Predictors of Clinical Outcomes in Adult COVID-19 Patients Admitted to a Tertiary Care Hospital in India: an analytical cross-sectional study

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Abstract. Background: The outbreak of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic has resulted in exponential rise in the number of patients getting hospitalised with coronavirus disease 2019 (COVID-19). There is a paucity of data from South East Asian Region related to the predictors of clinical outcomes in these patients. This formed the basis of conducting our study. Methods: This was an analytical cross-sectional study. Demographic, clinical, radiological and laboratory data of 125 patients was collected on admission. The study outcome was death or discharge after recovery. For univariate analysis, unpaired t-test, Chi-square and Fisher’s Exact test were used. Receiver operating characteristic (ROC) curves were plotted for Sequential Organ Failure Assessment (SOFA) score and few laboratory parameters. Logistic regression was applied for multivariate analysis. Results: Elderly age, ischemic heart disease and smoking were significantly associated with mortality. Elevated levels of D-dimer and lactate dehydrogenase (LDH) and reduced lymphocyte counts were the predictors of mortality. The ROCs for SOFA score curve showed a cut-off value ≥ 3.5 (sensitivity- 91.7% and specificity- 87.5%), for IL-6 the cut-off value was ≥ 37.9 (sensitivity- 96% and specificity- 78%) and for lymphocyte counts, a cut off was calculated to be less than and equal to 1.46 x 10^9 per litre (sensitivity- 75.2% and specificity- 83.3%). Conclusion: Old age, smoking history, ischemic heart disease and laboratory parameters including elevated D-dimer, raised LDH and low lymphocyte counts at baseline are associated with COVID-19 mortality. A higher SOFA score at admission is a poor prognosticator in COVID-19 patients. (www.actabiomedica.it)

Keywords: COVID-19; D-dimer; Outcomes; Predictors; SOFA score

Introduction

The highly contagious severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection which causes the Coronavirus Disease 2019 (COVID-19) has spread across the globe accounting for 20,405,695 confirmed cases including 743,487 deaths till date (1). The clinical spectrum of COVID-19 is
heterogeneous, with nearly 80% of the infected cases being either asymptomatic or have mild influenza-like illness (ILI) who recover without complications (2). About 15%-20% of mild cases progress to develop severe disease and one-fifth of severe cases become critically ill requiring intensive care management (3). The mortality in those who are critically ill is very high (>50%) despite the best management (4). Advanced age, co-morbid illnesses such as diabetes, hypertension, pre-existing cardiovascular diseases, chronic lung disease, chronic kidney disease, and malignancies are considered as risk factors for severity based on reports from China and rest of the world (4-7). However, complications and mortality have been reported in those without the aforementioned risk factors. Further, laboratory parameters and inflammatory markers including C-reactive protein, interleukin-6 (IL-6), lactate dehydrogenase (LDH) among others have been shown to predict severity of COVID-19 (7,8). India is presently witnessing a rapid surge in infections, hospital admissions and mortality. There is a paucity of data from South East Asian Region (SEAR) regarding the clinical outcomes and risk factors for mortality due to COVID-19. Therefore, the present study was undertaken to identify the predictors of clinical outcome, as early identification would be paramount in optimal utilization of medical resources in managing these high risk-patients.

Methods

Study design and participants

This analytical cross-sectional study was conducted in COVID-19 patients aged more than 18 years admitted at the All India Institute of Medical Sciences, Jodhpur, a tertiary care teaching hospital in western India. The diagnosis of COVID-19 was confirmed by real-time polymerase chain reaction (PCR) assay of nasopharyngeal and throat swabs of patients admitted in our hospital from April 2020 to June 2020. Cases admitted outside the study period and those referred to other facilities were excluded. Those fitting into the inclusion criteria were enrolled after obtaining informed written consent. Baseline demographic, clinical, radiological and laboratory parameters of each patient were recorded at the time of hospitalization. Our study outcome was either death or discharge from the hospital after recovery. A total of 125 patients were enrolled. The study was approved by the institutional ethics committee (ECR/866/Inst/RJ/2016/RR-19) of All India Institute of Medical Sciences, Jodhpur, India

