

## Original Research Paper

## RISK STRATIFICATION OF PATIENTS ADMITTED WITH COVID -19 TO A TERTIARY CARE HOSPITAL IN PUDUCHERRY USING ISARIC-4C MORATLITY SCORE

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**ABSTRACT:**

**Background:** Risk stratification of patients is the most important aspect in COVID-19 management. Prioritizing critical care services in situations of overwhelming numbers of patients is an absolute necessity. Globally many scoring systems have been specifically developed for risk stratification in COVID-19 patients. The ISARIC/WHO 4C Mortality score is a well validated risk stratification score. It is observed that the Covid disease present differently in different regions of the world. Hence the applicability of the ISARIC- 4C score in the Indian population needs to be studied. **Aims & Objectives** : The study was aimed (1) to find the association of various clinical and laboratory parameters as used by ISARIC/WHO 4C Mortality score with COVID19 mortality in a tertiary covid care centre. (2) to find the effectiveness of ISARIC-4C mortality score in predicting the in-hospital COVID19 mortality and validating its use in our population. **Material and Methods:** This is a single centre; retrospective medical record based observational study undertaken at a tertiary care hospital. 160 lab confirmed covid positive patients  $\geq 18$  years admitted in our institute during the peak of covid 2<sup>nd</sup> wave (May1, 2021 to May 31, 2021) were included. These 160 patients were divided into 2 groups. Group 1 had 80 patients who were treated and discharged and group 2 had 80 patients who died of the disease. The clinical data and laboratory parameters were retrospectively analysed from the health records of these patients. Data was compared between patients who were discharged and succumbed to death. Result: Age was significantly associated with the outcome of the patient. Higher age (age more than 60 years) had significantly higher proportion of deaths (58.8%) on comparison. Higher number of comorbidities (comorbidities more than 2) had significantly higher proportion of deaths (11.3%). There was significantly higher respiratory rate and lower SPO<sub>2</sub>, GCS score among those with bad outcome (death). There was a significantly higher CRP value among those with bad outcome (death). 4C Mortality risk score was significantly higher among those with bad outcome (death). Compared to those with Low & Intermediate risk, COVID 19 patients with High & Very high risk had 15.7 times higher chance of mortality which was significant. The Sensitivity analysis found that the risk stratification High & Very high risk had a sensitivity of 81.3% and specificity of 78.8% to detect bad outcome (death). The overall diagnostic accuracy was 80%. **Conclusion:** According to our study, the ISARIC 4C mortality score is highly predictive of in-hospital mortality and can be used to stratify and predict mortality in COVID-19 patients on admission to the hospital. It is an adaptable and good prognostic tool for use in Indian emergency departments and hospitals.

**KEYWORD:** ISARIC/WHO 4C Mortality score ( ISARIC/WHO 4C: International Severe Acute Respiratory And Emerging Infections Consortium / World Health Organisation-Coronavirus Clinical Characterisation Consortium)

**INTRODUCTION:**

Risk stratification of patients is the most important aspect in the management of COVID-19 as there is need to prioritize critical care services in situations of overwhelming numbers of patients. At the peak of the pandemic there were very less critical care beds available and there were a group of patients who initially appeared well but rapidly progressed to life-threatening illness requiring mechanical ventilation and ICU admission and many even succumbed to the disease. So the need to find out the most deserving patients using a very reliable risk stratification technique is a necessity. Globally many scoring systems have been specifically developed for risk stratification in COVID-19 patients. This study is conducted with the objective of finding out the association of various clinical and laboratory parameters as used by 'International Severe Acute Respiratory And Emerging Infections Consortium / World Health Organisation -Coronavirus Clinical Characterisation Consortium (ISARIC/WHO 4C)'Mortality score in predicting high risk patients of COVID-19. The 4C mortality score was derived and

validated within the ISARIC World Health Organization Clinical Characterisation Protocol UK study. The score was derived from a population of over 35,000 hospital in-patients. Validation on over 22,000 inpatient records indicated good discriminability. This is thus a well validated risk stratification score. It is observed that the Covid disease present differently in different regions of the world. Hence the applicability of the ISARIC -4C score in the local population needs to be studied. Ascertaining this ISARIC-4C risk score in our set up would help in triage of patients of severe disease at the outset, and shall prove beneficial in improving the standard of care.

**AIMS & OBJECTIVES\_:**

1. To find the association of various clinical and laboratory parameters as used by ISARIC/WHO 4C Mortality score with COVID19 mortality in a tertiary covid care centre.
2. To find the effectiveness of ISARIC-4C mortality score in predicting the in-hospital COVID19 mortality and validating its use in our population.

