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ORIGINAL RESEARCH CORONA EXPERIENCE

Analysis of clinical risk factors in COVID-19 mortality in ICU in various age groups: a retrospective observational study

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ABSTRACT

Background and Objective: COVID-19 has been associated with more than 770 million cases and 6.9 million deaths worldwide, since the first case was reported in 2019 in Wuhan, China. Various demographic and clinical factors have been associated with high mortality. We retrospectively analyzed data of patients admitted to our Intensive Care Unit (ICU) with moderate to severe disease for association of mortality with baseline clinical parameters and lab values.

Methodology: Retrospectively, data was collected for patients admitted to ICU of our hospital from March 2021 to August 2021, with moderate to severe covid infection. A total of 399 patients were included in the analysis after exclusion of patients with incomplete outcome data. Analysis was initially performed to find association of baseline parameters with ICU mortality; stratified analysis was further performed for association with various age groups.

Results: There was significant association of increased mortality with higher baseline heart rate (> 100 bpm), respiratory rate (> 30 bpm), low PaO_2/FiO_2 (< 100), Low oxygen saturation (< 80%), high neutrophil/lymphocyte ratio (> 10) and high baseline proBNP (> 500); however, subgroup analysis in the study showed that increased respiratory rate and increased neutrophil/lymphocyte ratio were not associated with increased mortality in patients with ages less than 50 y.

Conclusion: Baseline higher baseline heart rate, respiratory rate, low PaO_2/FiO_2, Low oxygen saturation, high neutrophil/lymphocyte ratio and high baseline proBNP were found to be associated with higher mortality in COVID patients. However, higher respiratory rate and higher neutrophil/lymphocyte ratio were not associated with increased mortality in patients with age less than 50 y.

Keywords: COVID-19, Heart rate, Respiratory rate, oxygen saturation, neutrophil/lymphocyte ratio, proBNP

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1. INTRODUCTION

Corona virus disease2019 which originated in Wuhan, China was a global pandemic causing major health concern all over the world.[1] It was caused by SARS COV-2 virus affecting primarily the respiratory system. The clinical manifestations varied from mild self-limiting disease to life threatening multiple organ involvement. It affected all age groups with significant morbidity and mortality rate and adverse outcomes becoming a global burden. [2]

Initially it was thought to involve respiratory symptoms, pneumonia and in severe cases progressing to ARDS requiring hospitalization. But now it is known to cause systemic inflammation affecting multiple organs including lung, heart, blood vessels, CNS, and other systems.

A systematic review of patients admitted in COVID ICU of our hospital was conducted. The aim of the study was to identify clinical predictors at the time of admission associated with mortality of COVID-19 patients of different age groups in our hospital admitted in intensive care unit during second wave.

2. METHODOLOGY

After getting clearance from Institutional ethics committee, data of moderate to severe COVID-19 patients admitted to our hospital from March 2021 till August 2021 was initially collected for analysis of epidemiological and clinical risk factors associated with the mortality in COVID-19 patients. Patients were excluded from this study if outcome data was unavailable, and 399 eligible patients were included in the study. The medical records of the patients were then retrospectively reviewed and data regarding heart rate (HR), respiratory rate (RR), oxygen saturation (SpO_2), partial pressure of oxygen, oxygen support, Neutrophil/Lymphocyte (N/L) ratio and Brain Natriuretic Peptide (BNP) at time of admission was collected for analysis.

Our primary predictor of interest was ICU mortality. Calculation of risk of death according to baseline values was done using Chi-square test. Stratified analysis was also performed using Chi-square test to calculate odds of mortality in various age groups (less than 50 y, 50-70 y, and more than 70 y).

3. RESULTS

A total of 399 patients admitted in our ICU during second wave of COVID were included in this study with an overall mortality of 232 (58.1%).

A baseline HR of more than 100 bpm at the time of admission was associated with a higher mortality (78.4%) compared to those with lower baseline HR (47.9%) (Figure 1). $\chi 2$ (1, N = 399) = 33.871, P ≤ .001.

Stratified analysis in age groups of less than 50 y, 50-70 y and more than 70 y revealed that the mortality difference was maintained in different age groups (Table 1).

