, Serum LDH, D- DIMER, procalcitonin, IL6 etc.), Chest X ray and chest computed tomographic (CT) scans on admission. The data thus collected was entered in an excel sheet. Those patients for whom adequate information was not available in records were excluded. Two study investigators independently checked the collected data of included patients.

Statistical Analysis

Data so collected was analysed to find mean ± SD of the continuous variables to identify the variables which were substantially elevated. Elevation of at least twice the normal values was considered substantial elevation. The variables which were identified like this, were given scores depending upon the level of elevation above normal according to following scheme : LDH <500 - 0, 500 to 1000 – 1, 1000 to 2000 – 2, 2000 to4000 – 3, > 4000 - 4; D Dimer <250 – 0, 250 to 500 – 1, 500 to 1000 – 2, 1000 to 2000 – 3, 2000 to 4000 – 4, > 4000 – 5; CRP < 3 – 0, 3 to 20 – 1, 20 to 50 – 2, 50 to 100 -3, > 100 – 4; S. Ferritin <250 – 0, 250 to 500 – 1, 500 to 1000 – 2, 1000 to 2000 – 3, 2000 to 4000 – 4, > 4000 – 5; N:L ratio < 3 – 0, 4 to 8 – 1, 9 to 12 – 2, 13 to 16 – 3, 17 to 20 – 4, > 20 – 5. Age was scored according to following age groups: >18 to 30 – 1, 31 to 40 – 2, 41 to 50 – 3, 51 to 60 – 4, > 60 – 5. As male gender and diabetes have been shown to be associated with increased risk of mortality in previous studies, females were given score 1 while males were given a score of 2 while hypertension and diabetes were given scores of 1 and 2 respectively. 1 point was added for any other comorbidity present. The scores were summed to find the individual scores from which mean severity score was calculated. Continuous variables with normal distribution are expressed as mean ± standard deviation (SD); nonnormally distributed continuous variables are reported as median.

Results

Total 200 patients were included. 136 (68%) were males and 64 (32%) were females. Mean age was 58.61±14.19 years.

Out of the 200 patients included, 81 (40.5%) had no comorbity, 46 (23%) were hypertensive, 25 (12.5%) had

Total (n)	200
Males/ Females	136/ 64
Mean Age (Years)	58.61 ± 14.19 years
Age category	
20 – 30	2 (1%)
31 – 40	21 (10.5%)
41 – 50	30 (15%)
51 – 60	49 (24.5%)
61 - 70	63 (31.5%)
71 - 80	23 (11.5%)
81 - 90	11 (5.5%)
91-100	1 (0.5%)

Comorbidity	
None	81 (40.5%)
Hypertension	46 (23%)
Diabetes mellitus	25 (12.5%)
Both DM & Hypertension	24 (12%)
Chronic Kidney Disease	13 (6.5%)
Ischemic heart disease	9 (4.5%)
Hypothyroidism	7 (3.5%)
Hepatitis	7 (3.5%)
CV stroke	6 (3%)

Table 1: Basic characteristics of study population

Type 2 diabetes while 24 (12%) had both. 13 (6.5%) patients had CKD, 9 (4.5%) had IHD, 7 (3.5%) each had hypothyroidism and hepatitis while 6 (3%) had CV stroke. History of epilepsy, CLD, HIV and bronchiectasis was found in two patients each while OSA, CN palsy, psychosis and Alzheimer's were seen in one patient each. One patient was pregnant. 58 (29%) patients developed AKI, 30 (15%) developed sepsis, 7 (3.5%) developed CV stroke, four each had DKA, uremic encephalopathy, and pancreatitis; two each had atrial fibrillation, hypernatremia and SVT, while one each had pneumothorax, cellulitis, ICU psychosis, and emphysema. At admission, 76 (38%) needed mechanical ventilation, 65 (32.5%) needed BiPAP while 60 (30%) were on NRBM, although all of them had to be kept on mechanical ventilator later.