Data collection

Data of patients was extracted from the hospital electronic records. We collected baseline demographic, clinical, radiological and laboratory data at the time of hospital admission using a standard data collection form. Clinical and demographic data included age, sex, presenting complaints, recent history of travel to COVID-19 endemic zones, contact history/exposure to a laboratory-confirmed case of COVID-19, co-morbidities, cigarette smoking, vital signs at presentation, quick sequential organ failure assessment (qSOFA) and sequential organ failure assessment (SOFA) scores. Laboratory investigations included complete hemogram, liver function tests, kidney function tests, serum electrolytes, prothrombin time (PT)/ international normalized ratio (INR), D-dimer, activated partial thromboplastin time (APTT), lactate dehydrogenase (LDH), creatine kinase (CK), serum ferritin, interleukin-6 (IL-6), serum procalcitonin, and random blood sugar. Imaging studies included chest radiograph and computerized tomography (CT) scans of chest as per clinical requirement. Outcome was documented either as discharge or death.

Definitions

Disease severity of COVID-19 was assigned into the following groups in accordance with interim guidance given by World Health Organization (WHO) (9). These included asymptomatic, mild, moderate, severe, and critical disease. Asymptomatic infection was defined as laboratory-confirmed case of COVID-19 without any symptoms. Mild disease included fever, cough, sore throat, nasal congestion, anorexia, fatigue, myalgia, anosmia, ageusia, headache and gastrointestinal symptoms without evidence of viral pneumonia or hypoxia. Moderate disease was pneumonia without
any signs of severe pneumonia. Severe disease included pneumonia with one of the following: respiratory rate >30 breaths per minute, oxygen saturation (SpO2) < 90% on room air. Finally, critical disease included acute respiratory distress syndrome (ARDS), sepsis, and septic shock. ARDS was defined by the Berlin definition of 2013. Sepsis and septic shock were defined by the 2018 update of surviving sepsis campaign (10). Fever was defined as axillary temperature of more than 37.5°C.

For scoring of abnormality on chest radiographs, each lung was divided into three zones by using two horizontal lines as mentioned in the studies by Borgeshi et al and Bhalla et al (11,12). The upper line passes through the inferior wall of aortic arch and the lower line at the level of right inferior pulmonary vein. The upper zone is located above the upper line, mid zone is located between both lines and lower zone is located below the lower line. Within each zone, a score 0–4 is given with maximum score of 24. Zero for normal; one for up to 25%, two for up to 50%, three for up to 75% and four for >75% of area involved in each zone.

Statistical analysis

The data was analysed using Microsoft Excel 2016 and SPSS v.23. For univariate analysis of demographic and clinical parameters, unpaired t-test, Chi-square and Fisher’s Exact test were used. For univariate analysis of laboratory parameters, median values with IQR were calculated. Mann-Whitney U and Kruskal Wallis H tests were used to assess the statistical significance. ROC curves were plotted for SOFA score, IL-6 level, and absolute lymphocyte counts for predicting the outcomes of COVID-19. Logistic regression was applied for multivariate analysis for both demographic and clinical characteristics as well as laboratory parameters. Variables strongly associated with mortality during univariate analysis (present among ~100% non-survivors) were directly considered as predictors of mortality and were excluded from multivariate analysis. The goodness of fit for regression models was assessed by Hosmer-Lemeshow test. P-value <0.05 was considered as statistically significant.

