Characterization and Outcomes of ARDS secondary to pneumonia in patients with and without SARS-CoV-2: A single center experience

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Short Report

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Abstract

ARDS is the major cause of mortality in patients with SARS-CoV-2 pneumonia. We report a single-centre study comparing the characteristics of ARDS patients with and without SARS-CoV-2. A greater proportion of SARS-CoV-2 patients were from an Asian ethnic group (p=0.002). SARS-CoV-2 patients had lower circulating leukocytes, neutrophils and monocytes (p<0.0001), but higher CRP (p=0.016) on ICU admission. SARS-CoV-2 patients required a longer duration of mechanical ventilation (p=0.01), but had lower vasopressor requirements (p=0.016). While the clinical syndromes of SARS-CoV-2 and CAP-ARDS are similar, the dysregulated inflammation observed in SARS-CoV-2 may contribute to the increased duration of respiratory failure.

Introduction

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) pneumonia can progress to hypoxemic respiratory failure requiring mechanical ventilation, with patients fulfilling the Berlin criteria for Acute Respiratory Distress Syndrome (ARDS)[1-3]. Intensive Care Unit (ICU) mortality rates of up to 68% from SARS-CoV-2 ARDS have been reported[3,4]. It is unclear whether patients with SARS-CoV-2 ARDS are clinically distinct, therefore requiring alternative management strategies, compared to other ARDS patients[5]. This study provides clinical characterization of ARDS patients with and without SARS-CoV-2 admitted to a single center ICU.

Methods

This is a single-center, observational study from the ICU of the Queen Elizabeth Hospital Birmingham, UK. All data was routinely collected on the hospital's electronic patient records. Ethical approval was not required based on Health Research Authority classification of this study. Local governance approval was granted from the audit and quality improvement department. Two ICU cohorts of patients were analyzed: SARS-CoV-2 patients admitted between 11th March and 21st April 2020 and all patients with community acquired-pneumonia (CAP) from bacterial or viral infection who developed ARDS between 1st January 2017 and 1st November 2019. ARDS secondary to others causes were excluded. As patients were from the same institution, their management prior to ICU admission and on ICU were broadly similar following local evidence-based protocols[6]. All patients were intubated, sedated and mechanically ventilated with positive pressure ventilation. Baseline demographic, comorbidities, laboratory investigations, physiological parameters and severity scores (APACHE II, SOFA & Murray Lung Injury) were collected at ICU admission. Sequential physiological and laboratory parameters were collected for 7 days whist on ICU. Sequential data not available for all patients due to deaths of 15 SARS-CoV-2 and 5 CAP-ARDS patients within one week.

Statistical analysis was performed using GraphPad Prism v.8.0. Data distributions were non-parametric and are presented as median with interquartile range (IQR) for continuous variables and number (percentage) for categorical variables. Differences between patient groups were analyzed using Mann-Whitney-U test for continuous data and Fisher's exact test for categorical data. Two-sided tests were used for all comparisons with $p<0.05$ considered statistically significant

Results

111 patients with SARS-CoV-2 ARDS and 29 patients with CAP-ARDS met the inclusion criteria (Table 1). Many patients (n=33) screened for CAP-ARDS were excluded, as ARDS had developed >48 hours after hospital admission. Patient demographic details are shown in table 1, with both groups being broadly similar except for ethnic background. A greater proportion of SARS-CoV-2 patients were of Asian / Asian British ethnicity (p=0.002), and a lower proportion were of White ethnicity (0.012), compared to CAP-ARDS patients

On ICU admission, SARS-CoV-2 patients had significantly lower APACHE-II and SOFA scores than CAP-ARDS patients (see table 1: $p<0.0001$). SOFA scores remained lower in SARS-CoV-2 patients for 7 days following ICU admission (Figure 1A).

