Section: Research Paper

Study of the Clinic-Etiological Profile, Severity, Mortality Risk and Management of ARDS in Children

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Abstract

Background: Acute respiratory distress syndrome (ARDS) is one of the rapidly progressing disease contributing to high rate of morbidity and mortality. It causes fluid to leak into the lung making the oxygen difficult to get into the blood stream. **Methodology:** This study was carried out at a tertiary level pediatric multispecialty hospital. The study duration was for 14 months. A total of 30 children who were fulfilling the BERLINs criteria for ARDS were included in the study. Pao2/Fio2 ratio were noted and depending upon the BERLINs definition patient were classified into (mild/moderate/severe) type of ARDS. **Result:** In the present study (21/30)70% children had primary ARDS and 30 % (9/30) had secondary. Among the primary ARDS 63% had pneumonia, 6% had transfusion triggered injury and 3% had accidental hydrocarbon aspiration (kerosene poisoning). On scoring mortality risk by PRISM III, (16.6%) had score of less than 15 and 5/30 (83.3%) score of more than 15. 10% of the patients required noninvasive and 90% of children required invasive type of ventilation. **Conclusion:** Primary ARDS is the commonest etiology with pneumonia being the major cause. Conventional ventilation is the primary modality to maintain ventilatory status with few children requiring High Frequency Oscillatory therapy aiming at low tidal volume and higher PEEP.

Keywords: ARDS, mortality, risk, management, children.

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Introduction

Acute respiratory distress syndrome (ARDS) is a rapidly progressive disease with a high degree of morbidity and mortality. The key pathophysiology is pulmonary edema with an

increased permeability of pulmonary capillary endothelial cells and alveolar epithelial cells, leading to hypoxemia and respiratory failure that is refractory to usual oxygen therapy, often needing assisted ventilation.[1] Pediatric ARDS is different than adult ARDS in various aspects [2] , hence in 2015 the PALICC group (Paediatric Acute Lung Injury Consensus Conference) developed a nomenclature pertinent to pediatrics ARDS and included oxygenation index (OI), oxygen saturation index (OSI) and the pulse oximetric saturation to fraction of inspired oxygen ratio - S/F (SPO_2/FiO_2)[3-6]

The diffuse lung injury seen in this condition is caused by diverse pulmonary and non-pulmonary etiologies, and in children pneumonia and sepsis are the commonest causes. The clinical symptomatology manifests as rapidly progressive dyspnea, tachypnea and hypoxemia which then quickly evolves into respiratory failure. The management of ARDS remains supportive, and is aimed at improving gas exchange and preventing complications while the underlying disease that precipitated ARDS is treated. The improvement in survival we are currently witnessing is probably due to better ventilator strategies[7-11] and standardization of care as recommended by PALICC group in 2015. The treatment must be modulated according to the age of the patient and to the severity of the lung pathology, taking into account that supportive and adjunctive therapies can be extremely important in improving the final outcome. Patients who survived ARDS chronic or delayed sequelae may develop which include motor and mental disabilities. There are many scoring systems to predict the mortality of children with ARDS. PRISM III scoring system is used to evaluate severity of disease at the time of admission in IPCU.[12-14] There are very few studies from the India on pediatric ARDS and as the disease is associated with a high degree of mortality and morbidity. Hence, this study was conducted to study of the clinic-etiological profile, severity, mortality risk and management of ARDS in children.

Materials And Methods

Study place: This study was conducted at a tertiary level pediatric multispecialty hospital. The study was conducted for a period of 14 months, from April 2015 to June 2016.

Study design: Descriptive cohort study

Inclusion criteria: Children aged between (1 month to 15years) fulfilling the BERLIN definition of ARDS admitted attertiary care multispecialty hospital.

Exclusion criteria: Children with chronic lung injury, underlying heart disease, patients refusing to give consent for resuscitation, and Neonates (<1 month of age).

Sample size: 30 children fulfilling the BERLINs criteria for ARDS, during the study period were included in the study.

Data analysis: Data was charted on Microsoft excel. Data was analyzed using SPSS Software version15 and Sigma plot version 12. Appropriate statistical tests were applied. P-value of less than 0.05 was considered statistically significant. Quantitave data is presented with the help of Mean, Standard deviation, Median and IQR, comparison among two study group is done with unpaired T test. Qualitative data is presented with the help of Frequency and Percentage table association among various study parameter is assessed with Chi-square test (Fisher Exact test for 2*2 tables).

Ethical considerations: All the necessary ethical permissions were taken from the Institutional Ethics Committee of the tertiary care hospital. An informed consent from the parents and from the patient (as and when necessary) was obtained. Each patient data was recorded in case proforma.

All the vitals were checked and systemic examination was done. Pao2/Fio2 ratio were noted and depending upon the BERLINs definition patient were classified into (mild/moderate/severe) type of ARDS. Whenever recruitment /HFOV were required, then pre

and post ABGs were compared for the improvement in Pao2/Fio2 ratio. X-ray findings were recorded in children. All patients considering the worsening of respiratory symptoms, and pa02/fio2 ratio on various o2 devices and ventilatory support and x-ray finding, were categorized as mild, moderate and severe ARDS (as per BERLIN's definition). PRISM Score was used for estimating the mortality risk of patients admitted in IPCU with ARDS. Antibiotics were started as per IPCU protocol and requirement of inotropes (dopamine/adrenaline /noradrenaline) number of inotropes and blood products were noted. In present study type of ventilation (non- invasive /invasive), were noted.

