Original Research Article

Epidemiology and Management of adult Corona-virus disease patients, in Intensive care unit

Dantoor Suresh[1], Vikram Kumar Naidu[2*], Dodooju Veera Bhadreshwara Anusha[3], Noule Vamshi Krsihna[4], Saamala Sri Harsha[5]

[1]Associate professor, Department of Anaesthesia, RVM Institute of Medical Sciences and Research Centre, Siddipet, Telangana, India
[2]Associate professor, Department of Anaesthesia, RVM Institute of Medical Sciences and Research Centre, Siddipet, Telangana, India
[3]Assistant professor, Department of Community Medicine, RVM Institute of Medical Sciences and Research Centre, Siddipet, Telangana, India
[4]Assistant professor, Department of Radiology, RVM Institute of Medical Sciences and Research Centre, Siddipet, Telangana, India
[5]Senior Resident, Department of Radiology, RVM Institute of Medical Sciences and Research Centre, Siddipet, Telangana, India

Received: 21-09-2021 / Revised: 05-10-2021 / Accepted: 07-11-2021

Abstract

Context: Corona virus disease (COVID-19) is an infectious disease. About 5% become critically ill and need intensive care. Being a novel disease, there is need of research on safe and effective management especially in Intensive care unit (ICU). **Aims:** To know epidemiology and management of adult COVID-19 disease patients in ICU. **Settings and Design**: An observational study done in adult COVID-19 patients admitted in ICU of a tertiary care hospital. **Methods and Material:** Purposive sampling method was used and data in 241 adult COVID-19 patients was collected on sociodemograpy, comorbidities, clinical and radiological severity, risk categorization **(**by Quick Sequential Organ Failure Assessment (qSOFA) and Systemic Inflammatory Response Syndrome (SIRS)**).** Biochemical investigations done, treatment given and outcome were recorded. **Statistical analysis used**: Data analysed using SPSS 20. Chi-square test and Mann Whitney U test was used. P<0.05 was considered statistically used. **Results**: Out of 241 Patients, 69(28.6%) died. Mortality was significantly high in age group > 60 years. Patients with higher Lactate dehydrogenase (LDH), serum ferritin and procalcitonin levels, have high proportion of mortality. Patients with Diabetes mellitus (41.1%), cardiovascular disease (6.2%), CTSS score >18 (44.7%) and SIRS score 2-4(32%) have high mortality. Inotropes, anticoagulation, anti-inflammation and convalescent Plasma therapy was given in and awake proning practiced in 41.1%, 72.6%, 73.4%, 36.9% and 23.6% respectively. **Conclusions:** ICU Mortality of COVID-19 patient was 28.6%. Patients with age > 60 years, diabetes mellitus, cardiovascular disease, higher LDH, serum ferritin and procalcitonin have, significantly higher prevalence of mortality.

Key-words: Epidemiology, adult, Corona Virus disease, Intensive Care management.

Introduction

In December 2019, a local outbreak of pneumonia of unknown aetiology was identified in Wuhan (China), and was found to be caused by a novel coronavirus, later called as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) .Corona virus diseases (COVID-19) is a recent pandemic[1]. In India 30,752,950 were infected, with 405,939 deaths as on 9th July 2021[2].

Fever, cough, shortness of breath, chest pain were the most common presenting symptoms of patients with COVID-19 disease.

*Correspondence
Dr. T. Vikram Kumar Naidu
Associate professor, Department of Anaesthesia, RVM Institute of Medical Sciences and Research Centre, Siddipet, Telangana, India.
E-mail: anu.dvb@gmail.com

Of which 15% become seriously ill and require oxygen and 5% become critically ill and need intensive care. Complications include respiratory failure, acute respiratory distress syndrome (ARDS), sepsis, septic shock; thromboembolism and multiorgan failure[3]. Elderly patients with systemic comorbidities like diabetes, hypertension, ischaemic heart disease and polytrauma are more severely affected and have worse outcomes[4, 5].Being a novel disease, there is need of research on safe and effective management especially in Intensive Care Unit (ICU) to decrease the mortality. This study deals with epidemiology and treatment patterns in adult COVID-19 disease patients.

