Original Research Article

Initial investigations and clinical outcome in COVID-19 patients

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ABSTRACT

Background: Coronavirus disease 2019 (COVID-19) has significant impact on the health infrastructure all over the world including India. We wanted to see whether the routine initial investigations done in COVID 19 patients reflect the prognosis and outcome of the patient.
Methods: It is a retrospective study involving the confirmed covid 19 patients admitted between April 2021 to May 2021. The initial investigations done at the time of admission were studied in relation to outcome of the patient in the form of survival or death of the patient.
Results: A total of 364 patients were studied. 295 (81.05%) patients survived and 69 (18.96%) patients died. Highest mortality was observed in 60% of patients with hemoglobin below 7.0 mg/dl, 40.00% of patients with platelet count below 50000/cml, 28.80% with neutrophil lymphocyte ratio more than 5.5, 32.81% with CRP more than 100 mg/L, 100% with D dimer more than 5000 ng/ml, 33.33% with Ferritin more than 1500 ng/ml, 29.54% with IL-6 more than 100 pg/ml, 23.14% with Random blood sugar more than 200 mg/dl, 37.50% with creatinine more than 2.0 mg/dl, 75% with Bilirubin more than 2.0 mg/dl, 42.85% with SGOT more than 201 mg/dl, 22.22% with SGPT more than 201 mg/dl, 38.46% with serum Procalcitonin more than 2.0 mg/dl. CT Chest severity score of 21 to 30 and 31 to 40 lead to mortality of 19.51% and 40.00% respectively.
Conclusions: The physician who is taking care of COVID-19 patients must get extra cautious regarding prognosis if he gets above initial parameters deranged in isolation or combination.

Keywords: Initial investigations, Clinical outcome, COVID-19

INTRODUCTION

The novel corona virus was identified in December 2019 as a case of pneumonia in Wuhan China which rapidly spread over China followed by all over the world as a pandemic. The corona virus has infected more than 250 million peoples worldwide including more than 5 million deaths.[1] India has witnessed more than 34 million cases which includes more than 4lakhs of deaths.[1] We all have experienced the impact of such huge number of cases over our health infrastructure. In this study we have tried to see whether we could predict the clinical outcome of the patient in the form of survival or death on the basis of routine initial investigations done at the time of admission of the patient into the hospital.

METHODS

This is a retrospective study done at Apollo Hospitals Bilaspur, Chhattisgarh India. The patients who were admitted between April 2021 to May 2021 with confirmed diagnosis of COVID-19 infection with either RTPCR or Rapid antigen positive for COVID-19 were included in the study. The patients who were excluded from the study were those who were suspected cases of COVID-19 but had RTPCR or Rapid antigen negative. A total of 364

patients fulfilled the inclusion criteria and were included in the study. Data were collected from each file with the help of medical records department of Apollo hospitals bilaspur. Data were saved in MS Excel Sheet. The data included the routine initial investigations done at the time of admission of confirmed COVID-19 infection. This included demographic data like Age, sex, severity of covid infection, comorbidities and investigations included hemoglobin, TLC, NLR (neutrophil lymphocyte ratio), platelets, CRP, D dimer, ferritin, IL6, bilirubin, SGOT, SGPT, creatinine, blood sugar, procalcitonin and CT chest severity score. Each of the above data were analysed individually and clinical outcome was assessed in the form of either survival or death of the patient. Ethical committee approval was waived off in this study as this was a retrospective and observational study not requiring any direct patient intervention.

RESULTS

A total of 364 confirmed cases of COVID-19 were admitted during the period of study out of which 242 were males (66.48%) and 122 were females (33.52%). The number of patients who survived and discharged were 295 (81.04%) and the number of patients who died were 69 (18.96%).

