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Original Research Article

Clinical profile and outcome of elderly COVID-19 patients

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ABSTRACT

Background: Emerging and reemerging infectious disease have plagued mankind and have been potential killer since historic times. The current pandemic of COVID-19 is the latest crisis that has challenged leadership and health infrastructure globally. Since, elderly are more susceptible, understanding risk factor and clinical feature in them is critically important to improve the outcome and efficacy of treatment.
Methods: The prospective study included 1187 patients, aged ≥65 years diagnosed with COVID-19. Necessary record like demographic data, comorbidities and clinical features were collected. Relevant laboratory investigation done. Patients were grouped as survival and death. Different parameters were compared using t-test for continuous variables and Chi-square test for categorical data. Receiver operating curve (ROC) drawn using SPSS software.
Results: Out of 1187 elderly people,316 (26%) have succumbed to death. Mortality was more in Male (68.7%). Fever (42%), cough (33.2%), dyspnea (26.9%) were the major symptom. Among patient who succumbed to death 45.9% people had diabetes with hypertension, 15.2% had only diabetes, 17.1% had only hypertension, 12.3% had chronic kidney disease and 15.56% had IHD. ROC curve drawn for TLC (AUC=0.72), NLR ratio (AUC=0.844), LDH (AUC=0.842), D-dimer (AUC=0.851), CRP (AUC=0.82), ferritin (AUC=0.823) which were statistically significant as predictor of disease outcome. D-dimer at cut-off 1 mcg/ml has specificity 89% and sensitivity 76% which is highest among the parameter, followed by NLR ratio at 6.9 has specificity (82%), sensitivity (73%).
Conclusions: D-dimer of 1 mcg/ml, NLR ratio of 6.9 may assist in triaging patient requiring ICU care and deciding intervention. Also, elderly with multiple comorbidity should be treated aggressively, so that chance of survival can be increased.

Keywords: COVID-19, Neutrophil lymphocyte ratio, D-dimer

INTRODUCTION

Corona viruses are non-segmented positive-stranded RNA viruses with a roughly 30 kb genome surrounded by a protein envelope. Most coronaviruses cause diseases in their particular host species.[1] Those that can infect humans through cross-species transmission have become an important threat to public health. Two serious coronavirus disease outbreaks have happened in the past two decades: severe acute respiratory syndrome (SARS) in 2003 and Middle East respiratory syndrome (MERS) in 2012.[2,3] Since December, 2019, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has been recognized as the causal factor in a series of severe cases of pneumonia originating in Wuhan in Hubei province, China.[4]

This disease has been named coronavirus disease 2019 (COVID-19) by WHO. SARS-CoV-2 has been shown to cause disease via a mechanism analogous to the SARS coronavirus, with potential damage to vital organs such as lung, heart, liver, and kidney, and infection poses a considerable risk to patients by the high prevalence of pneumonia.[5] All age groups are generally susceptible to coronavirus, but elderly people with underlying diseases

are more susceptible. The underlying diseases are diabetes, hypertension, cardiovascular disease, chronic kidney disease and cerebro-vascular disease.[6] The elderly are more susceptible to severe illness and are admitted to the HDU and intensive care unit (ICU), and the mortality of elderly patients is higher.[7]

In this pandemic, the urban facilities in the country have been overwhelmed with the treatment of severe cases. Understanding risk factor and clinical feature of severe cases is critically important to improve the outcome and efficacy of treatment. Still more and more studies are required for understanding the pathology and formulating standard care of treatment.

METHODS

The prospective study was carried out between March 2020 to December 2020 at Victoria hospital, BMCRI, Bengaluru. Approval and clearance were obtained from the institutional ethics committee.

The study included patients aged ≥65 yrs of both the gender, diagnosed with COVID-19 infection by RT-PCR technique. The study excluded patients <65 yrs and those not willing to provide signed informed consent prior to the study. Case record form with follow-up chart was used to record the demographic data, duration of illness, comorbidities and clinical features of the disease. .

