Incidence of acute respiratory distress syndrome: a comparison of two definitions

A Y T Goh, P W K Chan, L C S Lum, M Roziah

Abstract

Objectives—To determine the incidence and outcome of acute respiratory distress syndrome (ARDS) in children by comparing two commonly used definitions: the lung injury score and the American-European Consensus Conference definition. The causes and risk for developing ARDS were also studied.

Methods—Part prospective and retrospective analysis of 8100 consecutive hospital admissions from 1 June 1995 to 1 April 1997.

Results—Twenty one patients fulfilled the criteria for ARDS. Both definitions identified the same group of patients. The incidence was 2.8/1000 hospital admissions or 4.2% of paediatric intensive care unit admissions. The main causes were sepsis and pneumonia. Mortality was 13 of 21. Factors predicting death were a high admission paediatric risk of mortality (PRISM) score (30.38 × 18.75) and the presence of multiple organ dysfunction syndrome (92% ± 25%).

Conclusion—Both definitions identified similar groups of patients. The incidence in this population was higher than that reported elsewhere, but mortality and cause were similar to those in developed countries. Poor outcome was associated with sepsis, a high admission PRISM score, and simultaneous occurrence of other organ dysfunction.


Keywords: acute respiratory distress syndrome; lung injury score; American-European Consensus Conference

Ashbaugh and colleagues1 2 first described a group of patients with a characteristic pattern of respiratory distress, with hypoxaemia refractory to supplementary oxygen, decreased lung compliance, and diffuse alveolar infiltrates. This was secondary to widespread alveolar capillary damage from various pulmonary and systemic disorders, leading to permeability pulmonary oedema. The identified risk factors were sepsis, aspiration of gastric contents, trauma, pneumonia, fractures, and disseminated intravascular coagulopathy. According to a large population study in New York, the reported incidence in adults is about 150 000 cases/year.3 The incidence in children has not been well studied,4 with a mortality of 50% from five retrospective studies.5 6 All of these studies were conducted in developed countries, which have different patient and population characteristics from a developing country like Malaysia.

Part of the difficulty in determining the incidence of acute respiratory distress syndrome (ARDS) results from the heterogeneity of definitions used. In children, this is compounded by unavailability and the age and size dependent variability in measurements of pulmonary capillary wedge pressure, which formed the cornerstone of earlier definitions of ARDS. Murray and colleagues7 offered a useful and practical definition of ARDS that did not rely on pulmonary capillary wedge pressure measurements, using the lung injury score. A lung injury score of > 2.5 indicates ARDS. The American-European Consensus Conference (A-ECC) definition for ARDS was introduced in 1994 in an effort to streamline current definitions of ARDS, with the exclusion of positive end expiratory pressure (PEEP) values and compliance measurements to improve detection of early and true cases.8 We set out to determine the incidence and outcome of ARDS in Malaysia in children together with identification of its aetiology, and in the process compare the accuracy of both definitions.

Materials and methods

We carried out a part prospective and retrospective analysis of 8100 consecutive admissions to our paediatric department from 1 June 1995 to 1 April 1997, the last six months being prospective. Cases of respiratory failure were routinely admitted to the paediatric intensive care unit (PICU) and detailed analysis was carried out on these patients. The University Malaya Medical Centre is located in Kuala Lumpur, the capital of Malaysia. It serves a local population of 2.1 million and forms a tertiary referral centre for the nation. The paediatric department has 116 non-intensive care beds and a six bedded multidisciplinary PICU, which is staffed by one intensivist and has 24 hour physician coverage.

The lung injury score was determined by two to four criteria, each individually based on a four point scale (table 1). The score was derived by dividing the aggregate sum by the number of components used. The worst daily values were used to calculate the PaO2/FiO2 ratio and PEEP score in determining the overall lung injury score. In addition, the absence of a clinically apparent cardiogenic cause for the pulmonary oedema was added as a criterion. The radiographs were reported and scored by a radiologist for the appearance of bilateral diffuse alveolar infiltrates and absence of cardiomegaly. Patients were defined as having ARDS if any of the daily lung injury scores were > 2.5.
and there was no clinical evidence of cardiogenic pulmonary oedema. In addition, we applied the A-ECC definitions for ARDS (table 2) to determine their accuracy and to compare whether the two scores identified a similar population of patients. The A-ECC definitions excluded measurements of PEEP and the four point radiographic scoring system, and used the presence of bilateral alveolar infiltrates consistent with pulmonary oedema as criteria instead. The aetiology of ARDS was also studied in these patients together with their epidemiological data. The admission PRISM score was calculated and the presence of multiple organ dysfunction syndrome was noted using Wilkinson’s criteria. Factors associated with mortality were determined and compared using the $\chi^2$ test.