Out of the total of 364 patients admitted 6 patients (1.64%) were of below 18 years of age and 5 (83.34%) of them survived and 1 died (16.66%), 102 patients (28.02%) were between 18 to 40 years of age and out of which 90 patients (88.23%) survived and 12 patients (11.77%) died, 162 patients (44.40%) were between 40 to 60 years of age and out of which 133 (82.10%) survived and 29 (17.90%) died, and 94 patients (25.82%) were more than 60 years of age and out of which 67 (71.27%) survived and 27 (28.73%) died.

The number of patients who were admitted with mild category of disease were 58 (15.94%), moderate category of disease were 192 (52.74%) and severe category of covid 19 were 114 (31.31%). None of the patients who were admitted with mild and moderate category of disease died while 69 patients (60.52%) who were admitted with severe category of disease died during the course of treatment. The number of males who died were 47 (68.11%) and the number of females who died were 22 (31.89%).

The number of patients who had only DM as a comorbidity were 45 (12.36%) out of which 7 (15.55%) died and 38 (84.44%) survived. The number of patients who had only Hypertension as a comorbidity were 38 (10.43%) and out of which 9 (23.68%) died and 29 (76.31%) survived. The number of patients who had both DM and HT as a comorbidity were 46 (12.63%) and out of which 11 (23.91%) died and 35 (76.08%) survived.

The hemoglobin of 348 patients were documented at the time of admission and out of which 5 (1.43%) patients had hemoglobin less than 7 mg/dl, 3 (60.0%) patients died and

2 (40.0%) survived. 21 (6.03%) patients had hemoglobin between 7 to 10 mg/dl out of which 7 (33.33%) died and 14 (66.67%) survived. 322 (92.52%) patients had hemoglobin more than 10 mg/dl and out of which 59 (18.32%) died and 263 (81.68%) survived.

The platelet count of 346 patients were documented at the time of admission and out of which 5 (1.44%) patients had platelet counts below 50000/cml and 2 (40.00%) died and 3 (60.00%) survived. None of the patients studied had platelet count between 50000 and 1.0 lacs/cml. 95 (27.45%) patients had platelet count between 1 lac and 1.5 lacs/cml and out of which 16 (16.84%) died and 79 (83.16%) survived. 233 (67.34%) patients had platelet count between 1.5 lacs and 4.5 lacs/cml and out of which 48 (20.60%) died and 185 (79.40%) survived. 13 (3.75%) patients had platelet count more than 4.5 lacs/cml and out of which 3 (23.07%) died and 10 (76.93%) survived.

Total leucocyte count (TLC) was documented in 346 patients and out of which 40 (11.56%) patients had TLC of less than 4000/cml and 35 (87.50%) survived and 5 (12.50%) died. 230 (66.47%) patients had TLC count between 4000 to 11000/cml and out of which 188 (81.73%) survived and 42 (18.27%) died. 76 (21.96%) patients had TLC more than 11000/cml and out of which 54 (71.05%) survived and 22 (28.95%) died.

Neutrophil lymphocyte ratio (NLR) was calculated in 346 patients at the time of admission and out of which 80 (23.12%) patients had NLR below 3.5 and 9 (11.25%) died and 71 (88.75%) survived. 82 (23.69%) patients had NLR between 3.5 to 5.5 and out of which 7 (8.53%) died and 75 (91.47%) survived. 184 (53.17%) patients had NLR more than 5.5 and out of which 53 (28.80%) died and 131 (71.20%) survived.

CRP was documented in 324 patients and out of which 41 (12.65%) patients had CRP below 6.0 mg/L and 2 (4.87%) died and 39 (95.13%) survived. 131 (40.43%) patients had CRP between 6.0 and 50mg/L and out of which 22 (16.79%) died and 109 (83.21%) survived. 46 (14.19%) patients had CRP between 50 and 75 mg/L and out of which 10 (21.73%) died and 36 (78.27%) survived. 42 (12.96%) patients had CRP between 75 and 100 mg/L and out of which 9 (21.42%) died and 33 (78.58%) survived. 64 (19.75%) patients had CRP more than 100 mg/L and out of which 21 (32.81%) died and 43 (67.19%) survived.

