Factors affecting the outcomes in patients with acute respiratory distress syndrome in a tertiary care setting

Muhammed Rashid^a, Manasvini Ramakrishnan^a, Deepa Sudalai Muthu^a,
Viji Pulikkel Chandran^a, Girish Thunga^a, Vijayanarayana Kunhikatta^a, Vishal Shanbhag^b,
Raviraja V. Acharya^c, Sreedharan Nair^{a,*}

^a Department of Pharmacy Practice, Manipal College of Pharmaceutical Sciences, Manipal Academy of Higher Education, Manipal, 576104, India

^b Department of Critical Care Medicine, Kasturba Medical College, Manipal Academy of Higher Education, Manipal, 576104, India

^c Department of Medicine, Kasturba Medical College, Manipal Academy of Higher Education, Manipal, Karnataka, 576104, India

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ABSTRACT

Purpose: The clinical profile and factors affecting outcomes in acute respiratory distress syndrome (ARDS) from adequately sample-sized Indian studies are still lacking. We aimed to investigate the clinical profile, treatment pattern, outcomes; and to assess factors affecting non-recovery in ARDS patients.

Patients and methods: A retrospective observational study was conducted among adult ARDS patients admitted during five year period (January 2014–December 2018) in a South Indian tertiary care setting. The relevant data were collected from the medical records to the data collection form. The univariate and multivariate logistic regression analyses were conducted to identify the predictors of outcomes using SPSS v20.

Results: A total of 857 participants including 496 males and 361 females with a mean age of 46.86 ± 15.81 years were included in this study. Fever (70.9%), crepitation (58.3%), breathlessness (56.9%), and cough (45%) were the major clinical presentation. Hypertension (25.2%), kidney disease (23.8%), and diabetes (22.3%) were the major comorbidities; and sepsis (37.6%), pneumonia (33.3%), and septic shock (27.5%) were the major etiological factors observed. Antibiotics and steroids were administered to 97.9% and 52.3% of the population, respectively. The recovery rate was 47.49%. The patients with scrub typhus, dengue, pancreatitis, and oxygen supplementation had significantly lower mortality. The factors such as advanced age, sepsis, septic shock, liver diseases, and ventilation requirements were observed to be the independent predictors of non-recovery in ARDS patients.

Conclusion: A comparable recovery rate was observed in our population. Advanced age, sepsis, septic shock, liver diseases, and ventilation requirements were the independent predictors of non-recovery.

1. Introduction

American-European Consensus Conference (AECC) criteria 1994 says that acute respiratory distress syndrome (ARDS) is acute damage of lungs with an arterial oxygen partial pressure to fractional inspired oxygen (PiO_2/FiO_2) ratio of less than 200 mmHg regardless of positive end-expiratory pressure (PEEP) level, which can be observed by a bilateral infiltrate on the frontal chest radiograph with a pulmonary

artery wedge pressure of <18 mmHg without evidence of left-sided hypertension or heart failure.¹ Later Berlin definition in 2012 recommends the following, i) the onset should be within a week time; ii) presence of bilateral opacities in the chest imaging which is not explained by effusions, collapse, or the nodules; iii) respiratory edema which is not explained by cardiac failure; iv) with a PaO_2/FiO_2 ratio of less than 200 mmHg.²

ARDS is a global threat with significant health and economic burden

; ARDS, Acute Respiratory Distress Syndrome; AECC, American-European Consensus Conference; CI, Confidence Interval; COVID-19, Coronavirus Disease; ICU, Intensive Care Unit; IEC, Institutional Ethics Committee; MODS, Multiple Organ Dysfunction Syndrome; OR, Odds Ratio; PEEP, Positive end expiratory pressure; PiO_2/FiO_2 , Arterial oxygen partial pressure to fractional inspired oxygen; RCT, Randomized Controlled Trial; SARS-CoV 2, Severe Acute Respiratory Syndrome Coronavirus 2.

* Corresponding author.

E-mail address: nair.sreedhar@manipal.edu (S. Nair).

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as it needs intensive medical and pharmaceutical care. Incidence differs from location to location, which ranged from 1.5 cases to 79 cases per 100 000 inhabitants.³ Indian studies reported an 11.4% incidence rate of ARDS among the ventilated patients and 41.8% of mortality among the ARDS patients⁴ whereas, Sharma et al., reported 56.2% of mortality rate in 28-days.⁵

The major risk factors for the development of ARDS include pneumonia, sepsis, gastric and/or oral and oesophageal contents aspiration, trauma, poison, acute pancreatitis, transfusion of blood and blood products, medication overdose, near drowning, and smoke inhalation.^{5,6} Whereas the risk factors such as age, trauma, oxygenation index, PaO₂/FiO₂ ratio, FiO₂, and PaO₂ level, blood pH, liver cirrhosis, non-pulmonary organ failure, Acute Physiology Score, peak pressure were the significant predictors for mortality in ARDS patients.^{5,7,8}

