Original Article

Clinical Profile and Outcome of Acute Respiratory Failure

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Abstract. ***Objective :*** To examine the etiological factors, clinical features, treatment modalities and outcome of acute respiratory failure in children. ***Methods :*** This hospital-based prospective observational study was conducted over 15 months. Fifty children with acute respiratory failure, diagnosed by serial arterial blood gas analysis, were consecutively enrolled. Ventilation therapy was initiated when the FiO_2 requirement went above 0.6. ***Results :*** Pulmonary diseases accounted for majority (68%) of cases, followed by nervous system (12%); and cardiovascular and skeletal muscle system diseases (10%, each). Bronchopneumonia was the commonest cause of acute respiratory failure (11 cases). The majority of cases were in the age group 1 month to < 1year (26 cases). The commonest signs were altered depth and pattern of respiration (100%), chest wall retractions (88%), flaring of alae nasae (88%), tachypnea (84%), tachycardia (82%), and irritability (64%). Cyanosis was noticed in only 26 (52%) cases. Thirty-six (72%) children required ventilation therapy. The overall mortality was 58%. The mortality was high (55.9% to 66.7%), irrespective of the primary system involved. Significantly higher mortality was associated with co-existent malnutrition ($p<0.001$), Type I failure ($p=0.039$) and ventilation therapy ($p<0.0001$). ***Conclusion :*** Acute respiratory failure has varied etiology and clinical manifestations, and a high mortality. Its outcome is independent of age of the child and the primary system involved. Malnutrition and Type I failure are factors associated with a poor outcome.
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Acute respiratory failure is a term used to describe any disruption in the function of the respiratory system (including malfunctions in the cardiovascular system, central and peripheral nervous systems, and the skeletal muscle system) that acutely impairs its primary function of delivering adequate oxygen to or removing carbon dioxide from the pulmonary capillary bed or both.[1-3] It is a condition which poses an immediate threat to life and it can develop over minutes to hours.[1-3]

Acute respiratory failure is often preceded by a compensated state (acute respiratory insufficiency) in which the patient, through increased effort, is able to maintain adequate gas exchange at the expense of increased work of breathing.[1-3] Mechanisms which lead to this failure of gas exchange in the lungs vary with the diseases that produce respiratory failure. These underlying diseases, in which acute respiratory failure can develop as a complication, are classified according to the primary system involved as pulmonary, cardiovascular, nervous, and skeletal muscle disorders.[3,4] However, the diagnosis, evaluation, and initial management of acute respiratory failure are the same regardless of the underlying cause.[1-3] The diagnosis is based on the presence of hypoxemia and /or hypercapnia and, therefore, relies primarily on doing serial arterial blood gas (ABG) analysis.[1-3] Acute respiratory failure can be of 3 types: (i) Type I (or hypoxemic or lung failure), when the partial pressure of arterial oxygen (PaO_2) is less than 50mm Hg; (ii) Type II (or hypercapnic or ventilation failure), when the partial pressure of arterial carbon dioxide ($PaCO_2$) is more than 50mm Hg; and (iii) Type III (or combined oxygenation-ventilation failure), when the PaO_2 is less than 50mm Hg and the $PaCO_2$ is more than 50mm Hg simultaneously; in a patient breathing room air.[1-3]

Even in developed countries information on its clinical profile and outcome in the pediatric age group is scanty.[1-3] The present study was therefore undertaken to examine the etiological factors, clinical features, treatment modalities and outcome of acute respiratory failure in children admitted to our hospital. To our knowledge, such a study has not been reported earlier from India or any other developing country.

MATERIALS AND METHODS

This prospective observational study was carried out at a tertiary level public hospital over a period of 15 months, from August 1998 to October 1999. Fifty children, aged between 1 month and 12 years, who were admitted to our hospital with various diseases, and in whom acute respiratory failure was diagnosed, were consecutively enrolled. These children were admitted either to the general pediatric wards or directly to the Pediatric Intensive Care Unit (PICU). For patients admitted to the

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wards, a diagnosis of impending acute respiratory failure was an indication to get transferred to the PICU. A 24-hour availability of ABG facility, radiographic and other laboratory services, along with skilled pediatric residents and nursing personnel helped us in diagnosing and managing patients with this condition. Neonates admitted in the neonatal intensive care unit, and children admitted in the pediatric surgical wards and pediatric surgical intensive care unit of our hospital were not eligible for inclusion in this study, since they were managed by other departments and whose treatment protocols were different.