Results

Table 1 depicts that there was a significant difference in the mean age of survivors (46.16 ± 16.99) and non-survivors (65.83 ± 9.21) of COVID-19. Almost three fourth (74.4%) of patients were male. The prevalence of smoking was significantly more among non-survivors (50.0%) as compared to survivors (12.9%). None of the deceased patients reported any travel history in the recent past. About half of the patients had history of contact with a confirmed case of COVID-19. Co-morbidities like hypertension, diabetes and ischemic heart disease were significantly more common among non-survivors as compared to survivors. Symptoms including fever, sore throat, cough, fatigue, dyspnea and headache were also significantly more common among non-survivors. Other reported symptoms were myalgia, diarrhea and abdominal pain. Two-third of the patients had received Bacille Calmette-Guerin (BCG) vaccination during childhood. Abnormalities in clinical parameters like temperature > 37.5°C, pulse rate ≥100 per minute, respiratory rate ≥30 breaths per minute, SpO2 <90% and blood pressure (hypotension or hypertension) were significantly more common among non-survivors. Compared to 13.9% among the survivors, all patients in the non-survivor group had respiratory distress at presentation (p<0.001). The means of SOFA and q-SOFA score were significantly higher among non-survivors. As much as 58.4% of the survivors were either asymptomatic or had mild symptoms (26.7%); while all the non-survivors were either severely ill or critically ill at presentation.