SARS-CoV-2 patients had lower circulating leukocytes, neutrophils and monocytes ($p<0.0001$ for all) than CAP-ARDS patients on ICU admission. Leukocytes and neutrophil counts remained lower in SARS-CoV-2 patients for 3 days following ICU admission, whereas monocyte counts remained lower for 6 days (Figures 1B-D). Albumin was lower (p=0.003) whilst CRP (p=0.016) and platelet count (p=0.029) were higher at ICU admission in SARS-CoV-2 patients. Differences in CRP and albumin between patient groups increased with duration of ICU stay (Figures 1E-F). There was no difference in lymphocytes, eosinophils, bilirubin or creatinine between groups on ICU admission.

Peak end-expiratory pressure (PEEP) was higher in SARS-CoV-2 patients on ICU admission (p=0.003). However, there was no difference in other ventilator parameters between groups on ICU admission, including driving pressure, peak inspiratory pressure and PaO_2 / FiO_2 ratio. SARS-CoV-2 patients required a lower dose of vasopressors on ICU admission (p=0.016).

SARS-CoV-2 patients required a longer duration of mechanical ventilation compared to CAP-ARDS patients (p=0.010). However, there was no significant difference in other major ICU outcomes between groups, including hospital mortality, ICU length of stay, time to death from ICU admission, development of moderate / severe ARDS, need for renal replacement therapy or need for tracheostomy.

Conclusions

The stark difference between patient numbers indicates that before the emergence of SARS-CoV-2, development of CAP-ARDS was comparatively rare. In keeping with previous findings, our study confirms

that SARS-CoV-2 pneumonia seems to disproportionately affect patients from some ethnic minority backgrounds compared to CAP-ARDS[7].

Patients with SARS-CoV-2 ARDS develop rapid respiratory failure, however other organ functions seem to be initially preserved, with reduced requirement for vasopressors on ICU admission. Similar observations were made in a study comparing patients with SARS-CoV-2 versus H1N1 Influenza[8], suggesting that SARS-CoV-2 pneumonia initially causes less cardiovascular compromise compared to CAP-ARDS patients who present with mainly bacterial infections or Influenza.

The lower circulating leukocyte and neutrophil count in SARS-CoV-2 ARDS is similar to that observed in a previous pediatric study comparing pneumonia patients with SARS-CoV-2 versus Influenza A[9]. However, in contrast to this study, we found that CRP was significantly elevated in SARS-CoV-2 patients. These findings suggest that in SARS-CoV-2 ARDS, a greater migration of neutrophils and monocytes into the alveolar space may occur, driving dysregulated inflammation.

Whilst the duration of mechanical ventilation in CAP-ARDS patients was similar to previous ARDS cohorts[6], the SARS-CoV-2 patients required an increased duration of mechanical ventilation. However, there was no significant difference in most ventilator parameters or other major ICU outcomes (e.g. mortality and ICU length of stay) between patient groups. Absolute differences in PEEP between patient groups on ICU admission were small. The requirement for prolonged ventilation support is a key feature of SARS-CoV-2 ARDS, which otherwise causes a clinical syndrome similar to that observed in CAP-ARDS.

In summary, we show that whilst the respiratory mechanics of SARS-CoV-2 and CAP-ARDS patients are similar, SARS-CoV-2 patients initially have less severe cardiovascular dysfunction, fewer circulating leukocytes, and require prolonged ventilation support. An important limitation of our study is its single-center observational nature. Further studies are required into whether the dysregulated inflammation observed in SARS-CoV-2 patients contributes to the increased duration of respiratory failure.

Declarations

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Guarantor statement: Rahul Y. Mahida is the guarantor of the content of the manuscript, including the data and analysis.

Author contributions: RYM, MC, and JA were responsible for data collection, data analysis and manuscript preparation. CP, AH, RD, EB and LEC were responsible for additional data collection. MNB, DP, JMP and DRT had overall responsibility for the methodology, data extraction and manuscript preparation.