Any critically ill child showing signs of acute respiratory insufficiency, in the form of increased work of breathing, was closely monitored by doing serial ABGs (every hourly) to detect acute respiratory failure at the earliest. Along with hourly ABG monitoring, the patient was also closely monitored for signs of acute respiratory failure.[2] These clinical signs included respiratory signs (tachypnea, altered depth and pattern of respiration, chest wall retractions, flaring of alae nasae, cyanosis, decreased or absent breath sounds, grunting, wheezing), cardiac signs (tachycardia, hypertension, bradycardia, hypotension, cardiac arrest), cerebral signs (restlessness, irritability, headache, confusion, drowsiness, seizures, coma) and general signs (fatigue, excessive sweating).[2] Any abrupt clinical deterioration in the patient's condition was an indication to do an urgent ABG. The diagnosis of acute respiratory failure was confirmed by the standard ABG criteria mentioned earlier.[1-3] For a patient with acute respiratory insufficiency, oxygen therapy was given using mask or hood or nasopharyngeal catheter. The fixed inspired oxygen concentration (FiO_2) requirement of each patient receiving oxygen therapy was checked regularly using a FiO_2 meter. In a patient with acute respiratory failure if the FiO_2 requirement went above 0.6 to maintain an oxygen saturation of 95%, ventilation therapy was initiated.[2] Ventilation therapy was given by conventional mechanical ventilators available in our PICU. When a ventilator was not available, ventilation therapy was given by the pediatric resident in the form of manual intermittent positive pressure ventilation (IPPV), using a self-inflating AMBU bag apparatus.

For every patient enrolled in the study, age, gender, nutritional status, the disease which led to acute respiratory failure, the primary system involved, the clinical signs and the type of failure at the time of diagnosing this condition, the treatment given and its outcome were documented in a structured proforma. The nutritional status of each patient was assessed and graded as per Gomez's classification.[5] For the underlying disease the necessary specific therapy was given.

The outcome in each patient was assessed in terms of survival or death. Survival meant that the patient recovered and was discharged from the hospital. The data was analyzed to examine the clinical profile and outcome of acute respiratory failure in the present study. The outcome was correlated with the age, gender and nutritional status of the patients, the primary system involved, the type of failure and the treatment received. The Chi-square test was used for statistical analysis and $p < 0.05$ was considered as significant.

RESULTS

The underlying disease and primary system involved in the 50 patients, and the type of failure detected at the time of diagnosis are shown in Table 1. The present study found out that pulmonary diseases accounted for the majority (68%) of cases, followed by nervous system (12%); and cardiovascular and skeletal muscle system diseases (10%, each); (Table 1). Bronchopneumonia (11 cases) was the commonest cause of acute respiratory failure (Table 1). The majority of patients (26 cases) were in the age group 1 month to < 1year (Table 2). There were 29 males and 21 females, the M: F ratio being 1.38: 1. The signs of acute respiratory failure documented were altered depth and pattern (deep, shallow, apnea, irregular) of respiration in all 50 (100%) patients, followed by, chest wall retractions (88%), flaring of alae nasae (88%), tachypnea (84%), tachycardia (82%), irritability (64%), cyanosis (52%), wheezing (38%), excessive sweating (32%), decreased or absent breath sounds (28%), grunting (24%), hypotension (16%), drowsiness (16%), coma (12%), bradycardia (4%) and cardiac arrest (2%). Majority of the cases with Type I failure (15 out of 19; 78.9%), and Type II failure (9 out of 12; 75%) required ventilation therapy, as compared to fewer cases with Type III failure (12 out of 19 ; 63.1%); but this difference was not statistically significant (p=0.39). Irrespective of the type of acute respiratory failure detected, the majority of children (36 out of 50; 72%) required ventilation therapy.

The overall mortality was 58%. Only 21 patients survived. The survivors included 4 cases of bronchopneumonia, 2 bronchiolitis, 2 laryngotracheobronchitis, 4 status asthamaticus, 2 foreign body aspiration, 1 chemical (kerosene) pneumonitis, 1 ventricular septal defect with pulmonary edema, 1 aorto-pulmonary window with pulmonary edema, 2 Guillain-Barre syndrome, 1 diaphragmatic eventration with bronchopneumonia, and 1 case of tetanus. Of the 29 patients who died, 19 had pulmonary diseases (7 had bronchopneumonia, 3 lobar pneumonia, 2 bronchiolitis, 1 congenital hypoplastic lung with bronchopneumonia, 1 laryngotracheobronchitis, 1 status asthmaticus, 2 interstitial viral pneumonia, 1 miliary tuberculosis, and 1 had foreign body aspiration).