Results

Table 1: Clinico-etiological factors

Clinico-etiological factors	Frequency	Percentage
Cough	21	70%
Fever	27	90%
Breathlessness	25	83.33%
Chronic disease	20	66.67%
Anaemia	27	90%
Renal Failure	9	30%
Liver failure	11	36.67%
Sepsis	12	40%

Table 2: Association study group between, PRISM (III) and Severity significant (0.003)

PRISM (III)	Severity			Total
	Mild	Moderate	Severe	
Less than 15	3(75.0%)	2(9.5%)	0 (0.0%)	5 (16.6%)
15 and above	1 (25.0%)	19 (90.5%)	5 (100.0%)	25(83.3%)
Total	4(100.0%)	21(100.0%)	5(100.0%)	30 (100.0%)

Table 3: Association between prism and outcome is insignificant (0.593)

PRISM (III)	OUTCOME		Total
	Discharged	Death	
Less than 15	1(20.0%)	4(80.0%)	5 (100.0%)
15 andabove	8(32.0%)	17(68.0%)	25(100.0%)
Total	9(30.0%)	21(70.0%)	30(100.0%)

Table 4. Association of study group between, type of ARDS and Severity is significant (0.049)

Type ofARDS	Severity			Total
	Mild	Moderate	Severe	
Primary	4(100.0%)	13(61.9%)	4(80.0%)	21(70.0%)
Secondary	0(0.0%)	8(38.1%)	1(20.0%)	9(30.0%)
Total	4(100.0%)	21(100.0%)	5(100.0%)	30(100.0%)

Table 5: Association of in between type of ventilation and severity is significant (0.016)

Type of ventilation	Severity			Total
	Mild	Moderate	Severe	
Invasive	2(50.0%)	20(95.2%)	5(100.0%)	27(90.0%)
Non Invasive	2(50.0%)	1(4.8%)	0(0.0%)	3(10.0%)
Total	4(100.0%)	21(100.0%)	5(100%)	30(100%)

Table 6: Association between severity and outcome is insignificant (0.501)

Severity	OUTCOME		Total
	Survivors	Non survivors	
Mild	2(50.0%)	2(50.0%)	4(100.0%)
Moderate	5(23.8%)	16(76.2%)	21(100.0%)
Severe	2(40.0%)	3(60.0%)	5(100.0%)
Total	9(30.0%)	21(70.0%)	30(100.0%)

Table 7: Comparison in oxygen between recruitment (pre and post) is significant (0.029)

	N	Mean	Std. Deviation	Paired T test	P-Value
P/F Ration 4	6	128.37	93.93	-3.026	0.029
P/F Ration 5	6	214.33	71.84	Difference is sig	

Discussion

21/30(70%) children presented with cough indicating respiratory etiology as major cause of ARD**.** 27/30 (90%)of children presented with fever. Fever could be due to sepsis, pneumonia (any infection/injury /inflammation). In our study we observed that the presence of fever did not have any impact on the survival outcome. 25/30(83%) children had breathlessness either in form of tachypnea or dyspnea. Suggesting that all cases (primary/secondary) had lung involvement at the time of presentation to hospital. All children were not maintaining saturation on room air requiring some 02 support (nasal prongs/hood/mask/NRM). In this study, we found there was significant association between fever and breathlessness to severity of ARDS. There are very few studies in literature discussing about the clinical presentation of children in ARDS. In our study out of 30 patients 20 (66%) were presented with chronic diseases like (hematological/chronic lung disease/renal/neurological /endocrine/immunological). Judith [15] et al. conducted a study thirty-two (56%) patients had an underlying chronic comorbidity with 18 (46%) having hematology–oncology conditions. Hence, high index of suspicion should be kept in mind when child with underlying systemic illness or condition develop respiratory symptoms and worsening of the symptoms, as comorbid conditions can lead severe presentation of the disease. Large studies need to be done to establish this correlation.

When haemoglobin concentration of children in the study were analyzed it was found that 27/30(90%) patients had anaemia, haemoglobin (< 10 gm/dl). Anaemia definitely contributes to tachypnea, tachycardia, and hypovolemic shock thus must be corrected in the management of ARDS, anaemia correction improves oxygen carrying capacity and may reduce ventilatory requirement. 9/30(30%) children had renal failure at the time of presentation of ARD. Out of 9 cases, 6 children had moderate ARDS,2 had severe and 1 had mild ARDS. Renal failure represents deteriorating organ functions and child then goes into MODS. Darmon M [16] et .al in their study AKI occurred in 31.3% of patients and was more common in patients with ARDS (44.3% versus 27.4% in patients without ARDS; *P*<0.001) In another study by Chetan

et .al children who developed acute renal failure and disseminated intravascular coagulopathy had 100% mortality. The hypothesis of AKI causing deterioration of clinical condition of ARDS is renal failure (AKI) is an important comorbid factor contributing to ARDS because positive-pressure ventilation reduce cardiac output and increase central venous pressure, thereby diminishing renal blood flow, free water clearance, or the GFR . Changes in arterial blood O_2 or CO_2 may influence renal vascularresistance, renal perfusion, or diuresis.