Material and Methods

An observational study was done in, adult (>18 years) COVID-19 patients in Intensive Care Unit (ICU) of a tertiary care hospital. COVID-19 patients were diagnosed by positive Reverse Transcription Polymerase Chain Reaction (RTPCR) and SARS-CoV-2 antigen-RDT.6]. During study Period (May 2020 to April 2021) 1232 COVID-19 patients were admitted in to the hospital of which 463 adult patients got either admitted in to, or shifted in to ICU. Outcomes measured were either death or discharge after recovery. Patients who got discharged against medical advice (DAMA) were excluded from the study.

Purposive sampling method was used. Sample size arrived at by using the formula for finite population.

Where, Z α is the standard normal deviate, 1.96 at 95% confidence interval.

P = Prevalence of COVID-19 patients with need for ICU care = 5%[3]. Hence P = 0.05, 1-P = (1-0.05)

e = Absolute precision taken as 2% (<5% is acceptable)

N = study population (adult patients with COVID-19 disease admitted in ICU during study period) = 463

$$Sample\ size(n) = \frac{\frac{z^2 X\ p(1-p)}{e^2}}{1+\frac{z^2 X\ p(1-p)}{e^2 N}}$$

$$Sample\ size(n) = \frac{\frac{(1.96)^2 X\ 0.05(1-0.05)}{(0.02)^2}}{1+\frac{(1.96)^2 X\ 0.05(1-0.05)}{(0.02)^2\ 463}}$$

$$Sample\ size(n) required\ is = 230$$

Corrected sample size with non response rate as 15% was 265.

Data collection

After obtaining institutional ethical committee clearance and informed consent from patients nearest kin, data on socio demographic factors, presenting symptoms, comorbidities, clinical status, severity and risk categorisation, laboratory findings, radiological findings, treatment given and outcome were collected, in a structured questionnaire.

Procedure

Of the 265 Patients, 24 (DAMA) were excluded hence data analysed for 241 patients. Clinical severity assessed by following clinical guidance for management of adult COVID-19 patient by ministry of health family welfare Govt. of India. Radiological severity by CT chest severity score (CT-SS).

Clinical severity assessed as, Mild disease: Upper respiratory tract symptoms (&/or fever) without shortness of breath or hypoxia. Moderate disease: Any one of: 1. Respiratory rate > 24/min, breathlessness 2. Oxygen saturation (SPO2): 90% to < 93% on room air. Severe disease: Any one of: 1. Respiratory rate >30/min, breathlessness 2. SPO2 < 90% on room air[6].

The CT-SS score was calculated based on the extent of lobar involvement. Each of the five lung lobes was scored with range 0–5, score 0 as no involvement, score 1 as < 5% involvement, score 2 as 5–25% involvement, score 3 as 26–49% involvement, score 4 as 50–75% involvement, and 5 as > 75% involvement. The total CT score given on a scale from Zero (no involvement) to 25 (maximum involvement)[7,8]. Lung involvement was graded as normal (CT-SS=0), mild (CT-SS <7), moderate (CT-SS = 8-17), and severe (CT-SS > 18).

Risk categorisation was done by Quick Sequential Organ Failure Assessment (qSOFA) and Systemic Inflammatory Response Syndrome (SIRS). qSOFA scored as 1 point each for altered mental state, systolic blood Pressure ≤100 mmHg, respiratory rate ≥22 breaths/min; score range, 0–3 Points[9]. SIRS scored as 1 point each for temperature >38 ℃ or <36 ℃, heart rate > 90 beats/min, respiratory rate >20 breaths/min or partial pressure of carbon dioxide ($PaCO_2$) < 4.3 kilopascal (kPa), White blood cell count >12000 cells/mm^3 or < 4000 cells/mm^3**;** score range, 0–4 points[10].

Blood sample collected and ICU management done following, Infection prevention and control practices during health care by WHO[11]. Blood sample analysed for Complete blood picture, renal function tests, liver function tests, D dimer and inflammatory markers (C- Reactive Protein (CRP), Lactate Dehydogenase (LDH), Serum Ferritin and Procalcitonin) and arterial blood gases (ABG).