Mean hemoglobin was normal (12.5 ± 2.32 g/dl) while mean TLC was elevated (16818 ± 9999/cu.mm) with median N:L ratio being 18.2. Mean blood urea and serum creatinine both were elevated (71.68 ± 51.8 mg/dl and 1.94 ± 2.0 respectively). Mean HRCT score was 17.29 ± 5.44. Mean LDH and D DIMER were 1343 ± 807 IU and 3954.48 ± 3407.07 IU respectively. SGPT and PCT were within normal ranges (42 and 0.28 respectively). Medians of IL-6, CRP and S. ferritin were 455.40, 149.70 and 506.36 respectively. Thus, it was observed that LDH, D Dimer, CRP, N:L ratio and S. Ferritin were substantially elevated confirming the previous reports that these inflammatory biomarkers are related to more severe COVID-19 disease, hence were included in the scoring. Age, gender and comorbidity being established prognostic markers, were also included in the scoring scheme. IL-6 and PCT were not included as sufficient data was not available. We did a correlation analysis to find if any of these included variables were correlated and did not find any correlation between any two of these.

Lab investigations	.Mean ± SD	Normal range
Hemoglobin	12.55 ± 2.32	12 – 16 gm/dl
TLC	16818.83 ± 9999.16	4.5 – 11000/ul
N:L	18.2 (median)	3
Blood Urea	71.68 ± 51.85	6 – 24 mg/dl
S. Creatinine	1.94 ± 2.0	0.7 – 1.2 mg/dl
SGPT	42 (median)	7 – 56 U/L
S. Ferritin	398.25 (median)	20 – 250 (males), 20 – 120 (females) ng/ml
S. LDH	1343.33 ± 807.34	140- 280 U/L
PCT	0.28 (median)	< 0.05 ng/ml
D DIMER	3954.48 ± 3407.07	< 250 ng/ml
IL 6	79.38 (median)	0-16.4 pg/ml
CRP	73 (median)	< 3 mg/l
HRCT score	17.29 ± 5.44	> 30

Table 2: Mean values of lab investigations.

S.No.	Correlation between	R Value
1	D-Dimer and S. ferritin	0.097
2	D-Dimer and CRP	-0.066
3	D-Dimer and LDH	0.155
4	D-Dimer and Age	-0.194
5	Age and LDH	-0.163
6	Age and S. ferritin	-0.056
7	Age and CRP	0.125
8	S. ferritinand CRP	0.109
9	S. ferritin and LDH	0.217
10	CRP and LDH	0.117
13	N:L and LDH	-0.196
14	N:L and D-Dimer	0.088
15	N:L and CRP	-0.033
16	N:L and S. ferritin	-0.055
17	N:L and Age	0.076

Table 3: Correlation between different variables

As there was no correlation between any of them, we considered each of them an independent risk factor for mortality in COVID-19 disease and gave scores according to the predecided scoring criteria. The mean severity score was 19.22 ± 3.69. More than 95% of them had severity score ≥15.

Discussion

We have developed an eight variable AGIC (Age, gender, inflammatory markers and comorbidity) mortality score in patients admitted with covid-19. The mortality score uses patient demographics and blood parameters that are commonly available at the time of hospital admission and suggests a cutoff point above which most of the expired patients score. This study represents all mortal COVID 19 cases in a tertiary healthcare setting.

The use of parameters commonly available at admission in a tertiary care facility increases its applicability, avoiding the requirement for expensive markers.[14,15] Additionally, we used objective parameters. We did not use pulse rate and respiratory rate for prognostication as they may be altered by anxiety also which is a possibility considering the panic created due to the pandemic. The lab values do not get altered by any external factor and age, gender and comorbidities are also unalterable variables. Thus, the values were more reliably close to real ones. In previous studies on COVID-19 prognostic scores, the comorbidities were handled differently, some have considered them individually [16,17] giving equal weight [18] while others found no predictive effect.[19] Another recent study suggested an additive effect of comorbidity in patients with COVID-19 disease, with increasing number of comorbidities associated with poorer outcomes.[20] Hence in our study, comorbities were given individual scoring with scores added up upto a maximum of four comorbidities.