A baseline RR of more than 30 bpm at the time of admission was associated with higher mortality (73.9%) compared to those with lower RR (51.1%) (Figure 2). $\chi 2$ (1, N = 393) = 17.792, P ≤ .001.

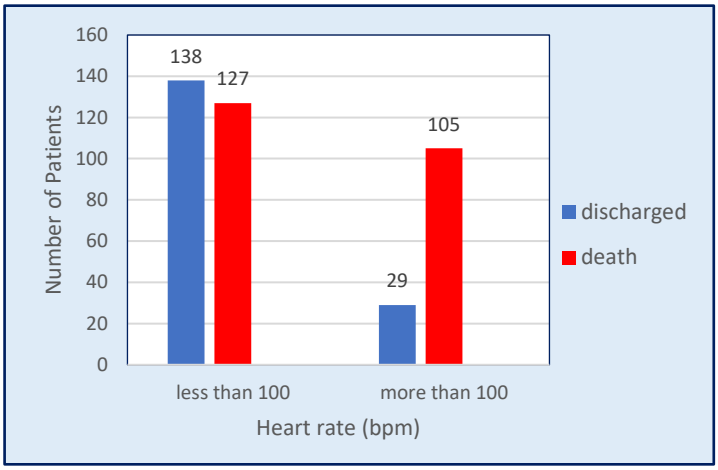

Figure 1: Patients with baseline HR more than 100 had higher mortality (78.4% ;105/134) as compared to patients with lower HR (47.9%;127/265)

Table 1: Mortality rates in different age groups: Significant mortality association was found in all age groups with increased HR.

Age group	HR < 100 bpm	HR > 100 bpm	p
Less than 50 y (133)	38.3% (31 deaths /81 patients)	65.4% (34 deaths /52 patients)	.002
50-70 (196)	47.4% (63 deaths /133 patients)	84.1% (53 deaths/63 patients)	.001
>70 (70)	64.7% (33 deaths /51 patients)	94.7% (18 deaths /19 patients)	.012

Table 2: Mortality rates in different age groups: Significant mortality association was not found in patients with age less than 50 y with increased respiratory rate (RR)

Age group	RR < 30	RR > 30	p
Less than 50 y (130)	49.5% (46 deaths /93 patients)	45.9% (17 deaths /37 patients)	.717
50-70 (194)	47.4% (62 deaths /131 patients)	84.1% (53 deaths /63 patients)	.001
>70 (69)	64.0% (32 deaths /50 patients)	94.7% (18 deaths /19 patients)	.011

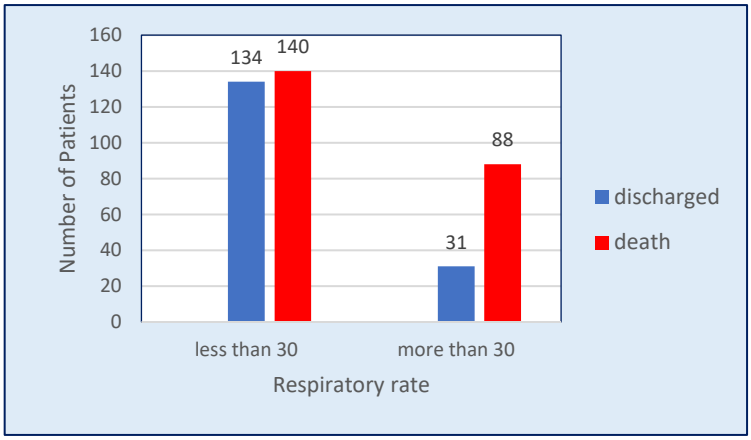

Figure 2: Patients with baseline respiratory rate more than 30 bpm had higher mortality (73.9%;88/119) as compared to patients with lower RR (51.1%;140/274).

A baseline RR of more than 30 bpm at the time of admission was associated with higher mortality (73.9%) compared to those with lower RR (51.1%) (Figure 2).

$\chi 2$ (1, N = 393) = 17.792, P ≤ .001.

However stratified analysis of age groups revealed that the increased RR was only associated with increased mortality in patients with age more than 50 y, and no significant difference was found in those with age less than 50 y (45.9% vs 49.5%) (Table 2). $\chi 2$ (1, N = 130) = .131, P = .717.

Hence increased RR might not be a prognostic marker in lower age groop patients.

