

Etiological factors and clinical outcomes in acute respiratory distress syndrome in a paediatric intensive care unit

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Abstract

Objective: To evaluate the aetiological factors of acute respiratory distress syndrome and their impact on disease severity and outcomes in paediatric intensive care patients.

Method: The cross-sectional study was conducted at the paediatric intensive care unit of The Children's Hospital, Lahore, Pakistan, from March 2023 to March 2024, and comprised -paediatric patients with acute respiratory distress syndrome diagnosed as per the criteria outlined by the second Paediatric Acute Lung Injury Consensus Conference. The patients were assigned into pulmonary and extrapulmonary groups. Data was obtained through a detailed review of medical records regarding demographics, clinical characteristics, radiological characteristics, oxygenation indices, type of ventilation, exposure to steroids and sepsis. The assessed outcomes were the severity of acute respiratory distress syndrome, survival, ventilation-free days, and the length of paediatric intensive care unit and hospital stay. Data was analysed using SPSS 23.

Results: Of the 90 patients, 49(54.4%) were boys with median age 8.00 years (interquartile range: 2.00-11.00 years) and 41(45.6%) were girls with median age 4.50 years (interquartile range: 3.00-7.00 years). The acute respiratory distress syndrome severity was mild in 31(34.4%) cases, moderate 34(38.9%) and severe 24(26.7%). There was no strong association between disease aetiology and severity. The results were greatly affected by the level of immunosuppression, the type of ventilation and the severity of acute respiratory distress syndrome. With increasing ARDS severity ($p < 0.001$) survival decreased significantly, survivors had longer PICU stay than non survivors ($p < 0.001$).

Conclusion: Disease severity and patient-specific factors were the main factors determining clinical outcomes in paediatric acute respiratory distress syndrome independently of aetiology.

Keywords: Respiratory distress syndrome, Non-invasive ventilation, Immunosuppression. (JPMA 76: 1851; 2026)

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Introduction

Acute respiratory distress syndrome (ARDS) is a severe inflammatory lung disease that is caused by the disruption of the alveolar-capillary barrier, which leads to permeability and pulmonary oedema affecting gas exchange. ARDS may be caused by direct pulmonary insults, including pneumonia, or indirect systemic processes, including sepsis.¹ ARDS is characterised by the acute onset of hypoxemia, bilateral pulmonary infiltrates on X-rays and the non-occurrence of left atrial hypertension.²

ARDS has a worldwide incidence of about 3% of paediatric intensive care unit (PICU) population and a mortality rate of 15-45%. The rates of mortality differ significantly and tend to be higher in the developing countries, which can be attributed to the differences in healthcare resources and management.³

In Pakistan, a study reported an incidence of 15.33%

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among PICU admissions with the help of oxygen saturation index (OSI) as the diagnostic criterion. Pneumonia, lower respiratory tract (LRT) infections, sepsis, aspiration, trauma and near-drowning were the most frequently reported aetiological factors.⁴

Pulmonary aetiologies, especially pneumonia and LRT infections, and extrapulmonary aetiologies, especially sepsis, are the most prevalent causes of ARDS in paediatric populations.⁵ Non-invasive oxygenation parameters, like the OSI and the peripheral capillary oxygen saturation / fraction of inspired oxygen (SpO_2/FiO_2) (SF) ratio, which are validated surrogates of the oxygenation index (OI), and partial pressure of oxygen / fraction of inspired oxygen (PaO_2/FiO_2) (PF) ratio, can be utilised to identify and manage paediatric ARDS in its early phases. Compared to the OI and PF ratio, which involve an arterial blood gas (ABG) test, OSI and SF ratio involves pulse oximetry, which is more viable and practical in assessing the oxygenation status in time, especially in limited resources.⁶ According to guidelines set out by the second Paediatric Acute Lung Injury Consensus Conference (PALICC-2), the severity of ARDS in children is determined by OI, with mild ARDS = OI 4-<8, moderate ARDS = OI 8-<16, and severe ARDS = OI 16 or greater. These limits assist in determining and treating

paediatric patients undergoing invasive mechanical ventilation.⁷

Treatment plans vary according to the patient's severity; if non-invasive ventilation proves inadequate, lung-protective ventilator techniques may be employed.⁸ It is pertinent to treat the underlying cause of ARDS accurately to offset the morbidity and mortality associated with ARDS.⁹ In a developing nation, paediatric ARDS is linked to a markedly increased mortality rate, and adds a substantial load on the PICU. The most frequent cause is still infection.¹⁰

Regardless of the available evidence, the contribution of ARDS aetiology to disease severity and outcomes among children is still uncertain, especially in low- and middle-income countries (LMICs). The majority of the available literature on paediatric ARDS is related to high-income countries (HICs), where treatment resources, treatment guidelines and the demographics of patients vary widely compared to those in Pakistan. To the best of our knowledge, local data assessing the prevalence of pulmonary and extrapulmonary aetiologies of ARDS and the specific effect on disease severity and survival outcomes in PICU is lacking in Pakistan.