Respiratory support started by oxygen therapy at 5 L/min delivered via a face mask. Flow rates titrated to reach target SPO2 ≥ 90%. In Patients with increasing oxygen requirement, High – Flow Nasal Cannula oxygenation (HFNO) or non – invasive mechanical ventilation (NIV) was used. NIV: setting - Pressure support (PS) 5-15 cm H2O adjusted to tidal volume (TV) of 5-7 ml/kg and Positive end expiratory pressure (PEEP) 5-10 cm H2O and fractional inspired oxygen (FiO2) @ 0.5 -1.0 titrated to target SPO2> 94%. HFNC settings: Started at a flow rate of 20 to 30L/min and an FiO2 of 40%; titrated flow rate up to a maximum of 60L/min increments of 5 to 10L/min based on respiratory rate, work of breathing and SPO2. If target SPO2 is not achieved with increasing flow alone, FiO2 was increased in steps of 5 to 10% up to a maximum of 100%.

If NIV was not tolerated, along with presence of haemodynamic instability, altered mental status or multi-organ failure, intubation was done. Started using lower TV (TV 4–8 ml/kg predicted body weight, PBW) and lower inspiratory pressures (plateau pressure <30 cm H_20). Lung protective ventilation strategy by ARDS net protocol was followed (TV 6ml/kg, RR 15-35/min, PEEP 5-15cm H2O; target plateau pressure < 30cm H2O, target SPO2 88-95% and/or partial pressure of oxygen (PaO2) 55-80mmHg). Prone ventilation considered, when there was refractory hypoxemia; PaO2/FiO2 ratio 0.6 with PEEP > 5cm H2O.

Data analysis

Data analysed for 241patients using SPSS version 20. Chi-square test and Mann Whitney U test was used. P<0.05 was considered statistically significant.

Results

Out of 241 COVID-19 patients, 69(28.6%) died and 172(71.4%) were discharged. Majority of patients belong to age group 41-60 years. Males were 69.7%. Mortality was significantly high in age group >60 years (35.9%) and males (33.3%). Mortality was slightly high in patients residing in rural area (29.4%). Habit of smoking (71.6%) and alcohol (73.7%) though slightly more in patients who got discharged was not statistically significant. (Table 1)

Out of 241 patients, 24(10%) have multiple pre-existing comorbidities. Diabetes mellitus (41.1%) was the most common comorbidity, followed by hypertension (22.8%), chronic lung disease (19.1%), cardiovascular disease (6.2%) and cerebro vascular disease (5.4%). Mortality was significantly high in patients with diabetes (36.4%) and cardiovascular disease (60%) compared with those who do not have diabetes and cardiovascular disease. Mortality was high in patients with hypertension, chronic lung disease and cerebro vascular disease but was not statistically significant (Table 1).

Table 1: Distribution based on socio-demographic characteristics and pre existing comorbidities

Socio demographic variables	Groups	Survived (172)	Died (69)	Frequency (n= 241)	X^2 / P value
Age	18- 40	29(93.5%)	2(6.5%)	31(12.9%)	X^2= 10.1613. P-0.006216
	41-60	77(72%)	30(28%)	107(44.4%)	
	>60	66(64.1%)	37 (35.9%)	103(42.7%)	
Sex	Male	112(66.7%)	56(33.3%)	168 (69.7%)	X^2 = 6.0026.
	Female	60(82.2%)	13(17.8%)	73(30.3%)	P- 0.014285.
Literacy status	Illiterate	11(57.9%)	8 (42.1%)	19(7.9%)	X^2 = 3.406.
	Primary school	47 (74.6%)	16 (25.4%)	63(26.1%)	P -0.33316 1
	Secondary school	67(68.4%)	31(31.6%)	98(40.7%)	
	Undergraduate & Post graduate	47(77%)	14(23%)	61(25.3%)	