It is evident from table 2 that median values of neutrophil count, serum ferritin, serum glutamic oxaloacetic transaminase (SGOT), serum glutamic pyruvic transaminase (SGPT), serum creatinine, LDH, prothrombin time, INR, D-dimer, IL-6, pro-calcitonin and creatinine kinase levels were significantly higher among non-survivors. No significant differences were observed in the white blood cell (WBC) count and platelet count between both the two groups. Chest radiography was done in a total of 38 patients (14 survivors and 24 non-survivors). The mean severity score of lung damage was significantly higher among non-survivors (12.29±4.19) as compared to survivors (1.24±3.49). Similarly, consolida-
| Variables                          | Survivor (n=101) | Non-survivor (n=24) | Total (n=125) | P value |
|-----------------------------------|------------------|---------------------|---------------|---------|
| **Age, years (Mean ± SD)**        | 46.16 ± 16.99    | 65.83 ± 9.21        | 49.94 ± 17.59 | <0.001  |
| **Sex**                           |                  |                     |               |         |
| Female                            | 25 (24.8%)       | 7 (29.2%)           | 32 (25.6%)    | 0.656   |
| Male                              | 76 (75.2%)       | 17 (70.8%)          | 93 (74.4%)    |         |
| **Smokers**                       | 13 (12.9%)       | 12 (50.0%)          | 25 (20.0%)    | <0.001  |
| **Positive Travel History**       | 19 (18.8%)       | 0 (0.0%)            | 19 (15.2%)    | 0.021   |
| **Known contact history**         | 52 (51.5%)       | 8 (33.3%)           | 60 (48.0%)    | 0.11    |
| **Comorbidities**                 |                  |                     |               |         |
| Hypertension                      | 13 (12.9%)       | 12 (50.0%)          | 25 (20.0%)    | <0.001  |
| Diabetes                          | 8 (7.9%)         | 8 (33.3%)           | 16 (12.8%)    | 0.001   |
| Ischemic Heart disease            | 5 (5.0%)         | 9 (37.5%)           | 14 (11.2%)    | <0.001  |
| Chronic lung disease              | 5 (5.0%)         | 2 (8.3%)            | 7 (5.6%)      | 0.517   |
| Malignancy                        | 2 (2.0%)         | 0 (0.0%)            | 2 (1.6%)      | 0.652   |
| Chronic kidney disease            | 1 (1.0%)         | 2 (8.3%)            | 3 (2.4%)      | 0.094   |
| BCG Vaccination done              | 69 (68.3%)       | 14 (58.3%)          | 83 (66.4%)    | 0.352   |
| **Presenting Symptoms**           |                  |                     |               |         |
| Fever                             | 42 (41.6%)       | 24 (100.0%)         | 66 (52.8%)    | <0.001  |
| Sore throat                       | 41 (40.6%)       | 23 (95.8%)          | 64 (51.2%)    | <0.001  |
| Fatigue                           | 41 (40.6%)       | 19 (79.2%)          | 60 (48.0%)    | 0.001   |
| Cough                             | 41 (40.6%)       | 24 (100.0%)         | 65 (52.0%)    | <0.001  |
| Myalgia                           | 0 (0.0%)         | 1 (4.2%)            | 1 (0.8%)      | 0.192   |
| Dyspnoea                          | 15 (14.9%)       | 24 (100.0%)         | 39 (31.2%)    | <0.001  |
| Headache                          | 0 (0.0%)         | 2 (8.3%)            | 2 (1.6%)      | 0.036   |
| Diarrhoea                         | 0 (0.0%)         | 1 (4.2%)            | 1 (0.8%)      | 0.192   |
| Abdominal pain                    | 0 (0.0%)         | 1 (4.2%)            | 1 (0.8%)      | 0.192   |
| Temperature >37.5°C               | 15 (14.9%)       | 19 (79.2%)          | 34 (27.2%)    | <0.001  |
| SpO₂ <90%                         | 12 (11.9%)       | 23 (95.8%)          | 35 (28.0%)    | <0.001  |
| Pulse rate ≥100 beats per min     | 10 (9.9%)        | 23 (95.8%)          | 33 (26.4%)    | <0.001  |
| Respiratory Rate ≥30 breaths per min | 14 (13.9%)    | 23 (95.8%)          | 37 (29.6%)    | <0.001  |
| **Blood pressure**                |                  |                     |               |         |
| Normotensive                      | 93 (92.1%)       | 13 (54.2%)          | 106 (84.8%)   | <0.001  |
| Hypotensive                       | 1 (1.0%)         | 9 (37.5%)           | 10 (8.0%)     |         |
| Hypertensive                      | 7 (6.9%)         | 2 (8.3%)            | 9 (7.2%)      |         |
| Respiratory distress              | 14 (13.9%)       | 24 (100.0%)         | 38 (30.4%)    | <0.001  |
| Altered sensorium                 | 0 (0.0%)         | 3 (12.5%)           | 3 (2.4%)      | 0.006   |
| **SOF A Score, (Mean ± SD)**      | 0.50 ± 1.44      | 7.42 ± 3.36         | 1.83 ± 3.35   | <0.001  |
| **q-SOF A Score, (Mean ± SD)**    | 0.20 ± 0.40      | 1.67 ± 0.56         | 0.48 ± 0.72   | <0.001  |
| **Disease Severity Status**       |                  |                     |               |         |
| Asymptomatic                      | 59 (58.4%)       | 0 (0.0%)            | 59 (47.2%)    | <0.001  |
| Mild                              | 27 (26.7%)       | 0 (0.0%)            | 27 (21.6%)    |         |
| Moderate                          | 0 (0.0%)         | 0 (0.0%)            | 0 (0.0%)      |         |
| Severe                            | 14 (13.9%)       | 5 (20.8%)           | 19 (15.2%)    |         |
| Critical                          | 1 (1.0%)         | 19 (79.2%)          | 20 (16.0%)    |         |
tation was significantly more common in non-survivors. ROC curves were plotted for SOFA score and IL-6 level for predicting mortality due to COVID-19. ROC for lymphocyte count was also plotted for the prediction of survival in COVID-19 (figure 1A-C). The identified cut-offs were used in regression modeling.

Table 3 depicts that among demographic and clinical parameters, older age group (AOR=5.81, 95%CI: 1.55-21.80), ischemic heart disease, (AOR=4.32,
95%CI: 1.02-18.38) and smoking (AOR=3.62, 95%CI: 1.05-12.46) were found as significant predictors of mortality in our patients. Amongst laboratory parameters, elevated D-dimer level (AOR=4.24, 95%CI: 1.16-45.16), elevated LDH levels (AOR=9.08, 95%CI: 1.17-70.67) and low absolute lymphocyte counts (AOR=8.95, 95%CI: 1.59-50.27) were significant predictors of mortality.