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Only data that were obtained as part of routine clinical care were collected for this study. All data were anonymised and entered by the Local Clinical Care Team, without linkage to any patient identifiers, in line with national and local guidance. The UK Health Research Authority guidance was followed (https://www.hra.nhs.uk/covid-19-research/guidance-using-patient-data/), and therefore consent and ethical approval was not required.

References

1. Guan WJ, Ni ZY, Hu Y, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. *The New England journal of medicine.* 2020;382(18):1708-1720.
2. Ranieri VM, Rubenfeld GD, Thompson BT, et al. Acute respiratory distress syndrome: the Berlin Definition. *Jama.* 2012;307(23):2526-2533.
3. Yang X, Yu Y, Xu J, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. *The Lancet. Respiratory medicine.* 2020;8(5):475-481.
4. Grasselli G, Zangrillo A, Zanella A, et al. Baseline Characteristics and Outcomes of 1591 Patients Infected With SARS-CoV-2 Admitted to ICUs of the Lombardy Region, Italy. *Jama.* 2020;323(16):1574-1581.
5. Gattinoni L, Chiumello D, Rossi S. COVID-19 pneumonia: ARDS or not? *Critical care (London, England).* 2020;24(1):154.
6. Bellani G, Laffey JG, Pham T, et al. Epidemiology, Patterns of Care, and Mortality for Patients With Acute Respiratory Distress Syndrome in Intensive Care Units in 50 Countries. *Jama.* 2016;315(8):788-800.
7. Aldridge RW, Lewer D, Katikireddi SV, et al. Black, Asian and Minority Ethnic groups in England are at increased risk of death from COVID-19: indirect standardisation of NHS mortality data. *Wellcome open research.* 2020;5:88.
8. Tang X, Du RH, Wang R, et al. Comparison of Hospitalized Patients With ARDS Caused by COVID-19 and H1N1. *Chest.* 2020;158(1):195-205.
9. Li Y, Wang H, Wang F, et al. Comparison of Hospitalized Patients with pneumonia caused by COVID-19 and influenza A in children under 5 years. *International journal of infectious diseases : IJID : official publication of the International Society for Infectious Diseases.* 2020.

Tables

Table 1: Demographics, Laboratory, and Physiological characteristics of SARS-CoV-2 ARDS and CAP-ARDS patients on admission to ICU.

	SARS-CoV-2 ARDS (n=111)	CAP-ARDS (n=29)	P value
Demographics			
Age at admission (years)	56 (47 – 63)	55 (41 – 59)	p=0.315*
Gender, Male (n, %)	84 (75.7%)	19 (65.5%)	p=0.358**
Body Mass Index	29 (27 – 34)	29 (26 – 33)	p=0.403*
Ethnicity White Asian / ***** British ***** / African / Caribbean Mixed / multiple Other	 54 (48.6%) 34 (30.6%) 9 (8.1%) 3 (2.7%) ** (9.0%)	 22 (75.8%) 1 (3.4%) 0 (0%) 1 (3.4%) 5 (17.2%)	 **p=0.012**** **p=0.002**** p=0.204** p=0.999** p=0.308**
Co-Morbidities None Hypertension Obesity Ischemic ***** Disease Diabetes Asthma / COPD Stroke / TIA Chronic kidney disease Cancer	 30 (27.0%) 44 (39.6%) 55 (49.5%) 6 (5.4%) 33 (29.7%) 12 (10.8%) 3 (2.7%) 9 (8.1%) 7 (6.3%)	 ** (34.5%) 9 (31.0%) 12 (41.4%) 1 (3.4%) 4 (13.8%) 4 (13.8%) 1 (3.4%) 1 (3.4%) 3 (10.3%)	 p=0.490** p=0.520** p=0.532** p>0.999** p=0.100** p=0.743** p=0.999** p=0.688** p=0.432**
Severity Scoring			
APACHE II	14 (12 – 18)	18 (16 – 24)	**p=0.0002***
SOFA Score	8 (7 – 10)	12 (9 – 14)	**p<0.0001***
Murray Lung Injury Score	2.75 (2.5 – 3.0)	2.75 (2.33 – 3.00)	P=0.645*
Laboratory parameters on ICU admission			
Leukocyte count (x10^9/L) Neutrophil count (x10^9/L) Lymphocyte ***** (x10^9/L) Monocyte count (x10^9/L) Eosinophil count (x10^9/L) *** (mg/L)	9.0 (5.9 – 12.6) 6.9 (4.5 – 10.2) 0.88 (0.57 – 1.20) 0.43 (0.29 – 0.65) 0 (0 – 0.03) 172 (113 – 241)	14.6 (10.6 – 22.9) 12.7 (9.0 – 21.0) 0.7 (0.5 – 1.2) 0.9 (0.6 – 1.3) 0 (0 – 0.1) 91 (40 – 235)	**p < 0.0001*** **p < 0.0001*** p=0.327* **p < 0.0001*** p=0.277* **p=0.016***
Platelets (10^9/L)	224 (174 – 305)	191 (111 – 294)	**p=0.029***
Creatinine (µmol/L)	77 (64 – 111)	87 (67 – 178)	p=0.260*
Bilirubin (µmol/L)	12 (9 – 20)	18 (8 – 45)	p=0.141*
	27 (24 – 32)	31 (27 –	**p=0.003***