The management strategies for ARDS include respiratory supports, prone positioning, administration of neuromuscular blockade, non-invasive oxygenation, fluid management, rescue therapies, and medical management depending on the co-morbidities and other complications in the patients.⁶

All this evidence indicates the epidemiological burden of ARDS is still high across the globe even in this era of modern medicine. Moreover, clinical data on the epidemiological pattern and factors affecting the outcomes in ARDS patients from developing countries like India still lacking. Moreover, the inadequate sample size in all of the published research, which ranged from the fifties to the hundreds, is a major issue.^{4,5} This study aimed to investigate the clinical profile, treatment pattern, and outcomes in adult patients with ARDS through a retrospective analysis of five-year data and also to assess the factors affecting non-recovery among this cohort of patients.

2. Methodology

2.1. Ethical consideration

This retrospective study was carried out after obtaining ethical approval from the relevant institutional ethics committee (IEC 549/2019).

2.2. Study setting and participants

A retrospective observational study was conducted in a tertiary care hospital located in South India, Karnataka. The data were collected from the medical records of the patients who are diagnosed with ARDS (ICD-10 code: J-80) during January 2014 to December 2018. The adult patients aged 18 years or above and diagnosed with ARDS according to the clinician's judgment were included without any gender restrictions.

2.3. Data sample

A total of 921 participants were identified, out of which 64 were excluded as they were aged less than 18 years, and the remaining 857 ARDS patients were included in this study.

2.4. Data collection and tools

The parameters such as patient demographics, admission details, signs and symptoms, co-morbidities, laboratory investigations, treatment characteristics, treatment outcome, and duration of hospitalization, ICU, and ventilation were collected to a case record form and it was transcribed to a password-protected laptop. The normal values of the laboratory parameters were considered as per the hospital in which the study was conducted to avoid mismatches.

2.5. Outcomes considered

The primary endpoint was recovery. The patients were categorized

into two groups, in which those patients who are completely recovered and discharged were considered as recovery group and those who were dead or discharged against the medical advice were considered as the non-recovery group. The secondary endpoints include duration of hospitalization, ICU stay, ventilation days, oxygenation days, and antibiotics days.

2.6. Statistical analysis

The statistical analysis was performed using Statistical Package for the Social Sciences version 20.0 developed by IBM.⁹ Descriptive statistics were performed and the results were presented as the frequency with percentages in case of categorical variables and mean (standard deviation) or median (interquartile range) in case of continuous variables, respectively. Following the exploratory analysis, a univariate logistic regression was used for preliminary identification of factors affecting non-recovery in ARDS patients. Factors showing significant association with non-recovery were used in multiple logistic regression for the identification of independent risk factors associated with non-recovery. The results of univariate and multivariate logistic regression were presented in terms of odds ratio (OR) along with its 95% confidence interval (CI). A probability of less than 0.05 was considered to be statistically significant.

3. Results

3.1. Demographic characteristics of included participants

A total of 857 participants including 496 (57.9%) male and 361 (42.1%) females with a mean age of 46.86 ± 15.81 years were included. Out of which, 407 were recovered which indicates 47.49% of recovery rate with ARDS. The mean age for non-recovered patients was higher (49.08 ± 16.57 years) than the recovered patients (44.41 ± 14.53 years). Among the included participants, 33 (3.9%) were smokers and 393 (45.9%) were non-smokers, however, the remaining 431 (50.3%) patients' smoking status was not available from the data. Similarly, 83 (9.7%) patients were alcoholics, 352 (41.1%) were non-alcoholics, and the remaining 422 (49.2%) couldn't be identified (Table 1).

3.2. Clinical manifestations, comorbidities, and risk factors

Majority of the participants observed to have fever ($n = 608$; 70.9%), followed by crepitation ($n = 500$; 58.3%), breathlessness ($n = 488$; 56.9%) and cough ($n = 386$; 45%) as a clinical presentation. 25.2% ($n=216$) had hypertension, 23.8% ($n=204$) had kidney disease, and 22.3% ($n=191$) had diabetes, respectively. A majority ($n=322$; 37.6%) of the included patients had sepsis as a risk factor for ARDS, followed by, pneumonia ($n=285$; 33.3%), septic Shock ($n=236$; 27.5%), and multi-organ dysfunction syndrome (MODS) ($n=126$; 14.7%) were the other major risk factors. A detailed demographic characters of the included participants, recovered and non-recovered group is presented in Table 1.

3.3. Laboratory parameters among the included participants

3.3.1. Vitals

The average vitals were observed to be near normal, which includes a temperature of 98.82 ± 0.80 F, heart rate of 98 ± 22 beats per minute, systolic blood pressure of 121.49 ± 25.36 mmHg, and diastolic blood pressure of 76.04 ± 12.56 mmHg. Whereas, respiratory rate (26.10 ± 8.94 breaths per minute) was observed to be higher than normal (Table 2).