Residence	Urban	71(72.4%)	27(27.6%)	98(40.7%)	$X^2 = 0.0942$. P - 0.758875
	Rural	101(70.6%)	42(29.4%)	143(59.3%)	
Smoking	Present	53(71.6%)	21(28.4%)	74(30.7%)	$X^2 = 0.0033$. P - 0.954
	Absent	119(71.3%)	48 (28.7%)	167(69.3%)	
Alcohol	Present	70(73.7%)	25(26.3%)	95 (39.4%)	$X^2 = 0.4113$. P - 0.521331.
	Absent	102(69.9%)	44(30.1%)	146(60.6%)	
Diabetes mellitus	Present	63(63.6%)	36(36.4%)	99(41.1%)	4.9171/ P -0.026592
	Absent	109(76.8%)	33(23.2%)	142(58.9%)	
Hypertension	Present	35(63.6%)	20(36.4%)	55(22.8%)	2.0855/P -0.148703
	Absent	137(73.6%)	49(26.3%)	186(77.2%)	
Chronic lung disease	Present	29(63%)	17(37%)	46(19.1%)	1.9286/ P -0.164908
	Absent	143(73.3%)	52(26.7%)	195(80.9%)	
Cardiovascular diseases	Present	6(40%)	9(60%)	15(6.2%)	7.7031/ P -0.005513
	Absent	166(73.5%)	60(26.5%)	226(93.8%)	
Cerebro vascular disease	Present	7(53.8%)	6(46.2%)	13(5.4%)	2.0649/ P - 0.150722
	Absent	165(72.4%)	63(27.6%)	228(94.6%)	

Multiple symptoms were seen in 93.3% of patients. Fever, body pains, sore throat/ cough and shortness of breath was seen in 89.6%, 90%, 76.8%, and 62.2% of patients respectively (figure 1).

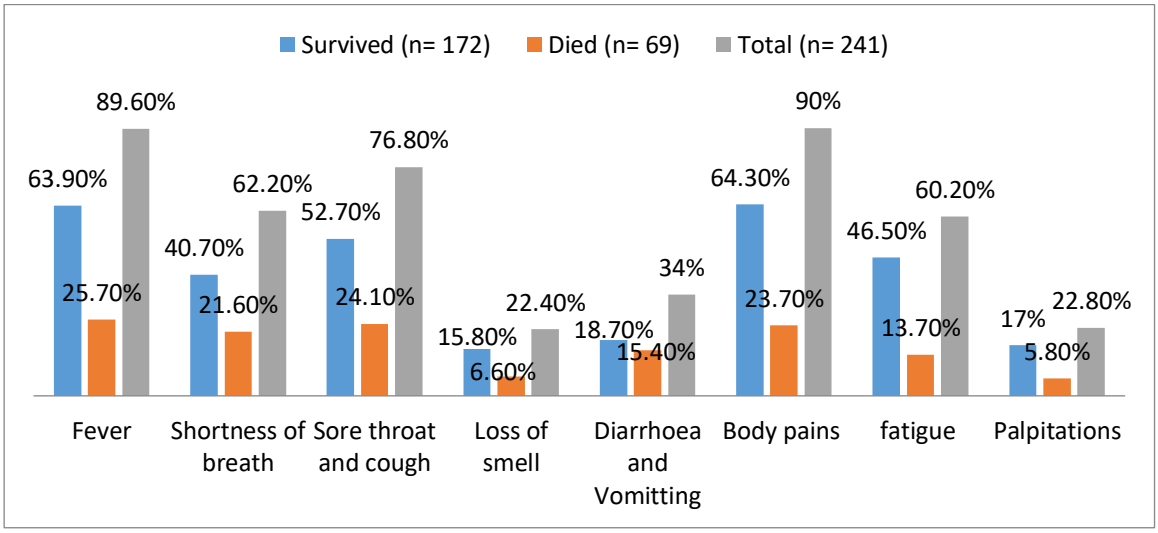

Fig 1: Distribution of patients by presenting symptoms at the time of admission

Median and Interquartile range of LDH, serum ferritin and procalcitonin was significantly higher in patients who died compared with patients who survived. Median and Interquartile range of White blood cell count (WBC count), CRP, D dimer and serum creatinine of died patients was higher compared to those who survived and it was not significant (Table 2).