D dimer was documented in 319 patients and out of which 133 (41.69%) patients had D dimer below 500 ng/ml and 12 (9.02%) died and 121 (90.98%) survived. 125 (39.18%) patients had D dimer between 500 and 1000 ng/ml and out of which 31 (24.80%) died and 94 (75.20%) survived. 36 (11.28%) patients had D dimer between 1000 to 2000 and out of which 10 (27.77%) died and 26 (72.23%) survived. 23 (7.21%) patients had D dimer between 2000 to 5000 and out of which 11 (47.82%) died and 12 (52.18%) survived. 2 (0.62%) patients had D dimer more than 5000 ng/ml and both died (100%).

Serum Ferritin levels were documented in 200 patients and out of which 139 (69.50%) patients had Ferritin levels below 500ng/ml and 18 (12.94%) died and 121 (87.06%) survived. 33 (16.50%) patients Ferritin level between 500 to 1000ng/ml and out of which 10 (30.30%) died and 23 (69.70%) survived. 25 (12.50%) patients had Ferritin level between 1000 to 1500 ng/ml and out of which 9 (36%) died and 16 (64%) survived. 3 (1.50%) patients had ferritin level more than 1500ng/ml and out of which 1 (33.33%) died and 2 (66.67%) survived.

Interleukin 6 (IL-6) was documented in 191 patients and out of which 25 (13.08%) had IL-6 below 7 pg/ml and 25 (100%) survived and no one died. 56 (29.31%) patients had IL-6 between 7 to 30 pg/ml and out of which 11 (19.64%) died and 45 (80.36%) survived. 43 (22.51%) patients had IL-6 levels between 30 to 60 pg/ml and out of which 10 (23.25%) died and 33 (76.75%) survived. 23 (12.04%) patients had IL-6 levels between 60 to 100 pg/ml and out of which 4 (17.39%) died and 19 (82.61%) survived. 44 (23.03%) patients had IL-6 levels more than 100 pg/ml and out of which 13 (29.54%) died and 31 (70.46%) survived.

Random Blood Sugar (RBS) was documented in 329 patients and out of which 45 (13.67%) had RBS below 100 mg/dl and 8 (17.77%) patients died and 37 (82.23%) survived. 176 (53.49%) patients had RBS between 100 to 200 mg/dl and out of which 35 (19.88%) died and 141 (80.12%) survived. 108 (32.86%) patients had RBS more than 200mg/dl and out of which 25 (23.14%) died and 83 (76.86%) survived.

Serum creatinine was documented in 338 patients and out of which 125 (36.98%) patients had creatinine below 1 mg/dl and 21 (16.80%) patients died and 104 (83.20%) survived. 179 (52.95%) patients had creatinine between 1.1 to 1.5 mg/dl and out of which 34 (18.99%) patients died and 145 (81.01%) survived. 10 (2.95%) patients had creatinine between 1.6 to 2.0 mg/dl and out of which 4 (40.00%) died and 6 (60.00%) survived. 24 (7.10%) patients had creatinine more than 2.0mg/dl and out of which 9 (37.50%) died and 15 (62.50%) survived.

Serum Bilirubin was documented in 324 patients and out of which 320 (98.76%) patients had Bilirubin below 2.0 mg/dl and 58 (18.12%) patients died and 262 (81.88%) patients survived. 4 (1.23%) patients had Bilirubin between 2.0 to 5.0 mg/dl and out of which 3 (75.00%) patients died and 1 (25.00%) patient survived. None of the patients had Bilirubin more than 5.0 mg/dl at the time of admission.

SGOT was documented in 328 patients and out of which 123 (37.50%) patients had SGOT below 50 mg/dl and 11 (8.94%) patients died and 112 (91.06%) patients survived. 156 (47.56%) patients had SGOT between 51 to 100mg/dl and out of which 31 (19.87%) patients died and 125 (80.13%) patients survived. 42 (12.80%) patients had SGOT between 101 to 200 mg/dl and out of which 17

(40.47%) patients died and 25 (59.53%) patients survived. 7 (2.13%) patients had SGOT more than 201 mg/dl and out of which 3 (42.85%) patients died and 4 (57.15%) patients survived.