3.3.2. Blood indices

The average levels of blood indices such as eosinophils count (1.04 ± 2.43), basophils (0.57 ± 1.68), and monocytes (5.88 ± 4.42) were within the normal. Whereas, the total leukocyte count ($12408.81 \pm$

Table 1
Demographic characteristics of included participants.

Parameter	Total participants (N = 857)	Recovery group (n = 407)	Non-recovery group (n = 450)
Age (Mean, SD)	46.86 (15.81)	44.41 (14.53)	49.08 (16.57)
Age (Median, IQR)	47 (35, 59)	45 (32, 55)	50 (36, 62)
Gender (n, %)			
Male	496 (57.9)	213 (52.34)	283 (62.89)
Female	361 (42.1)	194 (47.66)	167 (37.11)
Smoking status (n, %)			
Yes	33 (3.9)	14 (3.45)	19 (4.22)
No	393 (45.9)	194 (47.66)	199 (44.22)
Not Reported	431 (50.3)	199 (48.89)	232 (51.55)
Alcoholic status (n, %)			
Yes	83 (9.7)	39 (9.58)	44 (9.78)
No	352 (41.1)	175 (43.00)	177 (39.33)
Not Reported	422 (49.2)	193 (47.42)	229 (50.89)
Comorbidity (n, %)			
Yes	535 (62.4)	231 (56.76)	304 (67.55)
No	322 (37.6)	176 (43.24)	146 (32.45)
Risk factor (n, %)			
Yes	812 (94.7)	389 (95.58)	423 (94)
No	45 (5.3)	18 (4.42)	27 (6)
Signs and Symptoms (n, %)			
Fever	608 (70.9)	334 (82.06)	274 (60.89)
Cough	386 (45.0)	190 (46.68)	196 (43.55)
Breathlessness/ Shortness of breath	488 (56.9)	236 (57.98)	252 (56)
Creptitation	500 (58.3)	251 (61.67)	249 (55.33)
Rhonchi	98 (11.4)	53 (13.02)	45 (10)
Dyspnoea	77 (9.0)	28 (6.88)	49 (10.89)
Tachypnea	74 (8.6)	34 (8.35)	40 (8.89)
Abdominal Pain	134 (15.6)	83 (20.39)	51 (11.33)
Facial puffiness	13 (1.5)	10 (2.46)	3 (0.66)
Pitting or pedal edema	92 (10.7)	49 (12.04)	43(9.55)
Co-morbidities (n, %)			
Type 2 Diabetes Mellitus	191 (22.3)	94 (23.1)	97 (21.55)
Hypertension	216 (25.2)	93 (22.85)	123 (27.33)
Kidney diseases	204 (23.8)	79 (19.41)	125 (27.78)
Cardiovascular diseases	86 (10.0)	30 (7.37)	56 (12.44)
Liver diseases	47 (5.5)	7 (1.72)	37 (8.22)
Bronchial asthma/ COPD	37 (4.3)	18 (4.42)	19 (4.22)
Respiratory failure	25 (2.9)	10 (2.46)	15 (3.33)
Cancer	23 (2.7)	3 (0.74)	20 (4.44)
Others	231 (27.0)	113 (27.76)	118 (26.22)
Risk Factors (n, %)			
Pneumonia	285 (33.3)	109 (26.78)	176 (39.11)
Sepsis	322 (37.6)	73 (17.94)	249 (55.33)
Septic Shock	236 (27.5)	50 (12.28)	186 (41.33)
AIDS	7 (0.8)	1 (0.24)	6 (1.33)
Leptospirosis	75 (8.8)	42 (10.32)	33 (7.33)
Scrub typhus	124 (14.5)	107 (26.29)	17 (3.78)
Dengue	22 (2.6)	19 (4.67)	3 (0.67)
MODS	126 (14.7)	35 (8.60)	91 (20.22)
Poison	20 (2.3)	4 (0.98)	16 (3.55)
Burns	9 (1.1)	0 (0)	9 (2)
H1N1	112 (13.1)	50 (12.28)	62 (13.78)
Hepatitis	16 (1.9)	8 (1.97)	8 (1.78)
Pancreatitis	61 (7.1)	44 (10.81)	17 (3.78)
Others	349 (40.7)	196 (48.16)	153 (34)

SD: Standard deviation; IQR: Interquartile range; COPD: Chronic obstructive pulmonary disease; AIDS: Acquired immunodeficiency syndrome; MODS: Multiple organ dysfunction syndrome.

11977.08), neutrophils count (72.74 ± 16.93), and erythrocyte sedimentation rate (43.17 ± 31.09 mm/h), were higher than the normal; and the average levels of lymphocytes (13.23 ± 10.78 ; $n = 780$) were observed to be lesser than the normal (Table 2).