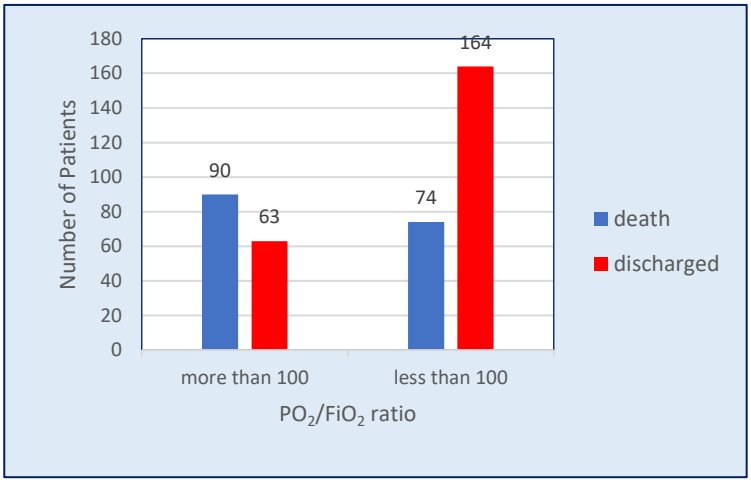

Figure 3: Patients with PO2/FiO2 ratio less than 100 had higher mortality (68.9%;164/238) as compared to patients with higher PO2/FiO2 ratio (41.2%;63/153).

A baseline PO_2/FiO_2 ratio of less than 100 at the time of admission was associated with a higher mortality (68.9%) compared to those with higher PO_2/FiO_2 ratio (41.2%) (Figure 3).

$\chi 2$ (1, N = 391) = 29.411, P ≤ .001.

Stratified analysis in age groups also revealed similar mortality differences however the results in individual age groups could not achieve statistical significance due to low number (Table 3).

Table 3: Mortality rates in different age groups: Similar mortality association was found in all age groups with low PO_2/FiO_2 ratios.

Age group	PO_2/FiO_2 > 100	PO_2/FiO_2 < 100	p
Less than 50 y (130)	39.6% (21 deaths /53 patients)	55.8% (43 deaths /77 patients)	.069
50-70 (194)	37.2% (29 deaths /78 patients)	73.3% (85 deaths /116 patients)	.001
>70 (67)	59.1% (13 deaths /22 patients)	80% (36 deaths /45 patients)	.07

Table 4: Mortality rates in different age groups: Significant mortality association was found in all age groups with decreased oxygen saturation

Age group	SpO2 > 80%	SpO2 < 80%	p
Less than 50 y (92)	28.8% (17 deaths /59 patients)	75.8% (25 deaths /33 patients)	.001
50-70 (132)	44.3% (35 deaths /79 patients)	83% (44 deaths /53 patients)	.001
>70 (52)	60% (21 deaths /35 patients)	100% (17 deaths /17 patients)	.002

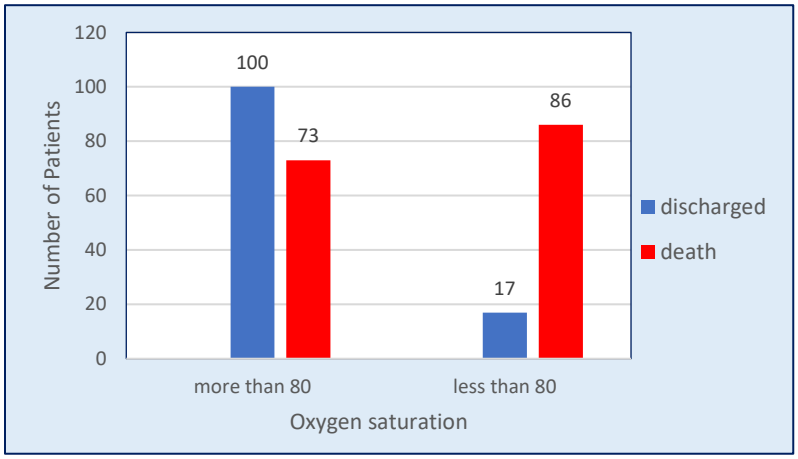

Figure 4: Patients with baseline oxygen saturation less than 80% had higher mortality (83.5%;86/103) as compared to pt's with higher oxygen saturation (42.2%;73/173).