Table 2: Distribution based on Biochemical investigations expressed as Median and inter quartile range (Q1- Q3)

Biochemical investigations (normal range)	Survived (172)	Died (69)	Total (n=241)	Mann-Whitney U Test/ P value
WBC count (4000-11000cells/cumm)/	7200 (4900-11500)	9400 (3400-21000)	8900 (5900- 11600)	U= 96/ P - 0.238.
CRP, (0-6 IU/mL)	21(12-57)	45(21-389)	27(12-384)	U-60/ P-0.0601
LDH (140-280 u/l)	421(229-456)	651(389-939)	562(341-865)	U-55.5/ P-0.03846.
Serum Ferritin (15-200ng/dl)	210(96- 342)	389(261-651)	271(96-367)	U – 51/ P-value - .02382
D dimer (uP to 500ng/ml)	567(423- 812)	785(321-1829)	678(423-1390)	U - 94.5/ P-value 0.41794
Procalcitonin (up to 0.05ng/ml)	0.11(0.02- 0.34)	0.41(0.15- 0.87)	0.22(0.04- 0.79)	U- 52.5/ P- 0.01314
Serum Creatinine (0.5-1.3mg/dl)	0.9(0.6- 1.2)	1.2(0.9- 3.2)	1.2(0.7- 1.6)	U- 93.5/ P-0.39532.

Mortality high in patients with Severe COVID-19 (34.2%) disease, CTSS score >18 (44.7%) and SIRS score 2-4(32%) which was statistically significant compared to patients with moderate COVID-19 disease, CTSS score <18, and SIRS score range 0-1. Patients with qSOFA score 2-3(30.2%) have high mortality compared to patients with qSOFA score range 0-1. but was not statistically significant. (Table 3). Complications

detected in patients include respiratory failure (12%), ARDS (63.1%), septic shock (41.1%) thromboembolism (17.9%) and multiorgan failure (2.4%).

Table 3: Distribution of study patients by disease severity and risk stratification.

Variables at the time of admission	Groups	Survived (172)	Died (69)	Frequency (n= 241)	X^2 / P value
Clinical severity	Moderate COVID-19 disease	72(80.9%)	17(19.1%)	89(36.9%)	6.2714/ P- 0.01227
	Severe COVID-19 disease	100(65.8%)	52(34.2%)	152(63.1%)	
CTSS severity score	Mild (≤ 7)	23(95.8%)	1(4.2%)	24(10%)	28.9137/ P- < 0.00001
	Moderate (8-17)	86(83.5%)	17(16.5%)	103(42.7%)	
	Severe (≥18 and more)	63(55.3%)	51(44.7%)	114(47.3%)	
qSOFA score	Score range 0-1	38(77.6%)	11(22.4%)	49(20.3%)	1.1502/ P- 0.28349
	Score range 2-3	134(69.8%)	58(30.2%)	192(79.7%)	
SIRS score	Score range 0-1	58 (80.6%)	14(19.4%)	72(29.9%)	4.2403/ P- 0.039475.
	Score range 2- 4	114(67.5%)	55(32.5%)	169(70.1%)	

Management by Invasive mechanical ventilation (IMV), inotropes, anticoagulation (Unfractionated heparin or low molecular weight heparin 4000 IU (LMWH) either twice or once, given subcutaneous), anti-inflammation (Methyl Prednisolone 1 to 2mg/kg Intra venous in 2 divided doses or 0.2-0.4mg/kg of dexamethasone), convalescent Plasma therapy and awake proning (conscious patient who is able to self prone with minimal assistance) done in 31.5%, 41.1%, 72.6%, 73.4%, 36.9% and 23.6% respectively. Ivermectin (92.1%) was most commonly given followed by azithromycin (76.4%), remdesivir (69.3%), hydroxychloroquine (51.5%), and favipiravir (30.7%).