11/30(40%) children had liver failure at the time of presentation of ARDS**.** Liver failure is an important part of MODS as well as comorbid factor for ARDS, as children with liver failure (due to underlying liver disease) may have hepato -pulmonary syndrome and poor coagulation which lead to poor oxygenation and worsening of ARDS. ARDS also causes poor ventilation oxygenation mismatch lead to liver injury. 12/30 (40%) Of the patients had blood culture positive(sepsis).

PRISM III score association with severity of ARDS is significant (p value 0.003) but no association with outcome. Although other scoring systems are also available to evaluate children with ARDS.PRISM score could be applied to estimate the severity of disease and probable mortality. In a study conducted by Singhal[17] et .al PRISM score showed a significant association with the mortality). The proportion of deaths which was only 8.2% among children with the scores 1-9 showed a gradual increase with higher scores, reaching 66.7% among the children with a score of > 30. Another study conducted by Bellad [18] et al. showed that PRISM 3 scoring system has high sensitivity to predict the outcome of children admitted in IPCU. Sensitivity in score 15 was 89%.

In present study 21/30(70%) children had primary ARDS and 9/30(30%) had secondary. In primary ARDS19/30(63%) had pneumonia ,2/30 (6%)had transfusion triggered injury and 1/21(3%) had accidental hydrocarbon aspiration (kerosene poisoning). Out of secondary ARDS children, 4/30(13%) had blood culture positive sepsis. In present study significant association was noted between type of ARDS with severity (p value 0.049). In study conducted by Chetan[19] et .al direct lung injury was the risk factor in 9(53%) children, pneumonia and hydrocarbon aspiration accounted for 35.2%, severe trauma and multiple transfusions were less commonly associated causes. Sepsis was the commonest cause of indirect lung injury (29.4) %.

In the present study, it was found that all children had worsening of respiratory complaints within 7 days of onset of illness, with x-ray suggestive of bilateral opacities which cannot be explained by effusion or nodules. Present study couldn't establish any significant association between severity and outcome. Large study conducted in JAMA [1](Task force), gave the BERLINs definition for ARDS found that, stages of mild, moderate, and severe ARDS were associated with increased mortality. The general support included sedation (continuous infusion of opioid and benzodiazepine), fluid maintenance, nutritional support, and antibiotics when indicated Whenever necessary, a muscle relaxant (vecuronium) was used to facilitate mechanical ventilation. Hemodynamic support with vasopressors/inotropes and/or fluids was administered through a central venous catheter when necessary. In our study, 27/30(90%) patients were anaemic, of which 23(85%) required blood transfusion.

Recruitment was done by, PEEP was increased from 5 cm H_2O to a maximum of 45 cm H_2O in steps of 5 cm H_2O, with each step lasting 2 minutes. During the PEEP titration phase, the PEEP is set to 25 cm H_2O and then further reduced by 5 cm H_2O in steps to the end-maneuver PEEP, with each step lasting 5 minutes. The end-maneuver PEEP was set to 5 cm H_2O (MRS-5) or 10 cm H_2O (MRS-10). When pre and post recruitment ABGs were compared (Pao2/Fio2) mean was 160, median 158, SD 83, range (47-400) as compared to post mean was 214, std d 71.8, median 193, range of (130- 320) suggestive of improvement in

oxygenation. Anupdas et al.[20] showed that the recruitment can be useful in improvement of oxygenation but not associated with survival. Hence, recruitment helps to engage the partially atelectatic alveoli, thereby improving the V/Q mismatch in the patients with ARDS thus improving oxygenation. All patients who underwent Recruitment had lower/worse Pao2/fio2 ratios and it showed improvement in oxygenation as seen by improvement in Pao2/fio2 ratio (p value 0.029), but didn't translate into survival benefit for all.

Children requiring invasive ventilation were put on Pressure Controlled Ventilation(mode) with optimal PEEP. Out of all ARDS children 27/30(90%) required invasive ventilator support, of which 5/5 (100%) severe ARDS, 2/4(50%) mild, and 20/21(95%) moderate ARDS. Association of invasive ventilation association with severity of ARDS was significant (p value 0.016). Hence, when there is worsening of the pao2/fio2 ratio more is possibility of invasive ventilation.

Conclusion

Primary ARDS is the commonest etiology with pneumonia being the major cause in this group and sepsis in secondary ARDS. In children with ARDS multiorgan dysfunction compounds the severity with liver dysfunction being the most common cause. Grading of children with ARDS according to Berlins criteria at onset of disease helps to predict the outcome. PRISM III score will help to predict the, mortality risk in IPCU, was found to be a useful application in children with ARDS also. Conventional ventilation is the primary modality to maintain ventilatory status with few children requiring High Frequency Oscillatory therapy aiming at low tidal volume and higher PEEP.

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