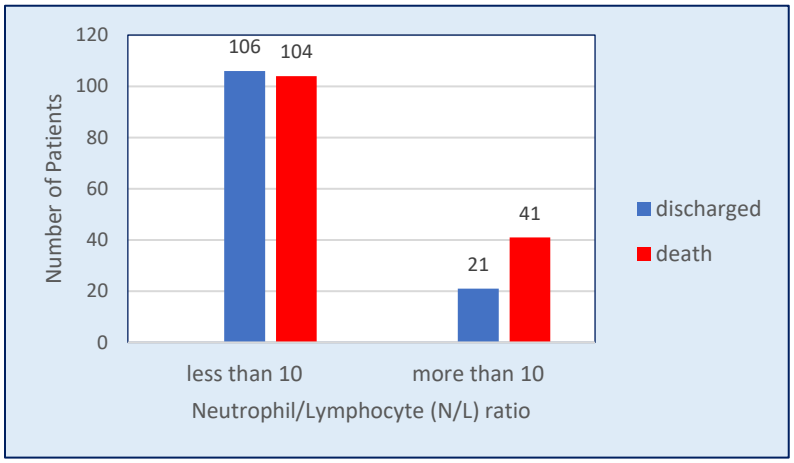

Figure 5: Patients with N/L ratio more than 10 had higher mortality (66.1%; 41/62) as compared to patients with lower N/L ratio (49.5%; 104/210)

A baseline oxygen saturation of less than 80 at the time of admission was associated with a higher mortality (83.5%) compared to those with higher oxygen saturation (42.2%) (Figure 4). $\chi 2$ (1, N = 276) = 45.09, P ≤ .001.

Stratified analysis in age groups also revealed similar mortality differences (Table 4).

A baseline N/L ratio of more than 10 at the time of admission was associated with a higher mortality (66.1%) compared to those with lower N/L ratio (49.5%) (Figure 5). $\chi 2$ (1, N = 272) = 5.303, P ≤ .021.

However, stratified analysis in age groups revealed that increase N/L ratio was only associated with increased mortality in patients with age more than 50 y and no significant difference was found in those with age less than 50 y (38.7% vs 37.5%) (Table 5). $\chi 2$ (1, N = 91) = .008, P ≤ .931.

Table 5: Mortality rates in different age groups: Significant mortality association was not found in patients with age less than 50 yrs. with increased N/L ratio.

Age group	N/L ratio < 10	N/L ratio > 10	p
Less than 50 y (91)	38.7% (29 deaths /75 patients)	37.5% (6 deaths /16 patients)	.931
50-70 (136)	52.9% (54 deaths /102 patients)	73.5% (25 deaths /34 patients)	.035
>70 (45)	63.6 (% 21 deaths /33 patients)	83.3% (10 deaths /12 patients)	.207

Table 6: Mortality rates in different age groups: Similar mortality association was found in all age groups with increased BNP

Age group	BNP < 500	BNP > 500	p
Less than 50 y (65)	29.5% (13 deaths /44 patients)	57.1% (12 deaths /21 patients)	.032
50-70 (103)	46.7% (28 deaths /60 patients)	65.1% (28 deaths /43 patients)	.064
>70 (41)	100% (7 deaths /7 patients)	79.4% (27 deaths /34 patients)	.187

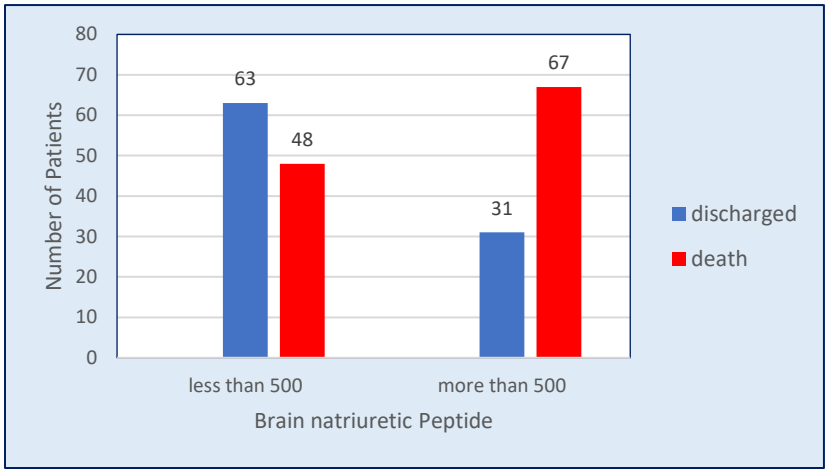

Figure 6: Patients with BNP more than 500 had higher mortality (68.4%;67/98) as compared to patients with lower BNP (43.2%;48/111).