Discussion

Our study is one of the earliest analytical studies in COVID-19 patients from India. We observed many similar and few contrasting findings when compared with international studies. Through univariate and multivariate analysis, we identified several demographic, clinical and laboratory parameters as predictors of mortality among the hospitalized patients with COVID-19.

Majority of our patients were males. The gender distribution was similar in survivor and non-survivor group. A preliminary Chinese study investigated the role of gender in COVID-19 and found that while males and females had the same prevalence, males had higher mortality as compared to women (13). In another study from Iran, male gender was significantly associated with the risk of death among COVID-19 patients (14). These findings are in contrast to the findings of our study.

It has been hypothesised that there may be some cross-protection provided by BCG vaccination against COVID-19 affected patients in developing countries (15). The BCG vaccine might reduce SARS-CoV-2 viraemia thus reducing the severity of COVID-19 leading to rapid recovery (16). In our study, there was no significant difference in the BCG status between the two groups of patients.

Advanced age is an independent risk factor for severe COVID-19 and mortality as in the case of SARS and Middle East respiratory syndrome-related coronavirus (17,18). In our study also, advanced age was found to be a significant predictor of mortality. Similar observations were made from the studies carried out in Wuhan and New York (7,19). Accelerated inflammation and immune senescence have been shown to be associated with worse clinical outcomes in elderly COVID-19 patients (20).

We found smokers to be at an increased risk of mortality as compared to non-smokers (AOR=3.62). Similar observations were made by Liu et al in a retrospective multicentric study from Wuhan (21). Apart
from immune suppression and predisposition to recurrent respiratory tract infections due to smoking, smokers have been found to have increased expression of angiotensin converting enzyme-2 (ACE2) receptor in the airways through which the SARS-CoV-2 virus gains entry into the cellular host tissue and increases susceptibility to active infection (22).

Symptoms like fever, cough, sore throat and dyspnoea were found to be significantly associated with mortality in our study. These findings are in line

| Table 3. Predictors of mortality in COVID-19 |
|---------------------------------------------|
| Variables                                   | OR (95% CI) | AOR (95% CI) |
| Demographics and clinical characteristics* |             |             |
| Age (years)                                 |             |             |
| >60                                         | 12.19 (4.11-36.13) | 5.81 (1.55-21.80) |
| ≤60                                         | 1           | 1           |
| Smoker (v/s non-smoker)                     | 6.77 (2.52-18.21) | 3.62 (1.05-12.46) |
| Comorbidities (present v/s absent)          |             |             |
| Hypertension                                | 6.77 (2.52-18.21) | 2.39 (0.65-8.83) |
| Diabetes Mellitus                           | 5.81 (1.91-17.71) | 1.47 (0.35-6.19) |
| Ischemic Heart Disease                      | 11.52 (3.39-39.06) | 4.32 (1.02-18.38) |
| Fatigue (present v/s not present)           | 5.56 (1.92-16.09) | 2.01 (0.53-7.56) |
| Laboratory Parameters*                     |             |             |
| SGPT (U/L)                                  |             |             |
| ≥40                                         | 5.00 (1.89-13.25) | 1.31 (0.26-6.59) |
| <40                                         | 1           | 1           |
| Serum Creatinine (mg/dl)                    |             |             |
| ≥1.2                                        | 5.53 (1.72-17.78) | 0.12 (0.01-2.12) |
| <1.2                                        | 1           | 1           |
| D-Dimer (ug/ml)                             |             |             |
| >1                                          | 16.04 (4.99-51.54) | 7.24 (1.16-45.16) |
| ≤1                                          | 1           | 1           |
| LDH (U/L)                                   |             |             |
| ≥250                                        | 35.29 (7.73-161.09) | 9.08 (1.17-70.67) |
| <250                                        | 1           | 1           |
| Creatinine Kinase (U/L)                     |             |             |
| ≥185                                        | 7.42 (2.72-20.20) | 4.02 (0.32-49.92) |
| <185                                        | 1           | 1           |
| IL-6 (pg/ml)                                |             |             |
| >37.9                                       | 23.74 (6.50-86.76) | 3.04 (0.56-16.64) |
| ≤37.9                                       | 1           | 1           |
| PT (secs)                                   |             |             |
| ≥16                                         | 5.81 (1.91-17.71) | 2.54 (0.32-20.04) |
| <16                                         | 1           | 1           |
| Lymphocytes 10^9 per L                      |             |             |
| <1.46                                       | 15.20 (4.74-48.72) | 8.95 (1.59-50.27) |
| ≥1.46                                       | 1           | 1           |