In the present study, although maximum mortality was in the 1 month to < 1 year age group, the age of the patient did not influence the outcome (p=0.38, Table 2). Neither did the gender influence the outcome (p=0.178). The mortality of acute respiratory failure was high, irrespective of the primary system involved (55.9% to 66.7%, Table 2). The mortality was highest for nervous

system diseases and lowest for pulmonary diseases. However this difference was not statistically significant (p=0.892, Table 2). Out of 50 patients, only 13 (26%) had a normal nutritional status. Of these 13 cases, 11 survived. Co-existent malnutrition was associated with a significantly higher mortality (p<0.001, Table 2). Patients with Grade III malnutrition had a very low survival rate as compared to those with Grade I or Grade II malnutrition (Table 2). However, the sample size was small for any meaningful subgroup analysis. Of the 19 patients with Type I failure at the time of diagnosis, 15 died. Patients with Type I failure had a significantly higher mortality rate as compared to patients with Type II or Type III failure (p=0.039, Table 2). Of the 14 patients who were treated with oxygen therapy (FiO_2 up to 0.6), only 1 died. The remaining 36 patients required ventilation therapy. Patients who required ventilation therapy had a significantly higher mortality, as compared to those who required only oxygen therapy (p<0.0001). Two patients with laryngotracheobronchitis received ventilation therapy with CPAP mode of ventilator and both survived. Twelve patients received ventilation therapy in the form of manual IPPV. The mean duration of manual IPPV was 14.8 hours (range 30 minutes to 70 hours, median 3 hours, and S.D. ± 11.08). Of these 11 died, and 9 died within 24 hours of initiation of IPPV therapy. The only patient who survived IPPV therapy (received for 70 hours) was a case of foreign body aspiration. This child's condition improved on removal of the foreign body by bronchoscopy. Twenty-two patients received ventilation therapy with a mechanical ventilator. Of these 17 died, and 8 died within 24 hours of initiation of therapy with a mechanical ventilator.

DISCUSSION

The present study has documented that acute respiratory failure has a varied etiology and a high mortality in the pediatric age group. This is in agreement with earlier descriptions of this condition in standard pediatric textbooks.[1-3] A detailed MEDLINE search revealed only one similar study, reported from the pediatric intensive care unit of the Children's Hospital of Philadelphia, USA.[4] In the present study the commonest diseases causing acute respiratory failure were bronchopneumonia, status asthmaticus, bronchiolitis, laryngotracheobronchitis, foreign body aspiration and, congenital heart disease. These diseases are similar to those reported in the USA study.

In the present study although age of the patient did not influence the outcome, the majority of cases (52%) were in the age group 1 month to < 1 year. In the USA study, almost two-thirds of the cases also occurred in the first year of life.[6] This remarkably high incidence in infancy can be attributed largely to structural immaturity of the chest wall, respiratory muscles, and the airway.[6,7]

The diagnosis of respiratory failure relies primarily on arterial blood gas analysis.[1-4,7] However, clinical assessment of arterial hypoxemia and hypercapnia is not always reliable.[1-4,7] Early diagnosis can be made by the physician who retains a high index of suspicion and who is aware of the clinical situations in which respiratory failure is likely to be a complication.[2,7] Any suspicion of acute respiratory insufficiency should be an indication for obtaining arterial blood gas measurements.[2,7] In the present study the commonest signs of acute respiratory failure were altered depth and pattern of respiration, chest wall retractions, flaring of alae nasae, tachypnea, tachycardia, and irritability. Chest wall retractions, flaring of alae nasae and tachypnea are signs of increased work of breathing.[2,7] Tachycardia is a sign of hypoxemia and irritability is a sign of both hypoxemia and hypercapnia.[2,7] Cyanosis was noticed in only 26 (52%) cases. It is important to remember that respiratory failure can exist without the presence of cyanosis.[1,2] In general, cyanosis becomes apparent only when the mean capillary concentration of reduced hemoglobin exceeds 5 g/dl.[8] Cyanosis is known to be a fairly late sign of respiratory failure.[1,2] In the present study the overall mortality was high irrespective of the primary system involved. But, Type I failure was associated with a significantly higher mortality, which is a known feature of this condition.[1-4]