Hence increased N/L ratio might not be a prognostic marker in lower age grp patients.

A baseline BNP of more than 500 at the time of admission was associated with a higher mortality (68.4%) compared to those with lower baseline BNP (43.2%) (Figure 6). $\chi 2$ (1, N = 209) = 13.275, P ≤ .001.

Stratified analysis in age groups also revealed similar mortality differences however statistical significance could not be achieved due to low number (Table 6).

4. DISCUSSION

COVID-19 was associated with a large impact on healthcare worldwide with many clinical risk factors studied for impact on mortality. In our study we analyzed the clinical risk factors in various age groups and their association with mortality.

A baseline HR of more than 100 bpm was associated with higher mortality in our study. Similar findings have been reported in a study conducted by Han Jin et al. on 136 patients in China, which showed significantly higher mortality among patients with tachycardia (HR > 100 bpm) as compared to those with moderate HR (80-90 bpm) and low HR (< 80 bpm).[3] However, study conducted by Ahmed Sameer Ikram et al. showed that there was no significant difference in admission HR between survivors and non survivors.[4] Age wise analysis in our study revealed that increased HR was associated with increased mortality in all age groups.

A baseline RR of more than 30 bpm was associated with increased mortality. Similar findings were found by many authors.[4-8] However subgroup analysis in our study revealed that it was significant only in patients with more than 50 y of age and that in younger age group increased RR was not a very reliable marker for mortality prediction.

A baseline PaO_2/FiO_2 < 100 is also known to be associated with increased moratlity.[9-10] Similar findings were there in our study with a low PaO_2/FiO_2 ratio associated with higher mortality in all age groups.

Low oxygen saturation is associated with increased mortality.[4,11] Analysis of baseline oxygen saturation revealed that patients with baseline SpO_2 < 80% had 83.5% mortality rate as compared to 42.5% in those with SpO_2 > 80%. The mortality difference was maintained in all age groups studied. Similar findings were reported by Peter M. Mphekgwana et al. who showed greater mortality in patients with SpO_2 < 95% in all age groups as compared to those with SpO_2 > 95% (P = 0.006).[12] Another study conducted by Fernando Mejia et al. showed that SpO_2 value on admission was lower in deceased patients compared to discharged patients (78% vs 91% P < 0.001).[13]

A high neutrophil/lymphocyte ratio has been associated with increased mortality in COVID-19 patients.[14-15] Similar results were found in our study but age group analysis further showed that high N/L ratio was only associated with increased mortality in patients more than 50 y old, with no significant association with mortality in lower age groups.

A high baseline proBNP levels have also been associated with increased mortality.[16-18] Similar results were there in our study with mortality association in all age groups.

5. CONCLUSIONS

Increased baseline heart rate, respiratory rate, low PaO_2/FiO_2, low oxygen saturation, high neutrophil/lymphocyte ratio and high baseline proBNP levels are associate with increased mortality in COVID-19 patients; however, subgroup analysis in our study showed that increased respiratory rate and increased neutrophil/lymphocyte ratio were not associated with increased mortality in patients with ages less 50 y and further studies may be required.

6. Data availability

The numerical data generated during this research is available with the authors.

7. Preregistration

The study was registered with Clinical Trials Registry-India (CTRI), hosted at the ICMR's National Institute of Medical Statistics (https://icmr-nims.nic.in) with registration number CTRI/2022/02/040638

8. Source of Funding

The study utilized the hospital resources only, and no external or industry funding was involved.

9. Conflict of interest

The authors declare that there was no conflict of interest.

10. Authors' contribution

MC, VS: Conduct of study; literature search; statistical analysis & manuscript editing

SK: Conduct of study; literature search; statistical analysis

AY, SS, HCS: Conduct of study; literature search

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