R²= 0.483, Hosmer-Lemeshow; R²= 0.685, Hosmer-Lemeshow; p=0.640
with the previous studies (7,23). This finding not only carries clinical significance but is also important from public health perspective as patients having one or more of these symptoms during the ongoing pandemic are the ones who need to visit a healthcare facility as early as possible to rule out the possibility of severe COVID-19.

Among the comorbidities mentioned in table 1, only ischemic heart disease was found to be independently associated with an increased risk of mortality. Similar findings have been observed during the COVID-19 outbreak in Italy (24). Presence of ischemic heart disease carries poor prognosis in COVID-19 (25).

We observed significantly elevated serum LDH levels among the non-survivors. Significant difference in serum LDH levels has been observed between non-severe and severe COVID-19 patients along with the demonstration of rise or fall in the levels that corresponded to radiologic progression or improvement (26). COVID-19 mRNA clearance ratio was shown to be significantly correlated with the decline of LDH levels suggesting that such reduction in LDH levels may be able to predict a favourable response in COVID-19 patients (27).

D-dimer has been found to be an important prognostic factor for mortality in COVID-19 patients (28). It was significantly elevated in non-survivors as compared to survivors in our study. Raised D-dimer levels is associated with increased mortality in patients without any evidence of pulmonary thromboembolism (PE) or deep vein thrombosis (29).

We observed a lower lymphocyte count at the time of admission in the non-survivor group. In one study, lower absolute lymphocyte count (ALC) was observed in ICU patients as compared to non-ICU patients, with an odds ratio of 3.40 (95% CI: 1.06-10.96) (30). Our study found AUC of 0.86 (0.76-0.95), cut-off of less than and equal to 1.46 x 10^9 per litre with sensitivity and specificity of 75.2% and 83.3% respectively. Pooled analysis in a study that included thirteen case series with 2282 patients of COVID-19 found lower lymphocyte count to be significantly associated with severe disease (31).

For SOFA score, the ROC curve showed AUC of 0.98 (95% CI 0.96-1), the cut-off value was ≥ 3.5 (sensitivity- 91.7% and specificity- 87.5%). An optimal cut-off value ≥3 could predict in-hospital mortality among critically ill COVID-19 cases (32). A SOFA score ≥ 2 was associated with poorer outcomes among hospitalized COVID-19 patients (33).

The ROC curve for IL-6 levels showed AUC of 0.87 (95% CI 0.80-0.94), the cut-off value was ≥ 37.9 pg/ml (sensitivity- 96% and specificity- 78%). IL-6 > 25 pg/ml was associated with severe disease and in-hospital mortality (34). A meta-analysis concluded that IL-6 levels are significantly elevated in severe COVID-19 disease as compared to mild to moderate disease (35).

**Strengths and Limitations**

This study has many strengths. First, ours is the first study from India that has identified predictors of clinical outcomes of COVID-19 in a comprehensive manner. Since India shares similar demographic and patient profile as that of SEAR countries, findings of our study are not only relevant for India but also for COVID-19 patients in these countries. Second, due to the prospective nature of this study, identification of patients and collection of data was done while patients were still in hospital, due to which no data was lost for any of the enrolled patient. This study has some limitations. First, duration of symptoms before hospitalization was not considered during analysis which may affect the clinical outcome. Second, chest radiography was done in limited number of patients. This is because during the initial period of COVID-19 outbreak, it was advised only in severe and critically ill patients.