Mortality was significantly high in patients who received inotropes (41.4%) and anti inflammatory drugs (24.1%). Mortality significantly low in patients who were given ivermectin (26.1% Vs 57.9%). Though mortality was high in patients on IMV (31.5%), anti coagulation (29.7%), hydroxychloroquine (31.5%), remdesivir (29.3%) and azithromycin (29.9%) it was not statistically significant. Mortality was low in patients on convalescent plasma therapy (28.1%) and favipiravir (27%) but was not significant. (Table 4).

Table 4: Distribution by treatment given to COVID-19 patients

ICU COVID-19 treatment		Survived (172)	Died (69)	Total (n=241)	X^2 / P value
Management of Hypoxia	Oxygen Mask	35(77.8%)	10(22.2%)	45(18.7%)	2.801/P-0.423336
	HFNO	41(75.9%)	13(24.1%)	54(22.4%)	
	NIV	43(65.2%)	23(34.8%)	66(27.4%)	
	IMV	53(69.7%)	23(30.3%)	76 (31.5%)	
Management of Shock	Inotropes Received	58(68.6%)	41(41.4%)	99(41.1%)	13.4374/ P-0.000247
	Inotropes Not Received	114(80.3%)	28(19.7%)	142(58.9%)	
Anticoagulation	Received	123(70.3%)	52(29.7%)	175(72.6%)	0.3672/ P -0.54454
	Not Received	49(74.2%)	17(25.8%)	66(27.4%)	
Anti inflammation	Steroid received	117(66.1%)	60(33.9%)	177(73.4%)	9.0509/ P 0.002626.
	Not received	55(85.9%)	9(14.1%)	64(26.6%)	
Convalescent Plasma therapy	Received	64(71.9%)	25(28.1%)	89(36.9%)	0.0202/ P- 0.886984
	Not Received	108(71.1%)	44(28.9%)	152(63.1%)	
Antivirals	Received Remdesivir	118(70.7%)	49(29.3%)	167(69.3%)	0.1344/ P- 0.713905
	Received Favipiravir	54(73%)	20(27%)	74(30.7%)	
Hydroxychloroquine	Received	85(68.5%)	39(31.5%)	124 (51.5%)	0.9947/ P- 0.318599
	Not received	87(74.4%)	30(25.6%)	117(48.5%)	
Ivermectin	Received	164(73.9%)	58(26.1%)	222(92.1%)	8.6446/ P- 0.00328
	Not Received	8(42.1%)	11(57.9%)	19(7.9%)	
Azithromycin	Received	129(70.1%)	55(29.9%)	184(76.4%)	0.605/ P- 0.436669
	Not Received	43(75.4%)	14(24.6%)	57(23.6%)	
Awake proning	Practiced	49(86%)	8(14%)	57(23.6%)	7.7835/ P- 0.005273
	Not practiced	123(66.8%)	61(33.1%)	184(76.4%)	

Discussion

Mortality in the current study in COVID-19 patients admitted in ICU was 28.6%, which was low compared to study by Rahim F et,al (77%) and Armstrong et,al (35.5%)[12,13]. Age group >60 years and male gender have statistically significant higher deaths in this study similar to study by Wang F et,al[14]. Smoking history though high in survivals was not significant in this study unlike study by Alqahtani JS where it was associated with mortality (38.5%)[15].

Mortality was significantly high in patients with diabetes (36.4%) and cardiovascular disease (60%). In patients with hypertension mortality though high, was not significant in the current study whereas, Wang F et al. stated that pre-existing hypertension, cardiovascular disease and diabetes were associated with increased risk of mortality in COVID-19 patient[14].

Mortality was significantly high in patients with higher LDH, serum ferritin and procalcitonin levels in this study similar to study by Faryal Khamis et al. White blood cell count (WBC count), CRP, D dimer and serum creatinine of patients who died was higher and it was not statistically significant in this study, unlike study by Faryal Khamis et al where it was significant[16].

In the current study mortality was more in severe COVID-19 disease, and SIRS score 2-4 which was statistically significant. Though mortality was more in patients with qSOFA score 2- 3 it was not significant unlike study by Elhadi M et,al where Lower quick SOFA scores were associated with better survival[17]. Jhang JG et al stated that low accuracy of SIRS and qSOFA prediction in COVID-19 clinical outcomes is that there are many "silent hypoxaemia" patients in severe COVID-19. SIRS and qSOFA has limitations in predicting the outcomes of COVID-19[10].

