



A COMPARATIVE STUDY OF CLINICAL AND BIOCHEMICAL PROFILE AMONG SURVIVORS AND NON SURVIVORS OF PATIENTS WITH COVID-19 INFECTION - A RETROSPECTIVE STUDY.

Dr. Tilak.N	Senior Resident, Department of Medicine, Ramaiah Medical College, Bangalore.
Dr. Abhijna Vithal Yergolkar	Intern, Ramaiah College of Pharmacy, Bangalore.
Dr Ashwin Kulkarni*	Associate Professor, Department of Medicine, Ramaiah Medical College, Bangalore. *Corresponding Author
Dr. T. Anil Kumar	Professor and HOD, Department of Medicine, Ramaiah Medical College, Bangalore.
Dr Sujatha.K.J	Assistant Professor, Department of Medicine, Ramaiah Medical College, Bangalore.
Dr Guruprasad Khandre	Post graduate student, Department of Medicine, Ramaiah Medical College, Bangalore.

ABSTRACT **BACKGROUND:** The pandemic caused by SARS-Corona Virus-2 (COVID-19) is far from over. There has been ongoing new infections across the globe. The clinical course of the disease is varied among different individuals. The prediction of severity and mortality is very difficult but quite essential for timely escalation of the treatment. This is a comparative study of clinical, biochemical parameters among the survivors and non survivors of COVID-19 infection. **METHODOLOGY:** This is a retrospective study conducted in a tertiary care hospital in South India. This study was an audit of 39 survivors and 39 non survivors of COVID-19 infection. These patients were matched with age and gender. The clinical profile, Biochemical parameters and the clinical course among the two groups were compared and analyzed. **RESULTS:** 39 survivors and 39 non survivors were included in the study. The two groups were age and gender matched. The symptoms were fever, cough, breathlessness, fatigue, myalgia, body ache, diarrhea. Breathlessness was more common among patients who did not survive. Pneumonia severity index was class 1 and class 2 among patients who survived. PSI was class 4 and class 5 among the patients who did not survive. This difference was statistically significant. It was seen that there were significant number of comorbidities and inflammatory markers like CRP, D DIMER, LDH, S. Ferritin seen among non survivors compared to the survivors. **CONCLUSION:** The study shows that presence of comorbidities has an adverse impact on the outcome of the patients with COVID-19 infection. The elevated inflammatory markers like CRP, D Dimer and LDH predicted poor outcome. Pneumonia severity index was a useful marker to predict the outcome among patients of COVID.

KEYWORDS : Survivors , Non survivors, Pneumonia severity illness, COVID-19.

INTRODUCTION

The pandemic caused due to Novel Corona virus-19 (COVID-19) is far from over. The initial infection started in Wuhan city of China and it has now rapidly spread to most of the countries. The pandemic has caused large number of deaths across the globe. The number of positive cases in India have now crossed 1 crore and more than 150 thousand deaths. The disease has myriad clinical features and has varied clinical presentations and outcome. The infection may be asymptomatic in some people and may be life threatening in some. The behavior of the disease is very difficult to predict. The dysregulated immune plays the central role in predicting disease severity. The cytokine storm has an impact in the survival of the patients. Critically ill patients had elevated levels of plasma inflammatory cytokines. (1). Early identification of patients who might have an adverse outcome is important for monitoring and timely escalation of treatment. Many scoring systems like Sequential organ failure assessment score (SOFA) have been used to predict outcome. Presence of comorbidities like diabetes, hypertension, Ischemic heart disease are known to cause greater risk of death among patients with COVID-19 infection (2)(3). The pneumonia severity index (PSI) or PORT Score is a clinical prediction rule that many physicians can use to calculate the probability of adverse outcome and death among patients with community acquired pneumonia (4). The CURB-65 scores and pneumonia severity index (PSI) are widely used to predict death in patients with community-acquired pneumonia. As of now, there is no scoring system to predict mortality in patients with COVID-19. The PSI scores performed significantly better than the CURB-65 score (5).

The present study was conducted to compare and contrast the clinical features, comorbidities, laboratory parameters and management strategies among survivors and non survivors of patients who were admitted with COVID-19 infection in tertiary care hospital. This study was conducted to assess the factors which can predict mortality among patients having COVID infection in a tertiary care center in India.

OBJECTIVES

1. To study and compare the clinical profile, laboratory parameters

among survivors and non survivors of COVID-19 infection.