**Conclusion**

Older age, smoking history, ischemic heart disease, elevated D-dimer, raised LDH level and low absolute lymphocyte counts at baseline are the risk factors for COVID-19 related mortality. A higher SOFA score at hospital admission is a poor prognosticator in COVID-19 patients.

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Author Contributions: N.K.C. conceived the study and its design, had full access to the data, and take responsibility for the integrity of the data and accuracy of the analysis. N.K.C., B.J.S., M.K.G., P.B.J., and D.M. organised and entered data. N.K.C., B.J.S., P.B.J. and M.K.G. contributed to data analyses. N.K.C., B.J.S., M.G., P.B., V.L.N., P.A.E., N.D., R.N.J., P.S., G.K.B., D.K., M.B., P.G., B.S., S.M., D.M., R.G., A.P. and M.M. contributed to data interpretation. N.K.C., B.J.S., M.K.G., P.B., N.D., G.K.B. and D.K. drafted the manuscript. All authors critically revised the drafted manuscript and approved the final version of the submitted manuscript.

References

1. https://covid19.who.int/ accessed on 13 August 2020.
2. Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet. 2020; 395:507-513.
3. Wu Z, McGoogan JM. Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72 314 Cases From the Chinese Center for Disease Control and Prevention (published online ahead of print, 2020 Feb 24). JAMA. 2020;10.1001/jama.2020.2648. doi:10.1001/ jama.2020.2648.
4. Yang X, Yu Y, Xu J, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. Lancet Respir Med. 2020; 8:475-1.
5. Epidemiology Working Group for NCIP Epidemic Response, Chinese Center for Disease Control and Prevention. (The epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19) in China). Zhonghua Liu Xing Bing Xue Za Zhi. 2020; 41:145-1.
6. CDC COVID-19 Response Team. Preliminary Estimates of the Prevalence of Selected Underlying Health Conditions Among Patients with Coronavirus Disease 2019 - United States, February 12–March 28, 2020. MMWR Morb Mortal Wkly Rep. 2020; 69:382-6.
7. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet. 2020; 395:1054-2.
8. Liu K, Chen Y, Lin R, Han K. Clinical features of COV-ID-19 in elderly patients: A comparison with young and middle-aged patients. J Infect. 2020; 80:14-8.
9. https://www.who.int/publications/i/item/clinical-management-of-covid-19?WHO/2019-nCoV/clinical/2020.5 accessed on 22 August 2020.
10. Levy MM, Evans LE, Rhodes A. The Surviving Sepsis Campaign Bundle: 2018 update. Intensive Care Med. 2018; 44:925-8.
11. Borghesi A, Maroldi R. COVID-19 outbreak in Italy: experimental chest X-ray scoring system for quantifying and monitoring disease progression. Radiol Med. 2020; 125:509-3.
12. Bhatia AS, Jana M, Naranje P, Manchanda S. Role of Chest Radiographs during COVID-19 Pandemic. Annals of the National Academy of Medical Sciences (India). 2020 Jul 4. doi:10.1055/s-0040-1714158.
13. Jin JM, Bai P, He W, et al. Gender Differences in Patients With COVID-19: Focus on Severity and Mortality. Front Public Health. 2020; 8:152.
14. Nikpouraghdam M, Jalali Farahani A, Alishiri G, et al. Epidemiological characteristics of coronavirus disease 2019 (COVID-19) patients in IRAN: A single center study. J Clin Virol. 2020; 127:104378.
15. Escobar LE, Molina-Cruz A, Barillas-Mury C. BCG vaccine protection from severe coronavirus disease 2019 (COV-ID-19). Proc Natl Acad Sci U S A. 2020; 117:17720-6.
16. Curtis N, Sparrow A, Ghebreyesus TA, Netea MG. Considering BCG vaccination to reduce the impact of COVID-19. Lancet. 2020; 395:1545-6.