SGPT was documented in 329 patients and out of which 181 (55.01%) patients had SGPT below 50 mg/dl and 27 (14.91%) patients died and 154 (85.09%) patients survived. 116 (35.25%) patients had SGPT between 51 to 100 mg/dl and out of which 24 (20.68%) patients died and 92 (79.32%) patients survived. 23 (6.99%) patients had SGPT between 101 to 200 mg/dl and out of which 9 (39.13%) patients died and 14 (60.87%) patients survived. 9 (2.73%) patients had SGPT more than 201mg/dl and out of which 2 (22.22%) died and 7 (77.78%) patients survived.

Serum Procalcitonin (PCT) was documented in 185 patients and out of which 110 (59.45%) patients had PCT below 0.15 ng/ml and 17 (15.45%) patients died and 93 (84.55%) survived. 62 (33.51%) patients had PCT between 0.15 to 2.0 ng/ml and out of which 18 (29.03%) died and 44 (70.97%) survived. 13 (7.02%) patients had PCT more than 2.0 ng/ml and out of which 5 (38.46%) patients died and 8 (61.54%) patients survived.

CT Scan Severity Score (CTSS) was documented in 260 patients and out of which 31 (11.92%) patients had CTSS below 10 and 2 (6.45%) patients died and 29 (93.55%) survived. 92 (35.38%) patients had CTSS between 11 to 20 and out of which 5 (5.43%) patients died and 87 (94.57%) patients survived. 82 (31.53%) patients had CTSS between 21 to 30 and out of which 16 (19.51%) patients died and 66 (80.49%) patients survived. 55 (21.15%) patients had CTSS between 31 to 40 and out of which 22 (40.00%) died and 33 (60.00%) patients survived.

DISCUSSION

A covid related deaths was audited in Mumbai medical college which included the COVID deaths that occurred between April 2020 to January 2021. They had 5762 covid admissions and out of which 763 deaths occurred. The mortality rate was 13.2%. The Mean age for death was 60-70 years and the Median age was 64.8 years.[2] We had 364 patients during the study period and 69 patients died. The mortality rate was 18.96%. This high mortality could be due to the fact that our hospital is a tertiary care hospital and receiving most of the very sick patients in the region. Our study showed that the deaths included patients of all age group however maximum number (28.73%) of deaths occurred in patients of more than 60 years of age. 68.11% of patients who died were males and 31.89% were females.

In our study we find that the maximum number of patients were of moderate category of covid (52.74%) and it was followed by severe category (31.31%) and only 15.94% of the patients admitted were of mild category. Being a tertiary care hospital, we admitted mostly moderate and

severe category of covid patients hence we had least number of mild cases.

The Hemoglobin is a basic investigation and our study has showed that a low hemoglobin at the time of admission spells a poor prognosis as 60% of patients having Hb below 7 mg/dl died, 33.33% of patients with Hb between 7 to 10 mg/dl died and only 18.32 % of patients with Hb more than 10mg/dl died. This could be because covid basically affects oxygenation and a low Hb further worsens the hypoxia. Masood et al in Iran studied the association between anemia at admission and covid outcomes in 1274 hospitalised patients and found that anemia was independently associated with mortality, ventilator requirement and the risk of ICU admission.[3]

TLC is again a basic investigation and our study has showed 66.47 % of patients had TLC count between 4000 to 11000/cml and 18.27% patient died, however death rate was increased to 28.95% in those patients having TLC more than 11000/cml at the time of admission. Death occurred in only 12.50% of patients having TLC of below 4000/cml at the time of admission. Bin et al studied 163 hospitalized patients and found that there was a significant decline of the cumulative survival rate(p<0.001) in those with WBC count >6.16×10^9/L.[4]