3.3.3. Arterial blood gas analysis

An average level of -5.15 ± 7.64 , 19.48 ± 5.11 , 18.20 ± 5.66 , 27.05 ± 14.80 , 14.37 ± 6.97 , and 34.84 ± 11.70 for ABEC, CHCO3 (st), CHCO3

Table 2
Laboratory parameters of included participants.

Laboratory parameters (Mean, SD)				
Parameter	Normal range	Total participants (N = 857)	Recovery group (n = 407)	Non-recovery group (n = 450)
Vitals				
Temperature (n = 565)	98.6 °F	98.82 (0.80) °F	98.88 (0.89) °F	98.77 (0.67) °F
Heart rate/Pulse rate (n = 724)	60-100 bpm	98 (22) bpm	96 (20) bpm	101 (24) bpm
Systolic blood pressure (n = 724)	<120 mmHg	121.49 (25.36) mmHg	121.85 (23.82) mmHg	121.08 (26.96) mmHg
Diastolic blood pressure (n = 716)	<80 mmHg	76.04 (12.56) mmHg	76.71 (12.28) mmHg	75.28 (12.83) mmHg
Respiratory rate (n = 500)	12-16 bpm	26.10 (8.94) bpm	24.64 (7.51) bpm	27.69 (10.03) bpm
Blood indices				
Total leukocyte (n = 846)	4000-10000 cells/ μ L	12408.81 (11977.08) cells/ μ L	12308.40 (13262.45) cells/ μ L	12501.02 (10660.15) cells/ μ L
Neutrophils (n = 786)	42-74%	72.74 (16.93) %	72.61 (14.28) %	72.85 (19.09) %
Eosinophils (n = 478)	1-8%	1.04 (2.43) %	1.01 (2.62)%	1.06 (2.24)%
Lymphocytes (n = 780)	18-44%	13.23 (10.78)%	14.57 (10.20)%	11.96 (11.15)%
Basophils (n = 418)	1-2%	0.57 (1.68)%	0.52 (1.40)%	0.62 (1.92)%
Monocytes (n = 764)	5-13%	5.88 (4.42)%	5.95 (4.00)%	5.81 (4.79)%
Erythrocyte Sedimentation Rate (n = 686)	0-20 mm/h	43.17 (31.09) mm/hr	42.87 (29.99) mm/hr	43.48 (32.17) mm/hr
Blood gas analysis				
ABEC (n = 809)	–	–5.15 (7.64)	–3.82 (6.72)	–6.39 (8.21)
CHCO3 (st) (n = 823)	–	19.48 (5.11)	20.47 (4.61)	18.55 (5.37)
CHCO3 (P) (n = 825)	–	18.20 (5.66)	18.95 (5.32)	17.50 (5.87)
CtCO2 (n = 826)	–	27.05 (14.80)	27.97 (14.49)	26.18 (15.04)
CtHb (n = 825)	13.5–17.5 g/dL	11.87 (8.40) g/dL	11.75 (7.65) g/dL	11.99 (9.04) g/dL
CtO2e (n = 827)	–	14.37 (6.97)	14.65 (5.37)	14.10 (8.18)
Hctc (n = 803)	–	34.84 (11.70)	35.28 (11.76)	34.42 (11.63)
PCO2 (n = 832)	35–48 mmHg	33.47 (15.43) mmHg	32.20 (16.85) mmHg	34.64 (13.87) mmHg
PO2 (n = 831)	83–109 mmHg	86.47 (52.31) mmHg	83.45 (42.47)	89.26 (59.85)
PH (n = 829)	7.35–7.46	7.59 (3.94)	7.60 (4.03)	7.59 (3.85)
SPO2 (n = 162)	95%	84.16 (14.93) %	87.12 (10.13) %	81.67 (17.62) %
SaO2 (n = 800)	95–99%	89.43 (12.99) %	90.97 (10.65) %	87.94 (14.75) %

bpm: Beats per minute; mmHg: millimetre mercury; mm/hr: millimetre/hour; cells/ μ L: cells/microliter; g/dL: grams/deciliter.

(P), CtCO2, CtO2e, and Hctc were observed among the included participants, respectively. A lower level of CtHb (11.87 ± 8.40), PCO2 (33.47 ± 15.43), SPO2 (84.16 ± 14.93), and SaO2 (89.43 ± 12.99) were observed, whereas PO2 (86.47 ± 52.31) were within the normal and PH was slightly higher than the normal (7.59 ± 3.94). The laboratory parameters and arterial blood gas analysis of the included participants are presented in Table 2.