2. To assess the utility of Pneumonia severity index to predict the mortality among patients of COVID-19

MATERIAL AND METHODS

This is a retrospective study conducted in Ramaiah Medical College and hospital, Bangalore. The study was conducted from 1st July 2020 to 1st October 2020. The medical records of the patients who were tested positive for COVID-19 by reverse transcriptase polymerase chain reaction (RT-PCR) and admitted to the hospital were studied. It was a random audit of 39 patients who survived and 39 patients who did not survive. In order to avoid the bias of the age, these groups were matched with respect to the age and gender. The treatment regimen followed as per the guidelines of Indian council of Medical research. Patients having mild disease were having symptoms of COVID infection and oxygen saturation more than 94 percent on room air. Patients with moderate disease were having symptoms of COVID and having oxygen saturation of 90-94 percent. The patients with severe infection were the one with oxygen saturation less than 90 percent. The standard of care was given to all the patients. Patients with mild illness received Hydroxychloroquine 400 mg BD or Doxycycline 100 mg BD and Tab Ivermectin 12 mg OD. The patients having moderate illness received system corticosteroids Methyl prednisolone and Low molecular weight heparin. Injection Remdesivir was advised to all patients with moderate and severe illness. It was given only in the patient or his attenders give consent. The treatment regimen followed as per the guidelines of Indian council of Medical research. The data was extracted from the patient files and electronic medical records. The clinical history, age, gender, comorbidities, inflammatory markers, chest X rays, CT scans were studied. The clinical course in the hospital was assessed. Pneumonia severity index was calculated for all the patients.

Pneumonia Severity Index

The pneumonia severity index (PSI) or PORT Score is a clinical prediction score that can be used to calculate the probability of

morbidity and mortality among patients with community acquired pneumonia.⁽⁶⁾

STEP- 1

1. Presence of age more than 50 years
2. Altered mental status
3. Pulse rate more than 125/minute
4. Respiratory rate more than 30/minute
5. Systolic blood pressure less than 90mm Hg
6. Temperature less than 35 C or more than 40 C.
7. History of Neoplastic disease
8. Congestive cardiac failure
9. Cerebrovascular disease
10. Renal disease

If non of the above parameter is present then the patients is assigned to be in Risk Class 1. If any of the above parameter is present then Step 2 has to be done

STEP- 2

1. Male (Age-years +)
2. Female (Age -10)
3. Nursing home resident (+10)
4. Altered mental status(+20)
5. Pulse rate more than 125/minute (+10)
6. Respiratory rate more than 30/minute (+20)
7. Systolic blood pressure less than 90mm Hg (+20)
8. Temperature less than 35 C or more than 40 C (+15).
9. History of Neoplastic disease (+30)
10. Congestive cardiac failure(+10)
11. Cerebrovascular disease(+10)
12. Renal disease(+10)
13. Liver disease(+20)
14. Arterial PH<7.53(+30)
15. Blood urea nitrogen>30mg/dL(+20)
16. Sodium<130mmol/litre(+20)
17. Glucose>250mg/dL(+10)
18. Hematocrit<30%(+10)
19. Partial pressure of oxygen<60mmHg(+10)
20. Pleural effusion(+10).

The total sum <70 is taken as Risk class 2, score of 71-90 is Risk Class 3, score of 91-130 is Risk Class 3, Score of more than 130 is Risk Class 4.

STATISTICAL ANALYSIS

Data was analyzed using SPSS 22 version software. Categorical data was represented in the form of frequencies and proportions. Chi square test was used as test of significance for qualitative data. Independent t test was used as test of significance to identify the mean difference between two quantitative variables. Median and IQR was calculated for non parametric data. Mann Whitney U test was used to test significance. P value of less than 0.05 was considered to be statistically significant.

RESULTS

39 survivors and 39 non survivors were included in the study. these two groups were age and gender matched. Mean age among survivors was 47.08 and among non survivors was 48.4 (Table-1). Among the groups of patients who survived 12 had mild infection, 18 had moderate and 9 were having severe COVID infection at the time of admission. Among the non-survivors group, 4 were having mild, 15 were having moderate and 20 were having severe COVID infection at the time of admission (Table-2). The symptoms of the patients are summarized in the Table-3. The symptoms were fever, cough, breathlessness, fatigue, myalgia, body ache, diarrhea. Breathlessness was seen among patients who did not survive. Pneumonia severity index was class 1 and class 2 among patients who survived. PSI was class 4 and class 5 among the patients who did not survive. This difference was statistically significant (Table-4). It was seen that there were significant number of comorbidities seen among non survivors compared to the survivors (Table-5). Among the patients who survived, 28 patients had received Remdesivir, 11 had not received. Among the patients who died, 11 had received Remdesivir and 27 had not received. This difference was statistically significant (Table-6). The inflammatory markers like CRP, D DIMER, LDH, S. Ferritin were all raised among patients who died compared to the patients who survived. This difference was statistically significant (Table-7). Mean CRP among patients who survived was 5.7 and among non survivors was 8.5. Mean NLR among survivors was 5.7 and among non survivors was 6.3. Mean LDH level

was 293mg/dl among survivors and 344 among non survivors. All these differences were statistically significant.