During an epidemic, there are high chances of coming across missing data during data collection [20], however, the assessment of missing data on model performance in novel COVID-19 risk stratification scores has been limited [18] or unexplored [19,16] till now. In this study also, PCT and IL 6 were excluded as complete data was not available for them. As PCT is more an indicator of development of secondary bacterial sepsis and not COVID-19 infection, the exclusion of this might not make much difference. Lack of data of IL-6 levels and its exclusion might be considered a weakness of this severity score but its inclusion would have made it more expensive and less feasible. Also, the markers that we have included are usually easily available, are in routine use and are not much expensive.

We did not evaluate and compare the predictive performance of several existing scores as they required a large number of parameters (for example, APACHE II), as well as several other COVID-19 prognostic scores that use computed tomography findings or uncommonly measured biomarkers. We could only give a tentative cutoff value which was scored by > 95% of those who met with mortality. However, we plan to validate the scoring system in a different validation cohort comparing those who did not survive with those who survived and thus give categories of scores at which the COVID 19 patients could be categorized as mild, moderate or severe at the time of admission for better management.

Conclusions

We have derived an easy-to-use eight variable scoring system that suggests a cutoff value above which most of those who did not survive scored. Validation of

the same on a different validation cohort and categorization into mild, moderate and severe categories will enable accurate stratification of patients with covid-19 admitted to hospital. Till the scores are validated, the cutoff value can be used as a guide to treat the COVID 19 patient more aggressively.

References

1. Centre for Evidence-Based Medicine. Global Covid-19 Case Fatality Rates. https:// www.cebm.net/ covid-19/global-covid-19-case-fatality-rates/ (accessed April 6, 2020).
2. International Severe Acute Respiratory and Emerging Infections Consortium (ISARIC). COVID-19 Report: 19 May 2020. https://media.tghn.org/medialibrary/2020/05/ISARIC_Data_Platform_COVID-19_Report_ 19 MAY 20. pdf
3. Henry BM, de Oliveira MHS, Benoit S, Plebani M, Lippi G. Hematologic, biochemical and immune biomarker abnormalities associated with severe illness and mortality in coronavirus disease 2019 (COVID-19): a meta-analysis. ClinChem Lab Med. 2020;58:1021–8.
4. Gao YD, Ding M, Dong X, Zhang JJ, KursatAzkur A, Azkur D, Gan H, Sun YL, Fu W, Li W, Liang HL, Cao YY, Yan Q, Cao C, Gao HY, Brüggen MC, van de Veen W, Sokolowska M, Akdis M, Akdis CA. Risk factors for severe and critically ill COVID-19 patients: A review. Allergy. 2021 Feb;76(2):428-455.
5. Setiati S, Harimurti K, Safitri ED, Ranakusuma RW, Saldi SRF, Azwar MK, Marsigit J, Pitoyo Y, Widyaningsih W. Risk factors and laboratory test results associated with severe illness and mortality in COVID-19 patients: A systematic review. Acta Med Indones. 2020 Jul;52(3):227-245. PMID: 33020334.
6. Henry BM, de Oliveira MHS, Benoit S, Plebani M, Lippi G. Hematologic, biochemical and immune biomarker abnormalities associated with severe illness and mortality in coronavirus disease 2019 (COVID-19): a meta-analysis. ClinChem Lab Med. 2020;58:1021–8.
7. Gao YD, Ding M, Dong X, Zhang JJ, KursatAzkur A, Azkur D, Gan H, Sun YL, Fu W, Li W, Liang HL, Cao YY, Yan Q, Cao C, Gao HY, Brüggen MC, van de Veen W, Sokolowska M, Akdis M, Akdis CA. Risk factors for severe and critically ill COVID-19 patients: A review. Allergy. 2021 Feb;76(2):428-455.
8. Setiati S, Harimurti K, Safitri ED, Ranakusuma RW, Saldi SRF, Azwar MK, Marsigit J, Pitoyo Y, Widyaningsih W. Risk factors and laboratory test results associated with severe illness and mortality in COVID-19 patients: A systematic review. Acta Med Indones. 2020 Jul;52(3):227-245. PMID: 33020334.
9. International Severe Acute Respiratory and Emerging Infections Consortium (ISARIC). COVID-19 Report: 19 May 2020. https://media.tghn.org/medialibrary/2020/05/ISARIC_Data_Platform_COVID-19_Report_19MAY20.pdf.
10. Henry BM, de Oliveira MHS, Benoit S, Plebani M, Lippi G. Hematologic, biochemical and immune biomarker abnormalities associated with severe illness and mortality in coronavirus disease 2019 (COVID-19): a meta-analysis. ClinChem Lab Med. 2020;58:1021–8.
11. Gao YD, Ding M, Dong X, Zhang JJ, KursatAzkur A, Azkur D, Gan H, Sun YL, Fu W, Li W, Liang