The current study was planned to fill the gap in literature by evaluating the aetiological factors of ARDS and their impact on disease severity and outcomes in PICU patients.

Patients and Methods

The cross-sectional study was conducted at the PICU of The Children's Hospital, (TCH) Lahore, Pakistan, from March 2023 to March 2024. After approval from the institutional ethics review committee, the sample size was calculated using the World Health Organisation (WHO) calculator, based on 5% prevalence of ARDS, 5% margin of error and 95% confidence level.¹¹ To improve precision and to strengthen the study power, the sample was inflated by >20%. Those included were paediatric patients aged between 1 month and 18 years diagnosed with acute lung injury that progressed to ARDS based on the PALICC-2 criteria.¹² Patients who had known valvular heart disease, congestive heart failure (CHF), chronic kidney disease (CKD) and fluid overload or who did not receive PICU care >6 hours were excluded. A non-probability consecutive method of sampling was used for the sampling process.

Informed consent was taken from the parents or legal guardians, and assent was obtained from children aged >7 years. Demographics, such as age, gender and weight, and the oxygenation condition during admission were noted. The number of breaths per minute (BPM) was recorded as the respiratory rate. Patients were divided into two groups

with respect to ARS aetiology; pulmonary ARDS (direct lung damage due to pneumonia or aspiration) and extrapulmonary ARDS (direct systemic damage due to sepsis or systemic inflammation). Parents and guardians were asked about the onset of symptoms. A thorough medical history was collected, chest radiographs were performed, and ABG analysis was used to calculate the PF ratio. To assess oxygenation impairment, key indices included PF, SF and OSI, which classified the impairment into mild, moderate and severe categories. A radiologist examined the anterior-posterior (AP) chest X-ray (CXR) to check for infiltrates. Children with prolonged hypoxemia and a high plateau pressure (Pplat) (>28cm of water [H₂O]) were treated with high-frequency oscillatory ventilation (HFOV) as rescue therapy as per the institutional protocol. To ensure that the cause of the pulmonary oedema was not cardiogenic, echocardiography was done on every patient. Systemic inflammatory reaction syndrome in the presence of, or as a result of a suspected or confirmed infection, defined sepsis. Within 14 days following admission, the use of systemic corticosteroids was classified as steroid exposure. This period is crucial for evaluating the potential impact of corticosteroids on patient outcomes. -free days (VFDs) were calculated based on the duration from the cessation of mechanical ventilation to study day 28. If extubation was successful after X days, VFDs were defined as 28-X. If a patient died within 28 days or required mechanical ventilation for >28 days, VFDs were recorded as 0. The ICU-free days were determined as the days between the first 28 days of admission, during which the patient was alive and not hospitalised in the PICU. In cases where the patient succumbed to death within 28 days or was still in ICU, the ICU-free days were counted as 0.

Data was analysed using SPSS 23. Data normality was checked by using the Shapiro-Wilk test. Age, length of hospital stay (LOS) and PICU duration were not distributed normally and were expressed as median with interquartile range (IQR). Qualitative data was expressed as frequencies and percentages. The chi-square test was used to evaluate association of demographic and clinical characteristics with ARDS severity. The Mann-Whitney U test (for non-normal data) was applied to compare medians for the duration of PICU stay and LOS between survivors and non-survivors. $P \leq 0.05$ was considered statistically significant.

Results

Of the 90 patients, 49(54.4%) were boys with median age 8.00 years (IQR: 2.00-11.00 years) and 41(45.6%) were girls with median age 4.50 years (IQR: 3.00-7.00 years). The acute respiratory distress syndrome severity was mild in 31(34.4%) cases, moderate 34(38.9%) and severe 24(26.7%). Demographic characteristics and clinical outcomes were

Table-1: Demographic characteristics, severity, comorbidities and clinical outcomes of acute respiratory distress syndrome (ARDS) patients in the paediatric intensive care unit (PICU) (n=90).