The demographic and clinical data collected were age, sex, clinical symptoms and comorbidities like hypertension, diabetes, renal, cardiac and respiratory disorders. Also, relevant laboratory investigation like haemoglobin, total leucocyte count, neutrophil%, lymphocyte%, neutrophil lymphocyte ratio (NLR), LDH, D-dimer, CRP, ferritin, chest X-ray and HRCT chest were done.

All the selected participants were followed up until discharge or death. As per the first discharge policy released by the state government, the patients were discharged after 14 days, if 2 consecutive throat/nasopharyngeal swabs taken 24 hrs apart were negative for SARS-CoV-2 RNA done using RT-PCR technique. If positive, test was repeated after 72 hrs. As per the revised discharge policy, patients who had mild and moderate symptoms were discharged after 10 days without throat/nasopharyngeal swab test for COVID-19 and symptom free for atleast 3 days and for severe patients, 14th day discharge policy based on negative swab test was adopted and those who were positive, the tests were repeated every 3rd day till obtaining a negative result. The demographics and clinical outcome were further correlated.

Statistical analysis was carried out using SPSS software. Continuous variables were expressed as means and standard deviation and categorical variables were presented as counts and percentages. Patients were grouped as survival and death. Different parameters were compared between the groups using t-test for continuous variables and Chi-square test for categorical data. The optimal cut points were estimated for significant continuous variables using receiver operating curve (ROC) analysis. Multiple regression analysis was carried out and odds ratio with confidence interval (CI) were estimated to determine the effect of significant factors on outcome death and survival. P value <0.05 was considered as statistically significant.

RESULTS

Study was conducted in Victoria hospital, Bangalore a designated referral centre for novel coronavirus infection. All the patient hospitalized were confirmed for RT-PCR. Out of 7259 COVID-19 patients admitted from march 2020 to December 2020, 1187 were elderly people (≥65 yrs) which accounts for 16% of total admission. Out of 1187 elderly people 316 people have succumbed to death with mortality of 26%. 871 people was discharged after recovering from illness. Clinical characteristic and laboratory investigation of survived and death were considered for comparison.

Average age of study population was 72.31±6.4 and mean age of survived and died were 71.95±6.1 and 73.3±7.04 respectively. So, patient >75 yrs were less likely to survive. Incidence in male was 60.5% and female was 39.5%. Mortality was also more in male than in female group of 68.7% and 31.3% respectively. Fever (42%), cough (33.2%) and dyspnea (26.9%) were the major symptom among study population. Only 6.6% was asymptomatic in mortality group, were as 24.5% patient were asymptomatic among survived group. Among patient who succumbed to death 45.9% people had diabetes with hypertension, 15.2% had only diabetes, 17.1% had only hypertension, 12.3% had chronic kidney disease and 15.56% had IHD.

Between the group biochemical parameter which showed statistical significance in predicting mortality were total leucocyte count, neutrophil%, lymphocyte%, neutrophil lymphocyte ratio (NLR), LDH, D-dimer, CRP, ferritin. These parameters were further considered for regression analysis. Since NLR is ratio neutrophil% and lymphocyte% only NLR was considered for multilogistic regression and ROC analysis. Odd ratio and CI are tabulated in Table 2 for significant variables. Odds ratio was highest for D-dimer i.e.; 1.366. ROC curve was drawn for TLC (AUC=0.72), N/L ratio (AUC=0.844), LDH (AUC=0.842), D-dimer (AUC=0.851), CRP(AUC=0.82), ferritin (AUC=0.823) and D-dimer at cut-off 1 had specificity 89% and sensitivity 76% which was highest among the parameter.

Based on saturation and severity at time of presentation patient was divided into 3 groups and comparison between the group is shown in Table 4. 30.8% were asymptomatic in group 1 and group 3 had fever (55.2%), cough (34.4%) and dyspnea (44.8%) as major symptom when compared

to another group. 46.8% people has both diabetes with hypertension in group 3. Lab parameter like total leucocyte count, neutrophil lymphocyte ratio (NLR), LDH, D-dimer, CRP, ferritin showed statistical significance in predicting severity of disease.

Table 1: Clinical feature and laboratory investigations were compared between survived and succumbed to death people.