Tables 1: Age distribution among survivors and non survivors

	SURVIVORS	NON SURVIVORS
Age in Mean (SD)	47.08 (9.8)	48.4 (9.5)

Table 2: Severity of Illness among survivors and non survivors

	SURVIVORS	NON SURVIVORS
Mild	12	4
Moderate	18	15
Severe	9	20

Table 3: Symptoms among survivors and non-survivors

	SURVIVORS	NON SURVIVORS
Fever	26	21
Cough	22	16
Breathlessness	13	20
Headache	2	4
Fatigue	13	0
Myalgia	3	0
Diarrhea	0	2

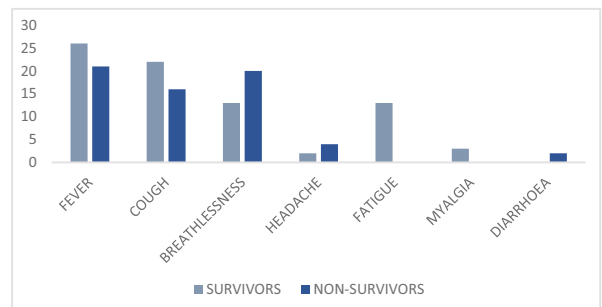


Table-4 PSI among survivors and non survivors

	SURVIVORS	NON SURVIVORS	CHI SQ	p value
Class I	11	3	41.72	0.000
Class II	25	6		
Class III	3	5		
Class IV	0	10		
Class V	0	15		

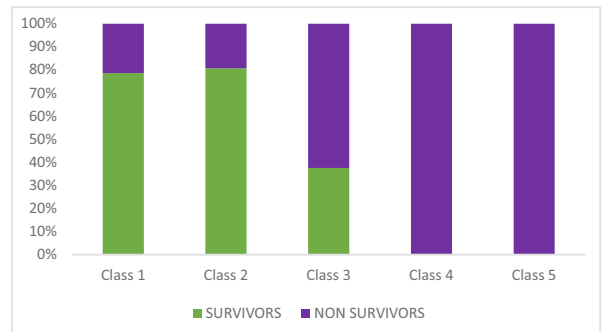


Table-5 : Comorbidities among survivors and non survivors

	SURVIVORS	NON SURVIVORS	CHI SQ	p value
Type II Diabetes Mellitus	9	9	10.55	0.032
Hypertension	11	12		
Heart Disease	3	6		
Hypothyroidism	5	1		
Chronic Kidney Disease	0	7		

Table-6 : Administration of Remdesivir

	Survivors	Non survivors	Chi Sq	P value
Received	28	11	10.06	0.002
Not Received	12	27		

Table-7 Laboratory Parameters survivors and non survivors

Parameter	Survivors Median (IQR)	Non-Survivors Median (IQR)	p value
Hb (g/dl)	13.8 (15-12.2)	12.7 (14.3 -10.01)	0.013

TLC (cells/cumm)	6100 (9100-5200)	7500 (10700-4700)	0.14
NLR	3.04 (6.08-1.98)	6.3 (12-3.8)	<0.001
CRP (mg/dl)	5.7 (13.6-0.89)	8.5 (19.4-5.03)	0.020
D-Dimer (mcg/ml)	0.84 (1.26-0.58)	1.3 (2.0-0.80)	0.004
LDH (U/L)	293 (412-236)	344 (536-271)	0.009
Ferritin (mcg/L)	153.5 (404-64.5)	443 (830 - 209)	0.003
BUN (mg/dl)	11 (14.7-9)	19 (49-10)	0.0016
Sr. Creatinine (mg/dl)	0.79 (0.97-0.58)	0.93 (2.07-0.68)	0.0013
AST (IU/L)	40 (49-29)	41 (61-26)	0.5
ALT (IU/L)	37 (49-26)	32 (38-21)	0.09