3.4. Treatment provided to the patients

Antibiotics were administered in 839 (97.9%), 401 (98.52%), and

438 (97.33%) of the overall population, recovered patients and non-recovered patients respectively. Whereas steroids were administered in half of the population, which is 52.3% (n=448), 52.82% (n=215), and 51.78% (n=233) of the overall population, recovered patients and non-recovered patients respectively. Among the included participants, 95.3% (n=817) of the patients were admitted to ICU; 70.1% (n=601) were taken to the ventilator and 35.1% (n=301) were given oxygen supplementation (Table 3).

3.5. Outcomes of ARDS in the patients

Among the total participants, 47.5% (n=407) of the population were completely recovered, whereas the remaining 52.5% (n=450) were not recovered. The average hospitalization days were observed to be 10.08 ± 7.96 days in the total population, which was more in the recovered group (12.55 ± 8.16 days) compared to the non-recovered population (7.86 ± 7.07 days). Similarly, higher average ICU days were observed with the recovered group (7.22 ± 6.08 days) compared to the non-recovered group (6.27 ± 5.55 days) where it was 6.72 ± 5.83 days in the overall population. Likewise, average ventilation days were higher in the non-recovered group (4.50 ± 5.00 days) compared to the recovered group (3.06 ± 5.00 days) where it was 3.82 ± 5.05 days in the overall population. The average oxygenation days and antibiotics days were observed to be higher in the recovered group (1.49 ± 2.24 and 12.00 ± 8.32 days) compared to the non-recovered group (0.66 ± 2.08 and 7.48 ± 7.01 days) where it was 1.05 ± 2.20 and 9.63 ± 7.99 days in the overall population, respectively. The treatment and outcomes in the included participants are provided in Table 3.

3.6. Factors affecting the outcomes

The factors such as scrub typhus (OR:0.138; 95%CI:0.073–0.263; $p < 0.001$); dengue (OR:0.183; 95%CI:0.049–0.679; $p < 0.001$); oxygen

Table 3
Treatments and outcomes in the included participants.

Parameter	Total participants (N = 857)	Recovery group (n = 407)	Non-recovery group (n = 450)
Treatment Provided (n, %)			
Antibiotics	839 (97.9)	401 (98.52)	438 (97.33)
Steroids	448 (52.3)	215 (52.82)	233 (51.78)
PPI or H2RA	757 (88.3)	362 (88.94)	395 (87.78)
ICU admission	817 (95.3)	381 (93.61)	436 (96.89)
Ventilation	601 (70.1)	226 (55.52)	375 (83.33)
Oxygenation	301 (35.1)	209 (51.35)	92 (20.44)
Outcomes			
Recovered (n, %)	407 (47.5)	407 (100)	NA
Not recovered (n, %)	450 (52.5)	NA	450 (100)
Hospitalization days (Mean, SD)	10.08 (7.96)	12.55 (8.16)	7.86 (7.07)
Hospitalization days (Median, IQR)	8 (5, 13)	10 (8, 15)	6 (3, 11)
ICU days (Mean, SD)	6.72 (5.83)	7.22 (6.08)	6.27 (5.55)
ICU days (Median, IQR)	5 (3, 9)	6 (4, 9)	5 (2, 9)
Ventilation days (Mean, SD)	3.82 (5.05)	3.06 (5.00)	4.50 (5.00)
Ventilation days (Median, IQR)	2 (0, 5)	1 (0, 4)	3 (1, 6)
Oxygenation days (Mean, SD)	1.05 (2.20)	1.49 (2.24)	0.66 (2.08)
Oxygenation days (Median, IQR)	0 (0, 2)	1 (0, 2)	0 (0, 0)
Antibiotics days (Mean, SD)	9.63 (7.99)	12.00 (8.32)	7.48 (7.01)
Antibiotics days (Median, IQR)	8 (4, 12)	10 (7, 14)	5 (3, 11)

PPI: Proton pump inhibitor; H2RA: Histamine 2 receptor antagonist; ICU: intensive care unit; SD: Standard deviation; IQR: Interquartile range.