Variables	Total (N=1187)	Survived (N=871)	Death (N=316)	P value
Age (years)	72.31±6.4*	71.95±6.1	73.3±7.04	0.001
Gender				
Male N (%)	718 (60.5)	501 (57.5)	217 (68.7)	0.001
Female N (%)	469 (39.5)	370 (42.5)	99 (31.3)	
Laboratory parameters				
Hemoglobin	12.4±4.2	12.5±4.6	12.0±2.3	0.532
Total WBC count	9321.5±4839.7	8143.5±3719.1	12534.6±5982.7	<0.0001
Neutrophil%	73.2±13.5	69.4±12.5	83.7±10.6	<0.0001
Lymphocytes%	18.4±10.9	21.5±10.3	9.78±7.1	<0.0001
Neutrophil lymphocyte ratio (NLR)	7.2±8.3	4.6±4.18	14.4±12.1	<0.0001
LDH	361.29±186.5	306.04±110.3	513.5±256.2	<0.0001
D-dimer	0.926±1.4	0.6±1.3	1.7±1.2	<0.0001
C-reactive protein	63.5±84.4	44.6±74.9	115.5±87.4	<0.0001
Ferritin	507.5±433.7	384.07±338.1	847.05±484.1	<0.0001
Clinical features				
Asymtomatic N (%)	234 (19.7)	213 (24.5)	21 (6.6)	<0.0001
Fever N (%)	498 (42)	327 (37.5)	171 (54.1)	0.001
Cough N (%)	394 (33.2)	283 (32.5)	111 (35.1)	0.394
Dyspnea N (%)	319 (26.9)	178 (20.4)	141 (44.6)	<0.0001
Sore throat N (%)	130 (11)	118 (13.5)	12 (3.8)	<0.0001
Myalgia N (%)	167 (14.1)	140 (16.1)	27 (8.5)	0.001
Others N (%)	12 (1)	10 (1.1)	2 (0.6)	0.433
Comorbidities				
None N (%)	296 (24.9)	242 (27.8)	54 (17.1)	0.0001
Diabetes only N (%)	151 (12.7)	103 (11.8)	48 (15.2)	0.258
Hypertension N (%)	229 (19.3)	175 (20.1)	54 (17.1)	0.246
Diabetes+hypertension N (%)	422 (35.6)	277 (31.8)	145 (45.9)	0.0001
Chronic kidney disease N (%)	99 (8.3)	60 (6.9)	39 (12.3)	0.003
IHD N (%)	141 (11.9)	92 (10.6)	49 (15.56)	0.02
Others N (%)	124 (10.4)	87 (10)	37 (11.7)	0.392

*mean±SD

Table 2: Multivariate logistic regression of the selected variables.

Variables	Odd ratio	95% CI	P value
Total lymphocyte count	1.00	1.00-1.00	0.141
Neutrophil lymphocyte ratio	1.137	1.097-1.179	<0.0001
LDH	1.005	1.004-1.006	<0.0001
D-dimer	1.366	1.118-1.669	0.002
CRP	1.004	1.002-1.006	<0.0001
Ferritin	1.001	1.001-1.002	<0.0001

Table 3: Cut points, AUC, specificity and sensitivity noted for potential predictors.

Variables	Area under curve	Cut-off	Specificity (%)	Sensitivity (%)
Total WBC	0.724	9950	77	60
N/L ratio	0.844	6.9	82	73
LDH	0.842	363.5	80	75
D-dimer	0.851	1.00	89	76
CRP	0.824	62.2	81	75
Ferritin	0.823	518	80	75