All 21 case notes were reabstracted after completion of the scoring and scored again. An abstraction/reabstraction ratio of $>0.8$ ($\kappa = 0.88$) was indicative of almost perfect interrater reliability. Proportions were compared where appropriate with the Fischer’s exact test and quantitative data were compared with the Student’s $t$ test. $p$ values $<0.05$ were considered significant.

Table 2: The American-European Consensus Conference definition of ARDS (1994)

<table>
<thead>
<tr>
<th>Oxygenation</th>
<th>$\text{PaO}_2/\text{FiO}_2 &lt; 200$ (regardless of positive end expiratory pressure level)</th>
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<tbody>
<tr>
<td>Chest radiograph</td>
<td>Bilateral infiltration seen on frontal chest radiograph</td>
</tr>
<tr>
<td>Pulmonary artery occlusion pressure</td>
<td>$\leq 18$ mm Hg when measured or no clinical evidence of left atrial hypertension</td>
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</table>

Results

Of the 494 patients admitted to the PICU, 21 fulfilled criteria for ARDS based on the lung injury score and A-ECC definitions for ARDS. The incidence of ARDS in our hospital during this study period was 2.8/1000 hospital admissions or 4.2% of all PICU admissions. Patients with ARDS had a median age of 28 months (range, 2–144), with more than two thirds being less than 5 years old. The boy to girl ratio was 1.4:1. Almost all patients fulfilled the criteria within 24 hours of admission to the PICU (20 of 21). One patient with pneumonia developed ARDS following aspiration of kerosene.

The median lung injury score was 3.6 with a mean (SD) of 3.36 (0.52). The median PRISM score was 28 with a mean (SD) of 25.9 (8.7). Multiple organ dysfunction syndrome was present in more than half of the patients. Sepsis was the main cause of ARDS (nine patients), followed by pneumonia (seven patients), dengue shock syndrome (two patients), aspiration of kerosene, meningitis, and drug induced (one patient each). The main bacteriological isolates (blood cultures) from the sepsis group were Gram negative in five patients and Gram positive in three others. None of the patients had an underlying illness, five had acute leukaemia and two had chromosomal disorders.

Death from ARDS was three times higher (13 of 21) than the overall PICU mortality of 17.2% ($p < 0.005$). Analysing subsets of patients, mortality was highest in the sepsis group and lower in pneumonia. Non-survivors had a higher mean PRISM score (30.38 $\pm$ 18.75; $p = 0.001$) and a higher incidence of multiple organ dysfunction syndrome (92% $\pm$ 25%; $p = 0.003$). There was no difference in the mean PEEP (8.1 $\pm$ 12.2), mean duration of PICU stay (11.2 $\pm$ 5.3 days), mean lung injury score (3.32 $\pm$ 3.49), and incidence of barotrauma between survivors and non-survivors, respectively. Survivors had a lower worst PaO$_2$/FiO$_2$ than non-survivors (72.4 $\pm$ 95.9; $p = 0.04$) (table 3).

Discussion

Since the classic description of ARDS by Ashbaugh 30 years ago,1 2 the study of ARDS and its risk factors has been hampered by the heterogeneity and lack of uniformity in definitions. Murray and colleagues proposed an expanded definition, in an effort to improve sensitivity and specificity, by including early and true cases of ARDS.3 This score has been used in several clinical studies.5-10 Studies in children have an additional compounding factor in that the previously accepted term for ARDS was the adult respiratory distress syndrome, implying that it occurred mainly in
The incidence of ARDS in our hospital population is higher than quoted elsewhere but mortality appears to be similar. This could be explained by the fact that University Hospital, Kuala Lumpur is a national referral centre for childhood oncology patients, who accounted for a significant proportion of the study group and a high percentage of those who died. In addition, patients in developing countries might present late as a result of socioeconomic and cultural factors, at the height of their illness, and with maximal organ failure. This was supported by the fact that criteria for ARDS and multiple organ dysfunction syndrome were met in almost all our paediatric patients with ARDS within 24 hours of admission to the PICU. Chronic shortage of PICU beds was a further compounding factor, with critically ill patients being cared for in non-intensive care areas, until further deterioration requiring ventilator support caused them to be transferred to the PICU.