**MATERIAL AND METHODS:**

**1. STUDY DESIGN:** Single centre, Retrospective Medical Record based Observational Study.

**2. STUDY POPULATION :** All lab confirmed covid-19 patients ≥18 years of admitted in our institute( SVMCH&RC) during the peak of Covid 2<sup>nd</sup> wave( MAY 2021).

**3. SAMPLING METHOD:** Random sampling technique.

**4. SAMPLE SIZE:** 160 COVID POSITIVE Case records of patients admitted during the peak of Covid 2nd Wave (MAY 2021). This 160 covid positive patients were divided into 2 groups. Group1 (80 patients )- Treated and discharged after Covid illness. Group 2 ( 80 patients) - who died of COVID illness.

**5. ELIGIBILITY CRITERIA:**

**INCLUSION CRITERIA:**

All lab confirmed covid-19 patients (Covid-19 Positive by RTPCR or CBNAAT) ≥18 years of admitted in our institute during the peak of Covid 2<sup>nd</sup> wave ( May 2021)

**EXCLUSION CRITERIA:**

Patients with clinical & radiological finding suggestive of Covid-19 but not lab confirmed.

Covid-19 patient treated in emergency room(ER) but not admitted.

Patients admitted with terminal illness and incidentally diagnosed Covid-19.

Case records found with missing information.

**DATA COLLECTION METHODS:**

This study was carried out in the General Medicine Department of Sri Venkateshwaraa Medical College Hospital and Research Centre, Ariyur, Puducherry, a tertiary care referral centre for covid-19 cases. Prior approval from the Scientific Research Committee and Institutional Ethics Committee was sought. Waiver for Informed consent was sought as the data for this study was collected retrospectively from hospital medical records. After obtaining ethical clearance, all the records were obtained from the MRD department of the Hospital. Data collection was performed in accordance with relevant guidelines and regulations. Confidentiality of data was ensured. A total of 160 lab confirmed covid positive patients meeting the above mentioned eligibility criteria were included in the study. These 160 patients were divided into 2 groups. Group 1 had 80 patients who were treated and discharged and group 2 had 80 patients who died of the disease. The clinical data and laboratory parameters were retrospectively analysed from the health records of these patients. Data was compared between patients who were discharged and succumbed to death. Data was analysed using SPSS version 23.0 software. Data was collected using ISARIC-4C Mortality Score Proforma. The ISARIC-4C score incorporates age, sex, comorbidities, respiratory rate, peripheral oxygen saturation, Glasgow Coma Scale, blood urea nitrogen, and C-reactive protein. The 4C score ranges from 0 to 21 with risk groups defined as Low (0-3), Intermediate (4-8), High (9-14), and Very high (≥15). Comorbidities were evaluated according to Charlson comorbidity index. Co-morbidities include, chronic cardiac disease, chronic respiratory disease (excluding asthma), chronic renal disease (estimated glomerular filtration rate ≤30), mild to severe liver disease, dementia, chronic neurological conditions, connective tissue disease, diabetes mellitus (diet, tablet, or insulin controlled), HIV or AIDS, malignancy and obesity.

**RESULTS :**

**TABLE 1. GENERAL CHARACTERISTICS OF STUDY POPULATION**

		Status, n(%)		p value*
		Alive	Dead	
Age category	≤ 60 years	51(63.7%)	33(41.3%)	0.004
	>60 years	29(36.3%)	47(58.8%)	
Gender	Male	45(56.3%)	54(67.5%)	0.143
	Female	35(43.8%)	26(32.5%)	

*\*p value by chi-square test*

Age was significantly associated with the outcome of the patient. Higher age (age more than 60 years) had significantly higher proportion of deaths (58.8%) on comparison. Gender was not significantly associated with outcome of the patient.

**TABLE 2. NUMBER OF CO-MORBIDITIES AND OUTCOME OF THE PATIENT**

		Status, n(%)		p value*
		Alive	Dead	
Number of Comorbidities	Nil	26(32.5%)	20(25.0%)	<0.001
	1	46(57.5%)	28(35.0%)	
	2	8(10.0%)	23(28.7%)	
	>2	0	9(11.3%)	

*\*p value by chi-square test*

The Number of comorbidities was significantly associated with the outcome of the patient. Higher number of comorbidities (comorbidities more than 2) had significantly higher proportion of deaths (11.3%) on comparison.