supplementation (OR:0.171; 95%CI:0.115–0.254; $p < 0.001$) and pancreatitis (OR:0.458; 95%CI:0.226–0.927; $p = 0.030$) were found to be independent predictors of better recovery. In a univariate analysis, the factors such as age of 60 years or above (OR:2.446; 95%CI:1.753–3.412; $p < 0.001$); male gender (OR:1.543; 95%CI:1.175–2.028; $p = 0.002$); presence of comorbidity (OR:1.586; 95%CI:1.201–2.095; $p = 0.001$); pneumonia (OR:1.756; 95%CI:1.314–2.346; $p < 0.001$); sepsis (OR:5.668; 95%CI:4.140–7.760; $p < 0.001$); septic shock (OR:5.030; 95%CI:3.543–7.142; $p < 0.001$); MODS (OR:2.694; 95%CI:1.777–4.084; $p < 0.001$); poison exposure (OR:3.714; 95%CI:1.231–11.203; $p = 0.020$); cardiovascular diseases (OR:1.786; 95%CI:1.121–2.845; $p = 0.015$); liver diseases (OR:5.575; 95%CI:2.468–12.591; $p < 0.001$); cancer (OR:3.714; 95%CI:1.231–11.203; $p = 0.020$); ICU admission (OR:2.125; 95%CI:1.094–4.129; $p = 0.026$); and ventilation requirement (OR:4.004; 95%CI:2.920–5.491; $p < 0.001$) were significantly associated with a higher risk of non-recovery. Whereas, in a multi variate analysis, the factors such as age of 60 years or above (OR:2.120; 95%CI:1.359–3.306; $p < 0.001$); sepsis (OR:2.600; 95%CI:1.701–3.972; $p < 0.001$); septic shock (OR:2.351; 95%CI:1.478–3.739; $p < 0.001$); liver diseases (OR:3.319; 95%CI:1.284–8.578; $p = 0.013$) and ventilation requirement (OR:3.792; 95%CI:2.481–5.795; $p < 0.001$) were observed to be the independent predictors of non-recovery in ARDS patients. The univariate and multi variate analysis on factors affecting non-recovery and recovery is provided in Table 4.

4. Discussion

ARDS is still a global concern with its high mortality and challenges in management even in this modern era of medicine. Currently, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV 2 or COVID-19) became another threat to the whole world which changed the complete face of the world.¹⁰ In our study, 57.9% were male and 42.1% were females, respectively. This was similar to the findings of the Indian studies conducted by Sharma SK et al., and Prabhu et al., in which they reported 60.9% and 60.7% male proportion, respectively.^{5,11} Our study population had an average age of 46.86 years, which was apparent to the findings of other south Indian studies.^{4,11} Also, we observed a recovery rate of 47.49%, which was almost near to the findings of other Indian studies.^{4,5,11}

The mean age for non-recovered patients was higher (49.08 ± 16.57 years) than the recovered patients (44.41 ± 14.53 years). Moreover, age greater than 60 years appeared to be an independent predictor of non-recovery in our group of patients. Similarly, numerous studies across the world observed that advanced age is an independent predictor of non-recovery or mortality in ARDS patients.^{7,12–14} Moreover, some studies interpreted that, younger age is an independent predictor of better recovery.^{15,16}

There were 496 (57.9%) males and 361 (42.1%) females in our study, with similar male domination in recovery (52.34% vs 47.66%) and non-recovery (62.89% vs 37.11%). Similar male domination was observed in studies from Pakistan,¹⁷ India,⁵ and other parts of the world.^{12,15,18,19} Being a male gender significantly affected the non-recovery in univariate analysis ($P = 0.002$), whereas, it was not an independent predictor ($P = 0.066$) in our study. Similar conflicting findings were observed in the previous studies, in which some studies identified that being a male gender is a risk factor for non-recovery or mortality among ARDS patients,^{12–14} whereas some studies didn't.^{16,18,19}

Sepsis, pneumonia, septic shock, and MODS were the major aetiological reasons for ARDS in our population. Pneumonia, sepsis, septic shock, MODS, poisoning were significant aetiological conditions that contributed to the non-recovery in our patients, in which sepsis and septic shock were the independent predictors of non-recovery. Similar findings were reported in other studies where they recorded that, sepsis, MODS, and refractory shock were the leading causes of death.^{5,17}

Table 4
Univariate and multi-variate analysis on factors affecting the outcomes.

VARIABLE	UNIVARIATE ANALYSIS		MULTIVARIATE ANALYSIS	
	Unadjusted odds ratio (95%CI)	P-value	Adjusted odds ratio (95%CI)	P-value
Age group				
<60 years (n = 652)	1	NA	2.120 (1.359–3.306)	0.001^a
60 or above (n = 205)	2.446 (1.753–3.412)	<0.001^a		
Gender				
Female (n = 361)	1	NA	1.398 (0.968–2.019)	0.074
Male (n = 496)	1.543 (1.175–2.028)	0.002^a		
Smoking status				
Not reported (n = 431)	1	NA	NA	
No (n = 393)	0.880 (0.669–1.157)	0.360		
Yes (n = 33)	1.164 (0.569–2.382)	0.677		
Alcoholic status				
Not reported (n = 422)	1	NA	NA	
No (n = 352)	0.852 (0.642–1.132)	0.270		
Yes (n = 83)	0.951 (0.593–1.524)	0.834		
Presence of co-morbidity				
No (n = 322)	1	NA	0.708 (0.477–1.051)	0.087
Yes (n = 535)	1.586 (1.201–2.095)	0.001^a		
Risk factors				
Pneumonia				
No (n = 572)	1	NA	1.119 (0.761–1.647)	0.568
Yes (n = 285)	1.756 (1.314–2.346)	<0.001^a		
Sepsis				
No (n = 535)	1	NA	2.600 (1.701–3.972)	<0.001^a
Yes (n = 322)	5.668 (4.140–7.760)	<0.001^a		
Septic Shock				
No (n = 621)	1	NA	2.351 (1.478–3.739)	<0.001^a
Yes (n = 236)	5.030 (3.543–7.142)	<0.001^a		
Acquired immunodeficiency syndrome				
No (n = 851)	1	NA	NA	
Yes (n = 6)	4.562 (0.531–39.211)	0.167		
Leptospirosis				
No (n = 782)	1	NA	NA	
Yes (n = 75)	0.688 (0.427–1.108)	0.124		
Scrub typhus				
No (n = 733)	1	NA	0.138 (0.073–0.263)	<0.001^a
Yes (n = 124)	0.110 (0.065–0.187)	<0.001^a		
Dengue				
No (n = 835)	1	NA	0.183 (0.049–0.679)	<0.001^a
Yes (n = 22)	0.137 (0.040–0.467)	0.001^a		
Multiple organ dysfunction syndrome				
No (n = 731)	1	NA	1.260 (0.746–2.127)	0.388
Yes (n = 126)	2.694 (1.777–4.084)	<0.001^a		