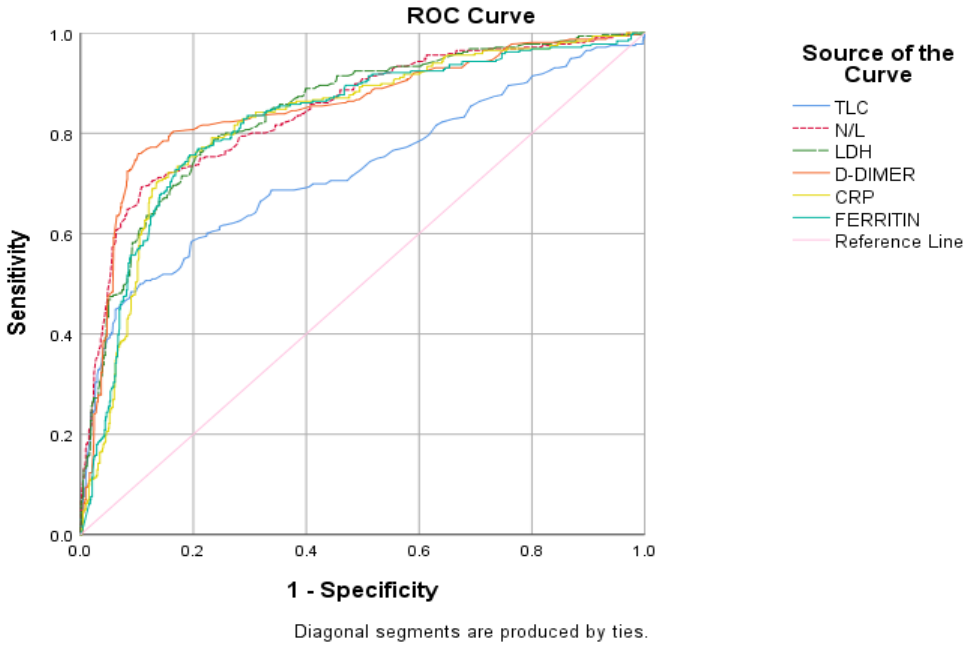

Figure 1: ROC curve for different variables showing area under curve

Table 4: Comparison of different variables cross 3 groups.

Variables	Group 1 (N=471)	Group 2 (N=408)	Group 3 (N=308)	P value
Age (years)	71.7±5.8*	72.4±6.7	73.04±6.8	0.024
Gender				
Male N (%)	257 (54.6)	251 (61.5)	210 (68.2)	0.001
Female N (%)	214 (45.4)	157 (38.5)	98 (31.8)	
Laboratory parameters				
Hemoglobin	12.5±2.08	12.6±6.5	11.9±2.3	0.101
Total WBC count	7547.5±2690.5	9019.2±4648.5	12400±6025	<0.0001
Neutrophil%	66.6±12.2	73.3±12	83.1±11.3	<0.0001
Lymphocytes%	23.69±10	18.5±10.1	10.2±7.8	<0.0001
Neutrophil lymphocyte ratio	3.7±2.5	6.1±5.7	14.2±12.1	<0.0001
LDH	285.5±89.6	333.23±128.5	514±258.6	<0.0001
D-dimer	0.47±0.4	0.8±1.9	1.7±1.3	<0.0001
C-reactive protein	34.7±63.5	59.2±88.9	113.2±84.3	<0.0001
Ferritin	314.7±305.9	481.9±364.9	835±490.7	<0.0001
Clinical features				
Asymtomatic N (%)	145 (30.8)	70 (17.2)	19 (6.2)	<0.0001
Fever N (%)	159 (33.8)	169 (41.4)	170 (55.2)	<0.0001
Cough N (%)	137 (29.1)	151 (37)	106 (34.4)	0.039
Dyspnea N (%)	89 (18.9)	92 (22.5)	138 (44.8)	<0.0001
Sore throat N (%)	55 (11.7)	64 (15.7)	11 (3.6)	0.0001
Myalgia N (%)	73 (15.5)	67 (16.4)	27 (8.8)	0.007
Others N (%)	4 (0.8)	4 (1)	4 (1.3)	0.826
Comorbidities				
None N (%)	151 (32.1)	91 (22.3)	54 (17.5)	<0.0001
Diabetes only N (%)	49 (10.4)	59 (14.5)	43 (14)	0.259
Hypertension N (%)	98 (20.8)	78 (19.12)	53 (17.2)	0.458
Diabetes+hypertension N (%)	135 (28.7)	143 (35)	144 (46.8)	<0.0001
Chronic kidney disease N (%)	30 (6.4)	34 (8.3)	35 (11.45)	0.048
IHD	52 (11)	41 (10)	48 (15.6)	0.059
Others N (%)	43 (9.1)	42 (10.3)	39 (12.7)	0.287