**TABLE 3. DISTRIBUTION OF CLINICAL PARAMETERS**

	Status, mean ( $\pm$ SD)		p value*
	Alive	Dead	
Respiratory rate	21( $\pm$ 3.0)	24( $\pm$ 5.0)	<0.001
SPO2	90( $\pm$ 5.4)	84( $\pm$ 11.9)	<0.001
Glasgow Coma Scale	15( $\pm$ .0)	15( $\pm$ .3)	0.002

\*p value by independent t test

All the vital parameters were significantly associated with the outcome of the patient. There was significantly higher respiratory rate and lower SPO2, GCS score among those with bad outcome (death).

**TABLE 4. DISTRIBUTION OF LABORATORY PARAMETERS**

	Status, mean ( $\pm$ SD)		p value*
	Alive	Dead	
Urea MG/DL	57( $\pm$ 19.0)	60( $\pm$ 36.2)	0.426
CRP MG/DL	12( $\pm$ 11.7)	27( $\pm$ 24.3)	<0.001

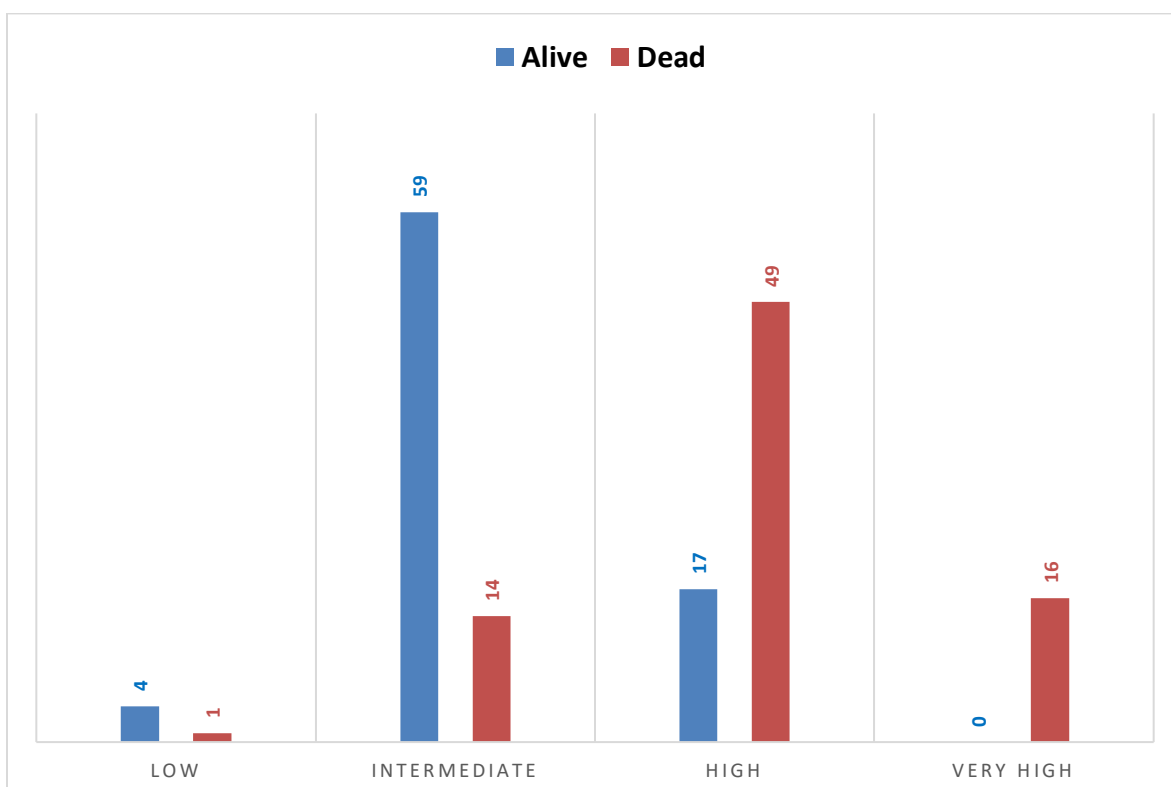
\*p value by independent t test

CRP value was significantly associated with the outcome of the patient. There was significantly higher CRP values among those with bad outcome (death). The Blood Urea levels was not significantly associated with outcome of the patient.

**TABLE 5: ASSOCIATION OF 4C MORTALITY SCORE AND RISK STRTIATIFICATION WITH THE OUTCOME OF THE PATIENT.**

		Status		p value
		Alive	Dead	
4C Mortality score, mean ( $\pm$ SD)		8( $\pm$ 4.6)	11( $\pm$ 3.5)	<0.002*
Risk, n (%)	Low	4(5.0%)	1(1.3%)	<0.001^
	Intermediate	59(73.8%)	14(17.5%)	
	High	17(21.3%)	49(61.3%)	
	Very high	0	16(20.0%)	

\*p value by independent t test; ^- p value by chi-square test



4C Mortality score and risk stratification were significantly associated with the outcome of the patient. The risk score was significantly higher among those with bad outcome (death).