The overall mortality rate was 58 per cent. Some of the factors which could have contributed to this higher mortality rate in the present study need to be discussed. Firstly, in the present study, 74 per cent of children had protein energy malnutrition and co-existent malnutrition was found to be associated with a significantly higher mortality (p<0.001). An experimental study carried out in adult humans has shown that clinical semi-starvation decreases the ventilatory response to hypoxia.[9] This experimental study has concluded that there should be greater awareness of the potential complications of respiratory insults in the malnourished patient.[9] A recent study from a Spanish PICU has stated that protein energy malnutrition is frequent in patients with acute respiratory failure, and emphasized the need for early and intensive nutritional intervention to reduce mortality in such patients.[10] In the present study, the second reason for the higher mortality was that these patients had presented to us at an advanced stage of their disease. Seventeen out of 50 patients died within 24 hours of admission. Lastly, 12 out of the 36 patients who required ventilation therapy received it in the form of IPPV therapy. Of these 12 patients, 11 died (9 within 24 hours of admission). In our study ventilation therapy was associated with a 77.8 per cent mortality rate which is higher than in the USA study, wherein it was associated with a 48 per cent mortality rate.[4] Non availability of a mechanical ventilator resulting in the patient receiving IPPV could be the third reason for the higher mortality rate in the present study.

In summary, acute respiratory failure is a complication of many disease processes, has varied clinical manifestations, and a high mortality. In the present study

Table 1. Distribution of Cases As Per the Underlying Disease, Primary System Involved and Type of Acute Respiratory Failure at the Time of Presentation

Primary system involved	Underlying disease	No. of cases	Type I	Type II	Type III
Respiratory system	Bronchopneumonia	11	6	1	4
	Lobar pneumonia	3	3	-	-
	Bronchiolitis	4	3	-	1
	Congenital hypoplastic lung with bronchopneumonia	1	-	-	1
	Laryngotracheobronchitis	3	-	-	3
	Status asthamaticus	5	-	2	3
	Interstitial viral pneumonia	2	1	-	1
	Miliary tuberculosis	1	1	-	-
	Foreign body aspiration	3	-	-	3
	Chemical (kerosene) pneumonitis	1	1	-	-
Cardiovascular system	Ventricular septal defect with pulmonary edema	3	2	-	1
	Aorto-pulmonary window with pulmonary edema	1	-	-	1
	Myocarditis with pulmonary edema	1	1	-	-
Nervous system	Pyogenic meningitis with raised intra-cranial tension	1	-	1	-
	Space occupying lesion with raised intra-cranial tension	2	-	2	-
	Cerebral malaria with raised intra-cranial tension	1	-	1	-
	Guillain-Barre syndrome	2	-	2	-
Musculo-skeletal system	Diaphragmatic eventration with bronchopneumonia	1	-	-	1
	Congenital diaphragmatic hernia with lung collapse	1	1	-	-
	Tetanus	2	-	2	-
	Paralysis following cobra bite	1	-	1	-
	Total	50	19	12	19

Table 2. Distribution of Cases of Acute Respiratory Failure As Per Age, Primary System Involved, Nutritional Status and the Type of Failure at Presentation and Their Outcome

Feature	No. of cases	Outcome				χ	p
		Survived	%	Died	%		
Age							
1 month to < 1 year	26	9	34.6	17	65.4	1.91	0.38
1 year to < 5 years	14	6	42.9	8	57.1		
5 years to 12 years	10	6	60	4	40		
Primary System							
Respiratory	34	15	44.1	19	55.9	0.0182	0.892
Cardiovascular	5	2	40	3	60		
Nervous	6	2	33.3	4	66.7		
Skeletal muscle	5	2	40	3	60		
Nutritional status							
Normal	13	11	84.6	2	15.4	10.84	<0.001
Malnourished	37	10	27.1	27	72.9		
(i) Grade I PEM	11	5		6			
(ii) Grade II PEM	10	3		7			
(iii) Grade III PEM	16	2		14			
Type of failure							
Type I	19	4	21.1	15	78.9	4.22	0.039
Type II	12	6	50	6	50		
Type III	19	11	57.9	8	42.1		

PEM = protein energy malnutrition; $p < 0.05$ = significant

its outcome was independent of age of the child and the primary system involved. Malnutrition and Type I failure were factors associated with a poor outcome. Ready availability of a ventilator is necessary to ensure optimum care of this life-threatening condition.

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