DISCUSSION

In the above study, it was seen that presence of comorbidities was a very important factor which could predict mortality among COVID patients. It was seen that among the patients who died, majority of them had hypertension, Diabetes and chronic kidney disease. It was also seen that the severity of the illness at which the patient got admitted to the hospital had a significant impact. The patients who died, had presented to the hospital when they were moderately or severely sick. Pneumonia severity index assessed at the time of admission was a useful parameter to predict disease severity. It was seen that PSI of patients who survived was in class 1 and 2, whereas PSI of patients who died was in class 4 and class 5. Hence PSI can be a powerful tool to stratify and predict the patients as per the severity. It was seen that Remdesvir was found to be beneficial. Among patients who survived, most of them had received Remdesivir. Remdesvir was not given in presence of Renal failure, refusal by patients and in the initial days of pandemic when Remdesvir was not available. It was also seen that serum inflammatory markers were statistically significant among the patients who survived and the patients who died. The findings of our study was similar to the study conducted by Fei Zhou(2020) in China, higher age, high SOFA score and D dimer had predicted poor prognosis even at early stage. This study reported comorbidity in 48 percent of patients, which hypertension and diabetes mellitus being the common comorbidities. (2)

It was also seen in our study that, serum inflammatory markers were high and statistically significant among the patients who did not survived compared to the patients who succumbed. These findings were concordant with the study conducted in Kurdistan by Zandkarimi (2020) in 1831 COVID patients. The results showed that patients suffering from Chronic lung disease, ischemic heart disease, kidney disease may face a greater risk of death. Higher CRP levels were associated with an increased risk for mortality (OR: 1.015, 95% CI: 1.008–1.021; $p < 0.001$). A study was conducted in Tukey by Celal Satici (2020) which assessed Pneumonia severity index among patients with COVID-19 infection .The PSI performed significantly better than CURB-65 (AUC: 0.91, 95% CI: 0.88–0.93 vs AUC: 0.88, 95% CI: 0.85–0.90; $p = 0.01$), and the addition of CRP levels to PSI did not improve the performance of PSI in predicting mortality (AUC: 0.91, 95% CI: 0.88–0.93 vs AUC: 0.92, 95% CI: 0.89–0.94; $p = 0.29$).⁽⁵⁾

A similar retrospective cohort study was conducted by Kim Ma(2019) to investigate the distribution of PSI class and whether PSI play a role in prognostic factors in viral CAP. The 30-day all-cause mortality rate was studied. It was found that the mortality rate of CAP was significantly increased according to the PSI class., regardless of respiratory virus detection.⁽⁷⁾

Comparative study of CURB-65, Pneumonia Severity Index and IDSA/ATS scoring systems in community acquired pneumonia in an Indian tertiary care setting by Madhu S(2017), found that the PSI was most sensitive in both predicting ICU admission and death whereas CURB-65 is most specific in predicting ICU admission and death. But CURB-65 is least sensitive in both predicting ICU admission and death. IDSA/ATS criteria had modest sensitivity and specificity in predicting ICU admission and death.⁽⁸⁾

CONCLUSION

The study shows that presence of comorbidities has an adverse impact on the outcome of the patients with COVID-19 infection. The elevated inflammatory markers like CRP, D Dimer and LDH predicted poor outcome. Pneumonia severity index was a useful marker to predict the outcome among patients of COVID. These parameters can be used for early detection of patients who might have an adverse outcome. Hence timely monitoring for and deterioration and early escalation of treatment may be done.

REFERENCES

- Huang C (2020), Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China; *The Lancet, volume- 395*.
- Zhou Fei (2020), Clinical course and risk factors for mortality of adult patients with COVID-19 in Wuhan, China, a retrospective study, *The Lancet, Volume 395, issue- 10229, page 1054-1062*.
- Zandkarimi E (2020), The prognostic factors affecting the survival of Kurdistan Province COVID-19 patients: A cross sectional study from February to May 2020. *International journal of Policy management 2020 August 22*
- Fine MJ (1997), "A prediction rule to identify low-risk patients with community-acquired pneumonia". *New England journal of Medicine, 336 (4): 243–250*.
- CelalSaticia"(2020) Performance of pneumonia severity index and CURB-65 in predicting 30-day mortality in patients with COVID-19 "; *International journal of Infectious diseases; Volume-98, Pages 84-8*.
- Fine, MJ; Auble, TE; Yealy, DM; Hanusa, BH; Weissfeld, LA; Singer, DE; Coley, CM; Marrie, TJ; Kapoor, WN; et al. (Jan 1997). "A prediction rule to identify low-risk patients with community-acquired pneumonia". *N Engl J Med, 336 (4): 243–250*.
- Kim MA (2019), Pneumonia severity index in viral community acquired pneumonia in adults. *PloSone, 2019 Mar 6; 14(3): e0210102*.
- Madhu S (2017) ,Comparative study of CURB-65, pneumonia severity index and IDSA/ATS scoring systems in community acquired pneumonia in an Indian tertiary care setting. *International Journal of Advances Medicine, 2017; 4(3):693-700*.