*mean±SD

DISCUSSION

In the present study of 7259 admitted patients, 16% was elderly people and mortality rate was 26%, which was way too much higher than any other age group that is affected. This demonstrated that the survival chances are lower for patient ≥65 yrs. There are many literatures to validate this association between age related COVID-19 severity and mortality. A rapid review and meta-analysis have also showed the positive association between increased age-related risk of COVID-19 disease severity, admission to ICU and mortality. The increased risk per age year noted for disease severity was 2.7%.[8] Similarly meta-analysis involving 6,11,583 reported that mortality was <1.1% in age group <50 yrs and largest increase in mortality was observed in patient between age group of 60-69 yrs.[9] Current study has showed fever, cough, dyspnea, myalgia followed by sore throat as common symptom. But fever and dyspnea was the major symptom present among patient who succumbed to death. A study conducted by Zhang et al evaluated clinical characteristics of 82 laboratory confirmed SARS CoV-2 death cases, reported that fever (78%), cough (64.6%), shortness of breath (63.4%) as prominent symptom reported in the succumbed victims.[10] The study by Gupta et al conducted in tertiary care centre in India also noticed fever and cough as major symptom.[11] In this study diabetes with hypertension coexistence followed by IHD was major association with the patient who succumbed to death. In concurrence with these finding, the study conducted by Saluka et al in government medical college, Kota, Rajasthan has also observed increased male preponderance. Hypertension was common associated co-morbidity followed by diabetes. Also, noted increased occurrence of severe illness and complication in patient age >60 yrs.[12] The data from Mexico has identified obesity, CKD, hypertension, diabetes and COPD are associated with increased mortality risk of COVID-19 patient. A review focusing on developing countries has reported that presence of comorbidities is linked to poor outcome of COVID-19 patients.[13]

Total leukocyte count, NLR, LDH, D-dimer, CRP and Ferritin were statistically significant as predictor of disease outcome. Among these variables the highest specificity (89%) and sensitivity (76%) was noted for D-dimer at 1mcg/ml followed by NLR ratio of 6.9 has specificity (82%), sensitivity (73%) and least for total leukocyte count. A study by Pomilla et al have assessed potential of routine infectious biomarker and haematological parameter in evaluating the disease severity in 100 adult COVID-19 patient. They suggested total leukocyte count of 8100/cumm has sensitivity 91%, specificity 62.5% and NLR ratio of 6.9 has sensitivity 91.7%, specificity 87.5% and may assist in triaging patient requiring ICU care and deciding on intervention.[14]

Zhang et al studied the clinical characteristics of 82 cases of death due to COVID-19 and most of the findings are in line with the present results. The researchers noted increased incidence of mortality in male subjects (66%) and more than half of the subjects who died were >60 yrs of age. The most common comorbidity noted in patients who died were hypertension (56.1%), followed by heart disease (20.7%), diabetes (18.3%), cerebrovascular disease (12.2%), and cancer (7.3%). Lymphopenia, neutrophilia, and thrombocytopenia were the common clinical finding observed on admission. In addition, elevated NLR of >5, systemic immune-inflammation index of >500, CRP, LDH, and D-dimer were also observed in most of the patients. Respiratory failure was identified as the main cause of COVID-19 and high level of IL-6 (>10 pg/ml) was indicative of cytokine release syndrome-mediated damage to other vital organs.[10] The present study holds significant relevance, as there is very limited literature evidence available on elderly with COVID-19 infection. More ever, it sheds light on several significant finding which would assist clinician in screening, treatment decision and estimating disease prognosis. Another strength of this study is good sample size, but generalization of finding is limited as the study was carried out in single centre.

CONCLUSION

In conclusion, D-dimer of 1 mcg/ml, NLR ratio of 6.9 may assist in triaging patient requiring ICU care and deciding intervention. Also, elderly with multiple comorbidity should be treated aggressively, so that chance of survival can be increased.

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