Variables	n (%)
Gender	
Male	49 (54.4)
Female	41 (45.6)
Severity	
Mild	31 (34.4)
Moderate	35 (38.9)
Severe	24 (26.7)
Underlying Immunosuppression	
Yes	30 (33.3)
No	60 (66.7)
Mechanical Ventilation	Non Invasive
38 (42.2)	
Invasive	52 (57.8)
Survival rate	
Survivors	48 (53.3)
Non Survivors	42 (46.7)
Pneumonia	
Yes	33 (36.7)
No	57 (63.3)
Sepsis	
Yes	22 (24.4)
No	68 (75.6)
Diabetic ketoacidosis	
Yes	23 (25.6)
No	67 (74.4)
Dengue fever	
Yes	15 (16.7)
No	75 (83.3)
Acute gastroenteritis	
Yes	29 (32.2)
No	61 (67.8)

Table-2: Comparison of demographic, clinical characteristics, and outcomes across different acute respiratory distress syndrome (ARDS) severity levels in paediatric patients [n (%)].

Variables	Severity of disease			Total	p-value
	Mild (n=31)	Moderate (n=35)	Severe (n=24)		
Gender					
Male	16 (32.7)	22 (44.9)	11 (22.4)	49 (54.7)	0.403
Female	15 (36.6)	13 (31.7)	13 (31.7)	41 (45.6)	
Study Group					
ARDS due to Pulmonary Causes	13 (28.9)	20 (44.4)	12 (26.7)	45 (50.0)	0.467
ARDS due to Extra pulmonary Causes	18 (40.0)	15 (33.3)	12 (26.7)	45 (50.0)	
Underlying Immunosuppression					
Yes	4 (13.3)	10 (33.3)	16 (53.3)	30 (33.3)	<0.001
No	27 (45.0)	25 (41.7)	8 (13.3)	60 (66.6)	
Mechanical Ventilation					
Non-Invasive	22 (57.9)	10 (26.3)	6 (15.8)	38 (42.2)	<0.001
Invasive	9 (17.3)	25 (48.1)	18 (34.6)	52 (57.8)	
Survival					
Survivors	25 (52.1)	13 (27.1)	10 (20.8)	48 (53.3)	0.001
Non Survivors	6 (14.3)	22 (52.4)	14 (33.3)	42 (46.7)	

noted in detail (Table 1).

There were 45(50%) patients in each of the two groups. In terms of outcome, there were 48(53.3%) survivors and 42(46.7%) non-survivors. Gender distribution showed no significant difference with respect to ARDS severity ($p=0.403$). Among those with pulmonary causes 13(28.9%) had mild disease, 20(44.4%) had moderate disease and 12(26.7%) had severe disease. In the extrapulmonary group, 18(40%) patients had mild ARDS, 15(33.3%) moderate, and 12(26.7%) severe. There was no statistically significant association between ARDS aetiology and disease severity ($p=0.467$). Underlying immunosuppression significantly correlated with increased ARDS severity ($p<0.001$), as did the type of mechanical ventilation, where non-invasive methods were more common in mild cases and invasive methods in severe cases ($p<0.001$). Additionally, survival decreased with increasing severity ($p<0.001$) (Table 2).

Age and gender did not significantly influence survival outcomes ($p>0.05$). ARDS severity had a significant impact on survival, with patients classified with mild ARDS exhibiting higher survival, and those with severe ARDS experiencing considerably lower survival rates ($p<0.001$). The duration of PICU stay and LOS had a significant relationship with survival ($p<0.001$) (Table 3).

Discussion

ARDS is a fatal critical illness that is linked to a high mortality rate of about 40% and is brought on by a variety of injuries.¹² Because of the great variability within the disease, the hunt for a suited ARDS treatment has proven to be ineffective. Three main levels of variance are clearly recognised in the presentation of ARDS: aetiological, physiological and biological.⁷ In children especially, it can result in respiratory failure, serious sickness and even death. Effective therapy for ARDS remains a problem despite new evidence of the effectiveness of mechanical ventilation and fluid management. Some effective treatment strategies include tidal volume, high positive end-expiratory pressure, advanced infection, and using less medications.¹³ A study from Pakistan has looked at mortality predictions in the PICU, evaluating all admissions and the other concentrating on 60 ventilated respiratory patients. The current study is the largest to assess the clinical profile, treatment and mortality predictors of ARDS patients in PICU.¹⁴

Table-3: Comparison of survivors and non-survivors across demographic and clinical variables in paediatric acute respiratory distress syndrome (ARDS) patients [n (%)].