Table 4 (continued)

VARIABLE	UNIVARIATE ANALYSIS		MULTIVARIATE ANALYSIS	
	Unadjusted odds ratio (95%CI)	P-value	Adjusted odds ratio (95%CI)	P-value
Poisoning				
No (n = 837)	1	NA	3.203 (0.902–11.373)	0.072
Yes (n = 20)	3.714 (1.231–11.203)	0.020^a		
H1N1				
No (n = 745)	1	NA	NA	
Yes (n = 112)	1.141 (0.765–1.701)	0.518		
Hepatitis				
No (n = 841)	1	NA	NA	
Yes (n = 16)	0.903 (0.336–2.428)	0.839		
Pancreatitis				
No (n = 796)	1	NA	0.458 (0.226–0.927)	0.030^a
Yes (n = 61)	0.324 (0.182–0.577)	<0.001^a		
Co-morbidities				
Type-2-diabetes mellitus				
No (n = 666)	1	NA	NA	
Yes (n = 191)	0.915 (0.663–1.262)	0.589		
Hypertension				
No (n = 641)	1	NA	NA	
Yes (n = 216)	1.270 (0.931–1.733)	0.132		
Kidney diseases				
No (n = 666)	1	NA	NA	
AKI (n = 168)	0.635 (0.271–1.488)	0.296		
Yes (n = 23)	1.071 (0.438–2.619)	0.880		
Cardiovascular disease				
No (n = 771)	1	NA	1.798 (0.962–3.358)	0.066
Yes (n = 86)	1.786 (1.121–2.845)	0.015^a		
Liver Diseases				
No (n = 810)	1	NA	3.319 (1.284–8.578)	0.013^a
Yes (n = 47)	5.575 (2.468–12.591)	<0.001^a		
Bronchial asthma/Chronic obstructive pulmonary disease				
No (n = 820)	1	NA	NA	
Yes (n = 37)	0.953 (0.493–1.842)	0.885		
Respiratory failure				
No (n = 832)	1	NA	NA	
Yes (n = 25)	1.369 (0.608–3.082)	0.448		
Cancer				
No (n = 837)	1	0.020^a	3.134 (0.829–11.847)	0.092
Yes (n = 20)	3.714 (1.231–11.203)			
Treatment provided				
Antibiotics use				
No (n = 18)	1	0.231	NA	
Yes (n = 839)	0.546 (0.203–1.469)			
Steroid use				
No (n = 409)	1	NA	NA	
Yes (n = 448)	0.959 (0.733–1.254)	0.759		

(continued on next page)

Table 4 (continued)

VARIABLE	UNIVARIATE ANALYSIS		MULTIVARIATE ANALYSIS	
	Unadjusted odds ratio (95%CI)	P-value	Adjusted odds ratio (95%CI)	P-value
<i>Intensive Care Unit admission</i>				
No (n = 40)	1	0.026^a	1.816	0.157
Yes (n = 817)	2.125 (1.094–4.129)		(0.795–4.151)	
<i>Ventilation requirement</i>				
No (n = 256)	1	<0.001^a	3.792	<0.001^a
Yes (n = 601)	4.004 (2.920–5.491)		(2.481–5.795)	
<i>Oxygenation</i>				
No (n = 556)	1	<0.001^a	0.171	<0.001^a
Yes (n = 301)	0.243 (0.180–0.329)		(0.115–0.254)	

NA: Not applicable.

^a Indicates the significant effect.