Albumin (g/L)		35)	
Ventilator parameters on ICU admission			
***** (cmH_2O)	27 (24 – 30)	28 (24 – 30)	p=0.578*
PEEP (cmH_2O)	10 (8 – 12)	8 (6 – 10)	**p=0.003***
Driving Pressure (cmH_2O)	16 (14 – 19)	19 (14 – 22)	p=0.178*
P/F ratio	15 (12 – 17)	15 (11 – 17)	p=0.895*
ICU Outcomes			
Hospital Mortality	40 (36.0%)	12 (41.4%)	p=0.668**
Time to death from *** admission (days)	** (8 – 18)	11 (7 – 17)	p=0.874*
ICU LoS (days)	17 (10 – 24)	13 (9 – 24)	p=0.344*
**** (P/F ratio kPa) Mild (>26.6 – 40) ******** (>13.3 ≤26.6) Severe (≤13.3)	 6 (5.4%) 58 (52.3%) 47 (42.3%)	 2 (6.9%) 15 (51.7%) 12 (41.4%)	 p=0.670** p=0.999** p=0.999**
Duration ** mechanical ventilation (days)	15 (9 – 20)	9 (3 –17)	**p=0.012***
Maximum noradrenaline dose on *** 1 of ICU ********* (µg/kg/min)	0.067 (0.015 – 0.120)	0.490 (0 – 0.623)	**p=0.016**
**** for RRT	46 (41.4%)	11 (37.9%)	p=0.833**
Need for tracheostomy	55 (49.5%)	16 (55.2%)	p=0.678**

Data are n (percentage) or median (IQR). COPD = Chronic obstructive pulmonary disease. LoS = Length of stay. TV = tidal volume. ICU = intensive care unit. PEEP = Peak end-expiratory pressure. P/F = PaO_2 / FiO_2 ratio. RRT = Renal Replacement Therapy * represents p-values from a Mann-Whitney U test, ** represents p-values from a Fisher's exact test.