HL, Cao YY, Yan Q, Cao C, Gao HY, Brüggen MC, van de Veen W, Sokolowska M, Akdis M, Akdis CA. Risk factors for severe and critically ill COVID-19 patients: A review. Allergy. 2021 Feb;76(2):428-455.

12. Setiati S, Harimurti K, Safitri ED, Ranakusuma RW, Saldi SRF, Azwar MK, Marsigit J, Pitoyo Y, Widyaningsih W. Risk factors and laboratory test results associated with severe illness and mortality in COVID-19 patients: A systematic review. Acta Med Indones. 2020 Jul;52(3):227-245. PMID: 33020334.
13. Izcovich, A., Ragusa, M. A., Tortosa, F., LavenaMarzio, M. A., Agnoletti, C., Bengolea, A., Ceirano, A., Espinosa, F., Saavedra, E., Sanguine, V., Tassara, A., Cid, C., Catalano, H. N., Agarwal, A., Foroutan, F., &Rada, G. (2020). Prognostic factors for severity and mortality in patients infected with COVID-19: A systematic review. *PloS one*, *15*(11), e0241955.
14. Tolksdorf K, Buda S, Schuler E, Wieler LH, Haas W. Influenza associated pneumonia as reference to assess seriousness of coronavirus disease (COVID-19). *Euro Surveill* 2020;25:2000258. doi:10.2807/1560-7917.ES.2020.25.11.2000258.
15. Song Y, Zheng S, Li L, Zhang X, Zhang X, Huang Z, et al. Deep learning enables accurate diagnosis of novel coronavirus (COVID-19) with CT images. medRxiv. 2020. doi:10.1101/2020.02.23.20026930.
16. Zhang H, Shi T, Wu X, Zhang Z, Wang K, Bean D, et al. Risk prediction for poor outcome and death in hospital in-patients with COVID-19: derivation in Wuhan, China and external validation in London, UK. medRxiv.2020. doi:10.1101/2020.04.28.20082222.
17. Williams RD, Markus AF, Yang C, Salles TD, Falconer T, Jonnagaddala J, et al. Seek COVER: Development and validation of a personalized risk calculator for COVID-19 outcomes in an international network. medRxiv. 2020. doi:10.1101/2020.05.26.20112649.
18. Liang W, Liang H, Ou L, et al. Development and validation of a clinical risk score to predict the occurrence of critical illness in hospitalized patients with COVID-19. 2020. https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2766086
19. Xie J, Hungerford D, Chen H, Abrams ST, Li S, Wang G, et al. Development and external validation of a prognostic multivariable model on admission for hospitalized patients with COVID-19. medRxiv.2020. doi:10.1101/2020.03.28.20045997
20. Guan W, Liang W, Zhao Y, et al. Comorbidity and its impact on 1590 patients with COVID-19 in China: a nationwide analysis. European Respiratory Journal. 2020. https:// erj.ersjournals.com/ content/55/5/2000547.