Variables	Survival		Total (n=90)	p-value
	Survivors (n=48)	Non-Survivors (n=42)		
Age (years)	6.00 (3.00-9.00)	5.00 (3.00-7.25)	5.00 (2.00 – 10.00)	0.450
Gender				
Male	25 (51.0)	24 (49.0)	49 (54.4)	0.394
Female	23 (56.1)	18 (43.9)	41 (45.6)	
Total	48 (53.3)	42 (46.7)	90 (100)	
Severity				
Mild	25 (80.6)	6 (19.4)	31 (34.4)	<0.001
Moderate	13 (37.1)	22 (62.9)	35 (38.9)	
Severe	10 (41.7)	14 (58.3)	24 (26.7)	
Study Group				
ARDS due to Pulmonary Causes	14 (31.1)	31 (68.9)	45 (50.0)	<0.001
ARDS due to Extra pulmonary Causes	34 (75.6)	11 (24.4)	45 (50.0)	
Duration of PICU (days)	8.00 (5.00-8.75)	4.00 (3.00-7.00)	10.00 (7.00 – 14.00)	<0.001
Duration of Hospital (days)	14.00 (11.00-16.00)	6.50 (3.00-12.25)	10.25 ((7.00 - 14.13)	<0.001

The majority of paediatric patients in this study appeared with moderate ARDS, followed by those with severe and mild ARDS. The mortality rate was 46.7%. There was a strong correlation between progressive worsening of ARDS and the lack of survival ($p<0.001$). Conversely, there was no significant association of ARDS aetiology (pulmonary versus extrapulmonary) with the severity of the diseases ($p=0.467$). Poorer outcomes were significantly related to immunosuppression and the use of invasive mechanical ventilation ($p<0.001$). Dahmer et al. in 2022 showed greater proportion of male with 61.4% compared to females 38.6%.¹⁵ In all subtypes, mortality was consistently correlated with both organ failure and the severity of the illness as determined by Paediatric Risk of Mortality III (PRISM III). In the complete model, OI at 24 hours was likewise linked to death, but not when limited to non-infectious ARDS.¹⁶

Most of the current children had moderate ARDS (38.9%), followed by mild (34.4%) and severe (26.7%). The mortality was 46.7%, which was higher than the 37.9% reported by Yan et al. in 2022.¹⁷

The current study observed a strong correlation between the ventilation mode and ARDS severity ($p<0.001$), and non-invasive ventilation was normally used in mild cases, while invasive ventilation was used in moderate and severe cases. This was in line with Khemani et al. who in 2015 reported that in paediatric patients with ARDS, severe disease and worse oxygenation were strongly related to the requirement of invasive mechanical ventilation, and such delays could affect the outcomes.¹⁸

ARDS severity was the best predictor of survival in the current study ($p<0.001$). There was a significant increase in

the days spent in PICU and in hospital ($p<0.001$) among the survivors. Goey et al. in 2024 also reported similar results.¹⁹

ARDS aetiology (pulmonary vs. extrapulmonary) and severity were not significantly associated ($p=0.467$), which was in line with the findings of Kim et al., who in 2020 reported that pneumonia and sepsis were the most frequent causes of ARDS, but severity and outcomes were more host-factor-related than insult type.²⁰

The current study used validated oxygenation indices and assessed the effects of immunosuppression and mode of ventilation on outcomes. The fact that it included pulmonary and extra-pulmonary causes added to its strength

and clinical relevance. The study, however, has limitations as it was conducted at a single centre with a small sample size and without a long-term follow-up. Possible variability in treatment practices may have limited the generalisability of the findings.

Conclusion

Elevated severity of ARDS was found linked to increased mortality, especially in individuals suffering from impaired immune systems. In cases of paediatric ARDS, early intervention and suitable breathing techniques are essential for increasing the survival rates.

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Conflict of Interest: None.

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Author Contribution:

MK: Data acquisition, analysis, interpretation, drafting and agreement to be accountable for all aspects of the work.

NS & MS: Critical review and final approval.

AR: Data acquisition and analysis.

SA: Concept and data analysis.

MKI: Data analysis and interpretation.