Supplemental oxygen therapy via face mask, HFNO and NIV was given in 68.5% and IMV in 31.5% in the current study where as in study by Oliveira et al 12 (9.2%) and 109 (83.2%) respectively. Inotropes, anticoagulation, anti-inflammation and convalescent Plasma therapy was given in and awake proning practiced in 41.1%,

72.6%, 73.4%, 36.9% and 23.6% respectively where as in study by Oliveira et al vasopressor used in 95 (72.5%), Convalescent Plasma in 49 (37.4%) and Corticosteroids in 77 (58.8%)[18].
In this study Ivermectin (92.1%) was most commonly given followed by azithromycin (76.4%), remdesivir (69.3%), hydroxychloroquine (51.5%), and favipiravir (30.7%). In study by Oliveira et al, azithromycin (93.9%), hydroxychloroquine (93.9%) and remdesivir (10.7 %.) was given[18]. This study shows no significant difference with remdesivir treatment similar to study by Mahajan, et al[19].

Conclusions

Intensive Care Unit mortality of COVID-19 patients was 28.6%. Patients with age >60 years, males, with diabetes mellitus, with cardiovascular disease, raised serum inflammatory markers (like higher LDH, serum ferritin and procalcitonin levels), Severe COVID-19disease, CTSS score >18 and SIRS score 2-4 have significantly higher prevalence of mortality. Acute Respiratory Distress Surgery was the most common complication. Mechanical ventilation provided to 31.5% of patients. Inotropes, anticoagulation, anti inflammation, convalescent plasma therapy was given in and awake proning practiced in 41.1%, 72.6%, 73.4%, 36.9% and 23.6% respectively. Ivermectin (92.1%) was most commonly given followed by azithromycin (76.4%), remdesivir (69.3%), hydroxychloroquine (51.5%), and favipiravir (30.7%). Mortality significantly low in patients given ivermectin. No significant difference with remdesivir treatment.

Recommendations

As ICU mortality was high multi-centric studies with emphasis on prognostic risk categorization, dealing with silent hypoxia and cytokine storm for further research is needed.

Limitations

This is an observational study from a single hospital.