**TABLE 6: ASSOCIATION TO FIND THE EFFECTIVENES OF 4C MORTALITY SCORE IN PREDICTING MORTALITY**

Risk	Status, n (%)		Odds Ratio (95% CI)	p value*
	Dead	Alive		
High& Very high	65 (81.2%)	17(21.3%)	15.7 (7.4- 35.1)	<b>&lt;0.001</b>
Low& Intermediate	15 (18.8%)	63 (78.7%)		

\*- *p value by chi-square test*

Compared to those with Low &Intermediate risk, COVID 19 patients with High &Very high risk had 15.7 times higher chance of mortality which was significant.

**TABLE 7: SENSITIVITY ANALYSIS AMONG HIGH AND VERY HIGH-RISK PATIENTS TO DETECT BAD OUTCOME**

Sensitivity analysis among high and very high-risk patients to detect bad outcome

Parameters	Value
Sensitivity	81.3%
Specificity	78.8%
Positive Predictive Value	79.3%
Negative Predictive Value	80.8%
Diagnostic Accuracy	80%

The Sensitivity analysis found that risk stratification High & Very high risk had a sensitivity of 81.3% and specificity of 78.8% to detect bad outcome (death). The overall diagnostic accuracy was 80%.

**TABLE 8 : ASSOCIATION BETWEEN COMORBIDITIES AND OUTCOME**

		Status, n (%)		p value*
		Alive	Dead	
<b>Diabetes Mellitus</b>	Yes	39(48.8%)	49(62.0%)	<b>0.042</b>
	No	41(51.2%)	30(38.0%)	
<b>Hypertension</b>	Yes	18(22.5%)	30(37.5%)	<b>0.038</b>
	No	62(77.5%)	50(62.5%)	
<b>Chronic Kidney Disease</b>	Yes	0	9(11.3%)	<b>0.002</b>
	No	80(100.0%)	71(88.8%)	
<b>Coronary Artery Disease</b>	Yes	0(0.0%)	7(8.8%)	<b>0.007</b>
	No	80(100.0%)	73(91.3%)	
<b>Respiratory Illness</b>	Yes	5(6.3%)	4(5.0%)	0.732
	No	75(93.8%)	76(95.0%)	

\*- *p value by chi-square test*

Presence of Diabetes Mellitus, Hypertension, Chronic Kidney Disease and Coronary Artery Disease were significantly associated with the outcome of the patient. There was significantly higher proportion of all the above co-morbidities among those with bad outcome (death).

## DISCUSSION:

We sought to confirm the predictability of this score in our community as this (ISARIC-4C) Study was conducted in England. ISARIC-4C considers the gender in risk prediction. Although male sex was associated to worse outcome in several reports, patient gender was not significantly associated to a different outcome in our study which is comparable to the result by Covino M et al. Our study concur with reports by Williamson EJ et

al, Mikami T et al, Feng Y et al and Onder G et al, that advanced age is a strong predictor of death from COVID-19. Higher number of comorbidities (>2) had higher proportion of deaths (11.3%). Presence of DM, S.HTN, CKD & CAD were significantly associated with higher proportion of bad outcome(death). Just like several other studies (Gong J et al, Henry BM et al, Ji W et al), our study also found that CRP levels were significantly associated with COVID-19 severity. In our

study, the ISARIC 4C mortality score was *highly predictive* of in-hospital mortality. COVID 19 patients with High & Very high risk had 15.7 times higher chance of mortality as per our study (Table 6). The mortality increased from 18% in the low & intermediate risk category to 80% in the high & very high risk category (Table 7). It is comparable to the results of Ali R et al who found mortality to increase from 10% in low risk to 80% in high risk. The Sensitivity analysis of our study found that risk stratification among High & Very high risk category had a sensitivity of 81.3% and specificity of 78.8% to detect bad outcome (death). The overall diagnostic accuracy was 80% (Table 7). This is in agreement with the study by Aaron Jones et al.

### CONCLUSION:

According to our study, the ISARIC 4C mortality score is highly predictive of in-hospital mortality and can be used to stratify and predict mortality in COVID-19 patients on admission to the hospital. It is an adaptable and good prognostic tool for use in Indian emergency departments and hospitals. It is especially of great significance among high or very high risk category and calls for aggressive ICU care in these patients from the outset. This score can help us improve the standard of care during the subsequent wave of Covid infection. We propose that this score be used in every COVID-19 patient who presents to the hospital.

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