The causes and risk factors for developing ARDS in our population were similar to those in developed countries. Sepsis remains the commonest cause of ARDS, often in immunocompromised children on long term chemotherapy. Severe pneumonia was the second commonest cause and had a better outcome, especially if there was no accompanying multiple organ dysfunction syndrome. Dengue virus infection is a known cause of ARDS in the tropics, especially cases of dengue shock syndrome. The pathophysiology of severe dengue infection is that of increased capillary permeability, which partially explains the changes in the respiratory system. Other recognised causes were central nervous system infections, drug ingestion, and aspiration pneumonia.

Sepsis, particularly Gram negative, was associated with a poor outcome. Severe Gram negative infection in chronically immunocompromised, debilitated children with malignancies and accompanying neutropenia was often fatal, once the stage of severe respiratory failure and organ dysfunction was reached. Only one patient with leukaemia, ARDS, and respiratory failure survived—a non-neutropenic child with *Pneumocystis carinii* pneumonitis without multi-organ dysfunction. Other authors have quoted survival rates of only 10% in this group of patients. ARDS in Gram positive sepsis had a slightly better prognosis because it was less likely to be associated with hypotension and multiple organ failure.

Multiple organ dysfunction syndrome is a primary life threatening situation in ARDS, arising from the same generalised activation of inflammatory cells responsible for the systemic inflammatory response seen in ARDS. Over half of our patients had multiple organ dysfunction syndrome, many of whom died. The commonest dysfunctional organ (other than the respiratory system) was haematological, with disseminated intravascular coagulopathy. As in most series of patients with multiple organ dysfunction syndrome, our paediatric patients with ARDS typically presented early, with maximal organ dysfunction at presentation or within 24 hours of PICU admission. This pattern differed from adult patients, who present with sequential organ failure, suggesting that there may be differing age related responses to similar insults.

A high admission PRISM score was also significantly associated with death. This score has been validated recently in Malaysia (Goh AYT, unpublished data, 1997) and shown to predict death across different diagnostic groups, as well as mortality risk intervals. The use of severity of illness scores using non-pulmonary factors has been used widely. Prognostic scores in ARDS should use routinely measured variables in these patients. Serial measurements of oxygenation index (\(\text{PaO}_2/\text{FiO}_2\)) and the total lung injury score were unreliable prognostic factors in our study. Surprisingly, non-survivors had a better \(\text{PaO}_2/\text{FiO}_2\) than survivors. The outcome appears to be linked more
to the cause of ARDS and associated organ dysfunction rather than the severity of the oxygenation deficit itself.

There were several problems associated with our study. It relied partly on retrospective data collection, which would weaken the incidence estimates because of the possibility of undiagnosed cases. We believe that this was minimised because all cases of respiratory failure/ALI/ARDS were managed in the PICU. The reliance on clinical assessment for absence of left atrial hypertension together with radiological interpretation of diffuse bilateral alveolar infiltrates could introduce bias. However, previous studies have shown the accuracy of these scores in diagnosing ARDS compared with a more rigid definition, which included static respiratory system compliance and pulmonary artery occlusion pressure measurements. The possibility of overestimating the lung injury score was limited by aiming for an abstraction/reabstraction ratio of > 0.8.

The current understanding of ARDS is that it is the severe end of a continuum of diseases affecting the respiratory system from both pulmonary and non-pulmonary insults, resulting in the characteristic clinical spectrum of arterial blood gas and chest radiographic abnormalities. Improved and accurate definitions would lead to better knowledge of its true incidence and outcome. This in turn would lead to better recognition of risk factors for ARDS, allowing preventive strategies and early treatment to improve outcomes in these critically ill children.