Pneumonia was found to be a predominant risk factor for ARDS and sepsis is the connecting link between pneumonia and ARDS.²⁰

The comorbidities such as kidney diseases, cardiovascular diseases, liver diseases, and cancer significantly affected the non-recovery, among liver diseases was an independent predictor. A similar observation regarded to the liver disease and worsening of ARDS was recorded by many studies.^{7,21} Interestingly, many studies observed that ARDS is usual comorbidity in liver disease patients, which further leads to a worse prognosis or death.^{22–24} This might be due to many associated conditions such as hepato-pulmonary syndrome, Porto-pulmonary hypertension, hepatic hydrothorax, and related hypoxemia.²³ Similarly, the patients who underwent a recent cardiovascular surgery, were more prone to develop ARDS and its further complications²⁵ though there is conflicting result on the impact of cardiovascular problems on mortality in ARDS patients.^{25–27}

The ICU admission and ventilation requirement was significantly associated with non-recovery in which ventilation requirement was observed to be an independent predictor in our population. Evidence indicates that wide use of ventilation is associated with higher mortality in ARDS.^{28,29} However, the factors such as scrub typhus, dengue, and oxygen supplementation were independent predictors of a better recovery. This might be due to the lesser severity and complication of the scrub typhus and dengue, which ultimately lead to a better recovery. Moreover, oxygen supplementation will be helpful to improve oxygen saturation which helps for better survival.

The antibiotics and steroids were used in 97.9% and 52.3% of the population, respectively, which was similar to the findings of the study conducted by Prabhu VA et al., where they reported 98.6% of antibiotic use and 48.6% of steroids use.¹¹ Though the use of antibiotics and steroids were observed to be clinically effective and associated with a better recovery rate, it was not significant. The use of steroids is highly controversial in ARDS concerning the onset of administration, dose, route of administration, and duration of treatment. Khan S et al. recorded the controversial effect of systemic corticosteroids in the management of ARDS, COVID-19, and Middle East Respiratory Syndrome due to their increased mortality and a higher likelihood of invasive mechanical ventilation.¹⁰

Drug utilization evaluations are the best way of method to estimate the use and effect of different types of medications used for a clinical condition.^{30,31} Hence, through assessing the use of antibiotics and steroids for the ARDS, it will be helpful to come up with further antibiotics policies and treatment guidelines. A previous study from our setting by Magazine R et al. recorded that all ARDS patients were prescribed antibiotics and 41.3% were prescribed corticosteroids.³²

Additionally, a very recent overview of meta-analyses by Rashid M et al. reported inconsistent evidence on the mortality reduction in the

steroid group among the ARDS patients. Their findings indicate significant mortality reduction in the observations of recent meta-analyses of randomized controlled trials (RCTs), whereas older studies are observed to have a non-significant effect. Moreover, an updated meta-analysis by the same researchers found a significant mortality reduction in the pooled estimation of RCTs, but not in cohort studies.³³

Though our study has the disadvantage of being retrospective, a significant portion of the sample will be useful in deriving appropriate conclusion. Lack of information due to retrospective study design, we had to exclude samples (negligible amount <20). The results of this study will help in the development of a tool or model for predicting mortality and treatment outcomes in ARDS patients. Further, well-controlled prospective studies are needed to assess the effect of steroids in ARDS patients. Additionally, location-based-treatment guidelines needs to be devised to reduce mortality from ARDS.

5. Conclusion

The non-recovery rate from ARDS is still observed to be more than the cure rate even in presence of this modern system of medicine. The patients with scrub typhus, dengue, and oxygen administration were observed to have better survival. Whereas, the factors such as advanced age, sepsis, septic shock, liver diseases, and ventilation requirements were the independent predictors of non-recovery in our population. Though the use of antibiotics and steroids improved the recovery, it was not statistically significant.

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Authorship statement

Conception and design of study: Muhammed Rashid (MR), Girish Thunga (GT), Sreedharan Nair (SN); **Acquisition of data:** MR; **Analysis and/or interpretation of data:** MR, Vijayanarayana Kunhikatta (VK), Viji Pulikkal Chandran (VPC); **Drafting the manuscript:** MR; **Clinical Inputs to the draft:** Vishal Shanbhag (VS), Raviraja V Acharya (RVA), GT; **Revising the manuscript:** Manasvini Ramakrishnan (RM), Deepa Sudalai Muthu (DSM), VK, SN, VS; **Approval of the version of the manuscript to be published:** MR, RM, DSM, VPC, GT, VK, VS, RVA, SN.

Data availability statement

The related to this work is not deposited in any repository. It will be available from the corresponding author on appropriate request.

Ethical committee statement

This retrospective study was carried out after obtaining ethical approval from the relevant institutional ethics committee (IEC 549/2019).

Declaration of competing interest

All authors report no conflicts of interest to declare. The listed authors are solely responsible for the originality and content of the manuscript. The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript.

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