NLR was also studied and the patients having NLR of more than 5.5 had maximum number of deaths (28.80%). Imran et al studied 63 patients in Pakistan in July 2020 and found that NLR was an statistically significant risk factor for severe COVID 19 pneumonia with sensitivity of 0.83 and specificity of 0.75.[4] A Chinese study done in March 2020 also showed that increased NLR was an independent risk factor for severe COVID 19.[5]

Our study has showed that the level of CRP at the time of admission correlates positively with the clinical outcome. We found that only 4.87% patients died when CRP was below 6.0 mg/L and it progressively rise to 16.79% to 21.73% to 21.42% to 32.81% as CRP rises from 6 to 50 mg/L and 50 to 75 mg/L and 75 to 100 mg/L and more than 100 mg/L respectively. Cheng et al in October 2020 also showed that higher levels of NLR and CRP at admission were associated with poor prognosis of individuals with moderate COVID-19 and were good predictors of progression to critical condition and death.[7] Another study done by Tan et al in Jul 2020 also showed that AUC of CRP on the first visit for predicting severe COVID-19 was significant with sensitivity and specificity of 83% and 91% respectively.[8]

COVID-19 is a primarily respiratory illness that can cause thrombotic disorders also, hence D dimer is an important marker for prognosis of the disease. Our study has showed that the d dimer below 500 ng/ml at the time of admission had mortality of 9.02% only however as we get higher D dimer at the time of admission spelled higher mortality i.e. a d dimer of 500 to 1000 ng/ml and 1000 to 2000 ng/ml and 2000 to 5000 ng/ml showed mortality of 24.80%,

27.77%, 47.82% respectively and a D dimer of more than 5000ng/ml showed mortality of 100%. A study done by Poudel et al in 2021 showed that D dimer on admission is an accurate biomarker for predicting mortality in patients of COVID 19 and found that1.5 mcg/ml as an optimal cut off for predicting mortality in COVID 19 patients.[9] Our study has also showed almost 50 % mortality with D dimer above 2000 ng/ml and 100% mortality with D dimer more than 5000 ng/ml. A systematic review and meta analysis done in Italy by Panagiotis et al also showed that serum D dimer concentrations in patients with severe COVID 19 were significantly higher when compared to non severe forms of COVID 19 disease.[10]

Serum ferritin is an intracellular form of iron storage and and an important molecule in the immune system leading the cellular defense against inflammation. Our study has showed a high level of ferritin at the time of admission lead to increased mortality. A ferritin level below 500ng/ml showed mortality of only 12.94% and a ferritin of more than 1500 ng/ml led to mortality of 33.33%. A study in Israil by Shani et al in Aug 2020 demonstrated that severe covid patients had significantly higher levels of ferritin (2817.6 ng/ml) than non-severe patients (708.6 ng/ml).[11] Another study done by Deng et al in April 2021 also showed that the median of ferritin concentration was about three times higher in death group than survival group (1722.25 mcg/L versus 501.90 mcg/L, p<0.01).[12]

Interleukin 6 (IL6) is an inflammatory interleukin mainly produced by macrophages and T lymphocytes in response to pathogens and its exacerbated production contributes to cytokine storm. Our study has showed that patients who had IL6 levels below 7pg/ml showed no mortality and mortality rised progressively with higher IL6 levels at admission and patients with IL6 more than 100pg/ml showed mortality of 29.54% of patients. A portugese study done by Cruz et al in 2021 showed that IL6 level was the most significant predictor of the non-survivor group when compared to age and CRP.[13] Another study a systematic review and meta-analysis done by Xiaohui et al showed IL6 is an adequate predictor of severe disease in COVID 19 infection.[14]

