Acute respiratory distress syndrome in the tropics: there is much to learn!

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First described more than five decades ago by Ashbaugh and colleagues,[1] today acute respiratory distress syndrome (ARDS) continues to be one of the most challenging clinical conditions with a high morbidity and mortality.[2] Till 1994, several definitions of ARDS were being used both for clinical care as well as for research purposes. The American-European Consensus Conference definition[3] provided a uniform standardised definition of ARDS and this facilitated meaningful comparison of research carried out on ARDS across the globe. As the American-European Consensus Conference definition of ARDS[3] was being used, several limitations with the use of this definition became evident. These limitations were addressed and the Berlin definition of ARDS[4] was published. While the earlier definitions relied on clinical features and chest imaging as surrogates, the Berlin definition[4] considered timing, i.e. onset within 1 week of clinical recognition of a trigger insult, bilateral opacities on chest radiograph or CT (not fully explained by lung collapse or effusion), respiratory failure (not fully explained by fluid overload or cardiac failure) and arterial hypoxaemia [based on ratio of partial pressure of oxygen (PaO_2) and fraction of inspired oxygen (FIO_2) at a positive end expiratory pressure (PEEP) ≥5 cm of water].[4] Further, the Berlin definition[4] classified the severity into three categories (mild, moderate and severe) based on the PaO_2/FIO_2 ratio and the PEEP to facilitate estimation of the prognosis of ARDS. Presently the Berlin definition[4] is being used world over in research on ARDS.

Recent clinical trial data suggest that pneumonia, aspiration of gastric contents and sepsis, were the most common aetiological causes of ARDS accounting for almost 85% of cases.[2] In tropical countries, in addition to these causes, other causes, such as tuberculosis,[5,6] malaria,[7] leptospirosis,[8] enteric fever[9] and scrub typhus,[10] have been documented to be the aetiological causes of ARDS. The aetiological spectrum of ARDS appears to be different in various parts of the world,[10,11] and this has necessitated periodically documenting the current aetiological spectrum of ARDS.

The prospective study by Balakrishnan et al.[12] featured in this issue of the *Journal of the Royal College of Physicians of Edinburgh*, attempted to describe the aetiology and short-term outcome of ARDS (n = 42; mean age 42.6 ± 15.3 years; 21 males) in the medical intensive care unit (MICU) at their tertiary care teaching hospital located in Puducherry, in south India. Of these, 22 patients has ARDS at admission and the rest developed ARDS during their in-hospital stay. Pulmonary ARDS was present in 13 out of 42 (31%) patients, with community-acquired pneumonia being the most common aetiological cause (n = 6), followed by hospital-acquired pneumonia. Majority of the cases were extrapulmonary ARDS [29 out of 42 (69%)], with sepsis (n = 16) being the most common cause followed by scrub typhus (n = 8). As per the Berlin criteria,[4] 13 (31%), 14 (33%) and 15 (36%) patients had mild, moderate and severe ARDS, respectively. Thirty three (79%) patients died; all the survivors (n = 9) had extrapulmonary ARDS. On univariate analysis, nonsurvivors had a significantly lower mean systolic blood pressure (BP), diastolic BP, mean arterial pressure and mean PaO_2/FIO_2 ratio; higher occurrence of complications such as acute kidney injury, thrombocytopenia, requirement for vasopressors and severe ARDS. Further, both acute physiology and chronic health evaluation II (APACHE II) and sequential organ failure assessment (SOFA) scores were significantly higher in nonsurvivors.

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Certain issues related to the study by Balakrishnan et al.[12] need consideration. It is a single-centre study with a small sample size. The patients were evaluated till discharge from hospital or till death; the median (interquartile range) duration of hospital stay was 6 (3.75–10) days. There were a large number of patients with viral pneumonia compared with other Indian studies,[10,13,14] which was explained by authors[12] to be due to seasonal increase in the place of study. In extrapulmonary ARDS, following sepsis, scrub typhus accounted for the majority of cases, which was attributed to endemicity of the disease.

In a recently published study[11] 3,022 out of 29,144 patients (10%) screened for inclusion in 459 ICUs in 50 countries fulfilled ARDS criteria during their ICU stay. In this study,[11] hospital mortality was 35%, 40% and 46% in patients with mild, moderate and severe ARDS, respectively. The mortality in the present study[12] (33 out of 42; 79%) was much higher than that reported in other recent studies where the in-hospital hospital mortality was 63 out of 170 (37%)[13] and 34 out of 75 (45%),[10] and 28-day mortality was 36 out of 64 (56%).[14] Balakrishnan et al.[12] attributed this high mortality to seasonal rise in H1N1 cases, and the fact that some patients were ventilated outside the ICU because of limited number of beds in ICU and transferred later on to ICU, and severe underlying organ dysfunction at admission. Furthermore, seven out of nine survivors had scrub typhus as the aetiological cause.

The study by Balakrishnan et al.[12] reiterates the importance of recognising treatable tropical infections as the aetiological causes of ARDS, as early initiation of appropriate antibiotic treatment has potential to significantly decrease the morbidity and mortality in patients with ARDS owing to these causes. Balakrishnan et al.[12] also reported the potential usefulness of critical illness scoring systems, such as APACHE II and SOFA score in predicting prognosis. These critical illness scoring systems have been validated in intensive care units (ICUs) outside India. Only univariate analysis has been carried out for predictors of survival. In an adequately powered study with an appropriate sample size, receiver–operator characteristic curve analysis, multivariable analysis could have better established the utility of critical illness scoring systems in predicting outcome in patients with ARDS requiring admission to MICU in the Indian scenario.

ARDS, with its varied aetiological causes, complex pathophysiological mechanisms and potential for lethal complications, still poses a major challenge even in developed countries and ARDS mortality still remains at approximately 40% globally.[11] In developing countries, with limited resources and sparsely available, accessible, affordable ICU care facilities, ARDS still remains to be a disease with high mortality for clinicians to contend with. In developing countries, especially in rural settings, variables required for satisfying Berlin definition,[4] such as arterial blood gas measurements and chest radiographs, may not be available and several cases of ARDS may, therefore, remain undiagnosed. To overcome this, other options such as the 'Kigali modification of Berlin' definition[15] have been proposed. Further, the utility of potential therapies for ARDS due tropical aetiological causes, such as use of extracorporeal membrane oxygenation, extracorporeal carbon dioxide removal and prone positioning, among others,[16] merits study. Further research is warranted on these issues in ARDS in the tropics.

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