17. Hong KH, Choi JP, Hong SH, et al. Predictors of mortality in Middle East respiratory syndrome (MERS). Thorax. 2018; 73:286-9.
18. Choi KW, Chau TN, Tsang O, et al; Princess Margaret Hospital SARS Study Group. Outcomes and prognostic factors in 267 patients with severe acute respiratory syndrome in Hong Kong. Ann Intern Med. 2003; 139:715-3.
19. Cummings MJ, Baldwin MR, Abrams D, et al. Epidemiology, clinical course, and outcomes of critically ill adults with COVID-19 in New York City: a prospective cohort study. Lancet. 2020; 395:1763-70.
20. Bonafè M, Prattichizzo F, Giuliani A, Storci G, Sabbatinielli J, Olivieri F. Inflamm-aging: Why older men are the most susceptible to SARS-CoV-2 complicated outcomes. Cytokine Growth Factor Rev. 2020; 53:33-7.
21. Liu W, Tao ZW, Wang L, et al. Analysis of factors associated with disease outcomes in hospitalized patients with 2019 novel coronavirus disease. Chin Med J (Engl). 2020; 133:1032-8.
22. Leung JM, Yang CX, Tam A, et al. ACE-2 expression in the small airway epithelia of smokers and COPD patients: implications for COVID-19. Eur Respir J. 2020; 55:2000688.
23. Giacomelli A, Ridolfo AL, Milazzo L, et al. 30-day mortality in patients hospitalized with COVID-19 during the first wave of the Italian epidemic: A prospective cohort study. Pharmacol Res. 2020; 158:10493.
tors of clinical outcomes of COVID-19 outbreak in Milan, Italy. Clin Immunol. 2020; 217:108509.
25. Inciardi RM, Adamo M, Lupi L, et al. Characteristics and outcomes of patients hospitalized for COVID-19 and cardiac disease in Northern Italy. Eur Heart J. 2020; 41:1821-9.
26. Wu MY, Yao L, Wang Y, et al. Clinical evaluation of potential usefulness of serum lactate dehydrogenase (LDH) in 2019 novel coronavirus (COVID-19) pneumonia. Respir Res. 2020; 21:171.
27. Yuan J, Zou R, Zeng L, et al. The correlation between viral clearance and biochemical outcomes of 94 COVID-19 infected discharged patients. Inflamm Res. 2020; 69:599-6.
28. Zhang L, Yan X, Fan Q, et al. D-dimer levels on admission to predict in-hospital mortality in patients with Covid-19. J Thromb Haemost. 2020; 18:1324-9.
29. Yao Y, Cao J, Wang Q, et al. D-dimer as a biomarker for disease severity and mortality in COVID-19 patients: a case control study. J Intensive Care. 2020; 8:49.
30. Wagner J, DuPont A, Larson S, Cash B, Farooq A. Absolute lymphocyte count is a prognostic marker in Covid-19: A retrospective cohort review (published online ahead of print, 2020 Jul 10). Int J Lab Hematol. 2020;10.1111/ijlh.13288. doi:10.1111/ijlh.13288.
31. Zhao Q, Meng M, Kumar R, et al. Lymphopenia is associated with severe coronavirus disease 2019 (COVID-19) infections: A systemic review and meta-analysis. Int J Infect Dis. 2020; 96:131-5.
32. Liu S, Yao N, Qiu Y, He C. Predictive performance of SOFA and qSOFA for in-hospital mortality in severe novel coronavirus disease (published online ahead of print, 2020 Jul 12). Am J Emerg Med. 2020; doi: 10.1016/j.ajem.2020.07.019.
33. Vaquero LM, Barrado MES, Escobar D, et al. C-Reactive protein and SOFA score as early predictors of critical care requirement in patients with COVID-19 pneumonia in Spain. medRxiv 2020.05.22.20110429.
34. Grifoni E, Valoriani A, Cei F, et al. Interleukin-6 as prognosticator in patients with COVID-19. J Infect. 2020; 81:452-82.
35. Ulhaq ZS, Soraya GV. Interleukin-6 as a potential biomarker of COVID-19 progression. Med Mal Infect. 2020; 50:382-3.