We have also studied the blood sugar levels at the time of admission in covid patients and clinical outcome. We had found that patients with RBS below 100 mg/dl has shown mortality of 17.77% and it increased to 19.88% in patients with RBS between 100 to 200 mg/dl. The mortality further increased to 23.14% in patients with RBS more than 200 mg/dl at the time of admission. A systematic review and meta-analysis done by Gilbert et al in January 2021 showed independent association between admission FBG and poor covid prognosis. They also showed a nonlinear relationship between admission FBG and severity where each 1 mmol/L increase augmented the risk of severity by 33%.15 Another study done by Yuli et al in 941 hospitalized patients in Wuhan China showed that a FBG >7 mmol/L was an independent risk factor for the

mortality of COVID-19 regardless of the presence or not of a history of diabetes.[16]

Our study has showed that a creatinine level of below 1 mg/dl and between 1.1 to 1.5 mg/dl has shown almost similar mortality rate of 16.80% and 18.99% respectively and a creatinine level between 1,6 to 2.0 mg/dl and more than 2,0 mg/dl has shown two times increase in mortality i.e. 40.00% and 37.50%. This spells a higher mortality in patients with acute kidney injury at the time of admission. A hospital based retrospective cohort study done by Hui-Xian et al found that serum creatinine and cystatin C were increased and eGFR was decreased in severe COVID patients as compared with those in mild covid patients.[17]

Raised serum bilirubin has also been showed to have increased mortality. A retrospective cohort study was done by Zeming et al in Wuhan China studied 1788 hospitalized patients and found that 5.8% of patients in the elevated serum bilirubin group died compared to 0.6% in the non-elevated bilirubin group.18 Our study has shown a mortality of 18.12% among the patients with Bilirubin below 2.0 mg/dl and 75.00% among the patients with bilirubin more than 2.0 mg/dl at the time of admission which also spells significant mortality in bilirubin elevated group.

Our study has showed that like bilirubin raised SGOT and SGPT at the time of admission are also associated with increased mortality. Only 8.94% and 14.91% of patients died respectively when SGOT and SGPT were below 50 mg/d, however it progressively raised to 42.85% and 22.22% when SGOT and SGPT respectively was more than 201 mg/dl at the time of admission. A retrospective study of 533 COVID patients admitted in ICU was done by Fikret et al from Turkey concluded that liver dysfunction was associated with significantly higher 7 day and 28-day mortality rates.[19]

Serum procalcitonin is an important biomarker for sepsis. 59.45% of the studied population had PCT below 0.15 ng/ml at the time of admission and only 15.45% of patients died in this group however 7.02% patients had PCT more than 2.0 ng/ml and 38.46% of them died which means that more than two-time mortality increased if patient has raised PCT. A systematic review of published literature on the prognostic role of serum PCT was done by Sibtain et al and found that 85% studies reported statistically significant association between PCT and severity.[20] A systematic review and meta-analysis done by Farshad Heidari et al also indicated higher PCT levels in patients with severe versus less severe COVID-19 disease.[21]

CT scan of chest and severity scoring was also commonly performed during the covid infections. It is a scoring system used to assess the lung changes and involvement. Our study showed that a CT severity score of below 20/40 at the time of admission showed a mortality of 5.43% to 6.45% only however a CT severity score of above 20 leads to mortality of 19.51% and 40.00% respectively for every 10 rise in severity score at the time of admission. A study done by Ran et al found that CT-SS were higher in severe COVID-19 when compared with mild cases (p<0.5) and also found that CT-SS threshold for identifying severe COVID-19 was 19.5 with 83.3% sensitivity and 94% specificity.[22]

Limitations of the study

The major limitation of our study is its small sample size. A larger, multicentric study is needed to affirm our findings.

CONCLUSION

A COVID patient may not look very sick at the time of admission, however his initial routine investigations may spell the prognosis. A low hemoglobin, raised TLC and NLR, a low platelet count, raised CRP, raised D dimer and serum ferritin, raised IL6, raised RBS, raised serum creatinine, deranged LFT along with raised serum PCT and elevated CT chest Scores individually or in combination may indicate the prognosis. The treating physician need to be extra cautious with the above prognostic factors.

ACKNOWLEDGEMENTS

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