References

1. World Health Organisation. WHO statement regarding cluster of pneumonia cases in Wuhan, China. Available at https://www.who.int/china/news/detail/09-01-2020-who-statement-regarding-cluster-of-pneumonia-cases-in-wuhan-china. Last accessed on 9th july 2021.
2. Gardner L. Mapping COVID – 19. COVID-19 Dashboard by the centre for systems science and Engineering (CSSE) at Johns Hopkins University (JHU). Available at https://www.arcgis.com/apps/dashboards/bda7594740fd40299423467b48e9ecf6. Last accessed on 9th july 2021
3. World Health Organisation. WHO Coronavirus disease (COVID-19) 12 October 2020 | Q&A. Available at https://www.who.int/emergencies/diseases/novel-coronavirus-2019/question-and-answers-hub/q-a-detail/coronavirus-disease-covid-19**.** Last accessed on 9th july 2021
4. Boulle A, Davies MA, Hussey H, Ismail M, Morden E, Vundle Z, et al. Risk factors for COVID-19 death in a population cohort study from the Western Cape Province, South Africa. Clin Infect Dis 2020:ciaa1198. Available at : https://pubmed.ncbi.nlm.nih.gov/32860699/. Last accessed on 9th july 2021
5. Bajwa SJ, Sarna R, Bawa C, Mehdiratta L. Peri-operative and critical care concerns in coronavirus pandemic. Indian J Anaesth 2020;64:267-74.
6. AIIMS/ ICMR-COVID-19 National Task Force/Joint Monitoring Group (Dte.GHS) Ministry of Health & Family Welfare, Government of India. April 22 2021. Clinical guidance for management of adult covid-19 Patient. Available at https://www.mohfw.gov.in/Pdf/COVID19ManagementAlgorithm22042021v1.Pdf. Last accessed on 9th july 2021
7. Francone M, Iafrate F, Masci GM, Coco S, Cilia F, Manganaro L, et,al. Chest CT score in COVID-19 Patients: correlation with disease severity and short-term Prognosis. Eur Radiol. 2020 Dec;30(12):6808-6817.
8. Pan F, Ye T, Sun P, Gui S, Liang B, Li L, et,al. Time Course of Lung Changes at Chest CT during Recovery from Coronavirus Disease 2019 (COVID-19). Radiology. 2020 Jun;295(3):715-721.
9. Seymour CW, Liu VX, Iwashyna TJ. Assessment of Clinical Criteria for Sepsis: For the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA.* 2016;315(8):762–774.
10. Jang JG, Hur J, Hong KS, Lee W, Ahn JH. Prognostic Accuracy of the SIRS, qSOFA, and NEWS for Early Detection of Clinical Deterioration in SARS-CoV-2 Infected Patients. J Korean Med Sci. 2020 Jun 29;35(25):e234. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7324266/. Last accessed on 9th july 2021.
11. WHO: World Health organization /Infection Prevention and control during health care when coronavirus disease (COVID-19) is suspected or confirmed: Interim guidance. Available at: https://www.who.int/Publications/i/item/WHO-2019-nCoV-IPC-2020.4. Last accessed on 9th july 2021
12. Rahim F, Amin S, Noor M, Bahadur S, Gul H, Mahood A, Usman M, Khan MA, Ullah R, Shahab K. Mortality of Patients With Severe COVID-19 in the Intensive Care Unit: An Observational Study From a Major COVID-19 Receiving Hospital. Cureus. 2020 Oct 12;12(10):e10906. doi: 10.7759/cureus.10906. Available at : https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7657313/. Last accessed on 9th july 2021
13. Armstrong RA, Kane AD, Kursumovic E, Oglesby FC, Cook TM. Mortality in patients admitted to intensive care with COVID-19: an updated systematic review and meta-analysis of observational studies. Anaesthesia. 2021 Apr;76(4):537-548.
14. Wang F, Cao J, Yu Y, Ding J, Eshak ES, Liu K, et,al. Corrigendum to: Epidemiological characteristics of Patients with severe COVID-19 infection in Wuhan, China: evidence from a retrospective, observational study. Int J Epidemiol. 2021 Jan 23;49(6):1940-1950.
15. Alqahtani JS, Oyelade T, Aldhahir AM, Alghamdi SM, Almehmadi M, Alqahtani AS, et al. Prevalence, Severity and Mortality associated with COPD and Smoking in Patients with COVID-19: A Rapid Systematic Review and Meta-Analysis. PLoS ONE 2020 may 11;15(5) :e0233147.: Available at: https://pubmed.ncbi.nlm.nih.gov/32392262/. Last accessed on 9th july 2021
16. Khamis F, Memish Z, Bahrani MA, Dowaiki SA, Pandak N, Bolushi ZA, et,al. Prevalence and predictors of in-hospital mortality of patients hospitalized with COVID-19 infection. J Infect Public Health. 2021 Jun;14(6):759-765.
17. Elhadi M, Alsoufi A, Abusalama A, Alkaseek A, Abdeewi S, Yahya M et, al. Epidemiology, outcomes, and utilization of intensive care unit resources for critically ill COVID-19 patients in Libya: A prospective multi-center cohort study. Plos one. 2021 ;16(4):e0251085.
18. Oliveira E, Parikh A, Lopez-Ruiz A, Carrilo M, Goldberg J, Cearras M, et,al. ICU outcomes and survival in Patients with severe COVID-19 in the largest health care system in central Florida. PloS One. 2021 Mar 25; 16(3):e0249038.
19. Mahajan L. Singh AP, Gifty. Clinical outcomes of using remdesivir in patients with moderate to severe COVID-19: A prospective randomised study. Indian J Anaesth 2021;65:41-6.

Conflict of Interest: Nil Source of support: Nil