Figures

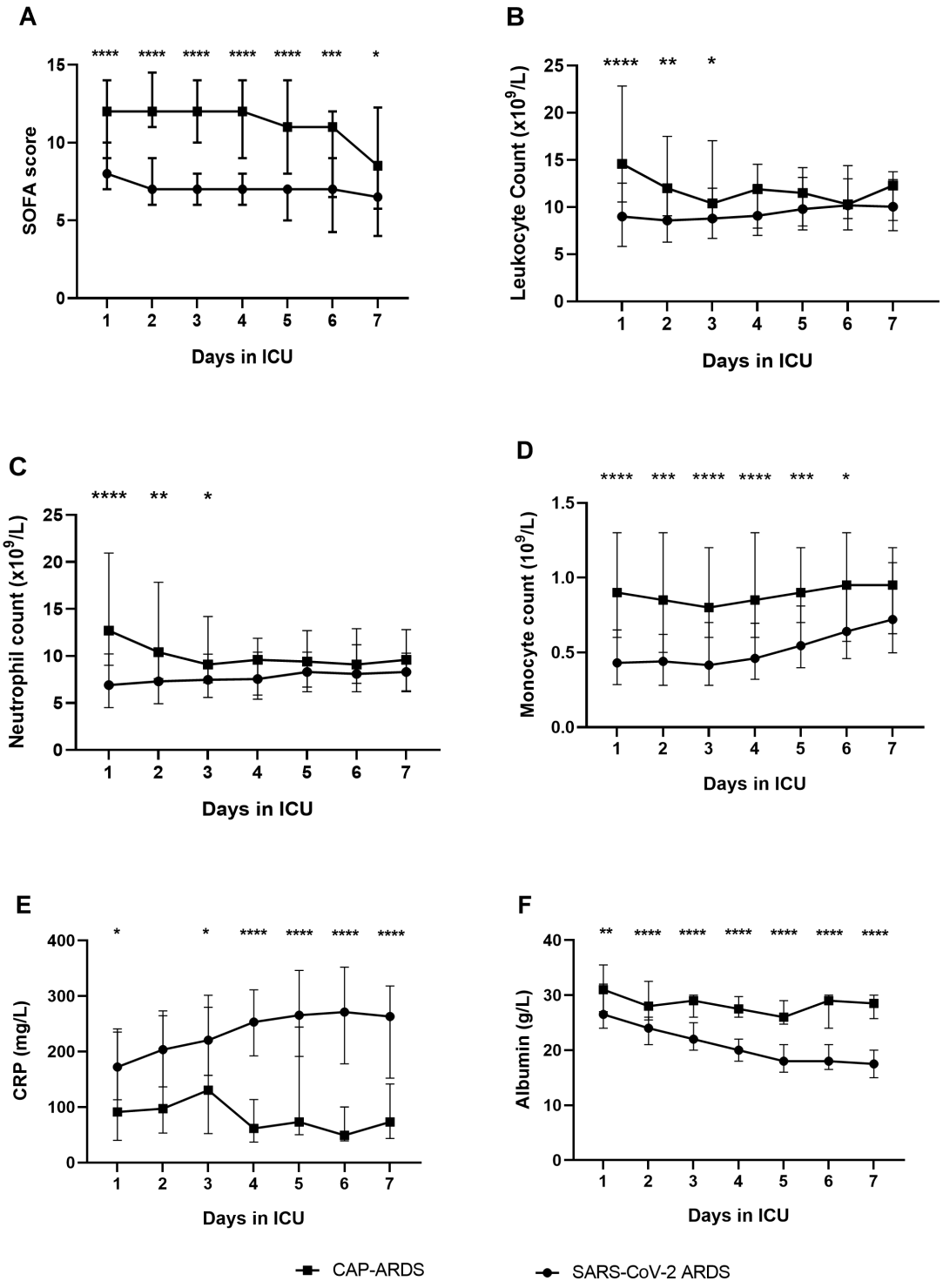

Figure 1

Figure 1: SOFA score and haematological parameters for SARS-CoV-2 and CAP-ARDS patients over the first seven days in the Intensive Care Unit. A: SOFA score. B: Leukocyte count. C: Neutrophil count. D: Monocyte count. E: CRP. F: Albumin. Data presented as daily median values and interquartile ranges for SARS-CoV-2 ARDS and CAP-ARDS patients. A Mann-Whitney U test was performed at each time point to compare both patient groups: ****p<0.0001, ***p<0.001, **p<0.01, *p<0.05.