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Factors affecting the mortality of children admitted with Acute Respiratory Distress Syndrome in the Pediatric Intensive Care Unit of a tertiary care hospital of Western Maharashtra

Kevin George[1], Aarti.A.Kinikar[2,] Naresh Sonkawade[3]
[1](Junior Resident, Department of Pediatrics, Byramjee Jeejeebhoy Medical College, Pune, India)
[2](Professor and Head of the Department, Department of Pediatrics, Byramjee Jeejeebhoy Medical College, Pune, India)
[3](Assistant Professor, Department of Pediatrics, Byramjee Jeejeebhoy Medical College, Pune, India)

Abstract:
Background*: Acute Respiratory Tract infections are the most common cause of morbidity and mortality among children globally as well as in India. . With advent of lung protective ventilation and other novel strategies mortality associated with Acute respiratory distress syndrome has showed a steep decline over the past few decades in many of the first world countries. Mortality rates were variable across these centres and have been shown to vary from 10-15% with mild cases to as high as 33% in severe disease. However this decline has not been reflected in studies conducted in Asian developing countries with an average mortality of 51% and some centres showing upto 70% death rate. This variability could be attributed to availability of resources, socioeconomic and cultural backgrounds. The aim of this study is therefore to evaluate the mortality associated with ARDS in a tertiary care centre of Western Maharashtra and to assess the risk factors associated with mortality.*
Materials and Methods*: In this prospective observational study conducted in a tertiary care centre, 57 children aged 1 month to 12 years, admitted to the pediatric intensive care unit with Acute Respiratory Distress Syndrome diagnosed based on Berlin definition were enrolled. They were prospectively observed for outcome(recovery/death). Total mortality rate was noted. Children who presented with comorbidities like anemia and malnutrition were observed and their effect on the outcome of Acute respiratory distress syndrome was evaluate.*
Results*: The total mortality rate associated with Acute respiratory distress syndrome was 61%. Mortality in boys and girls were 56.5% and 64.7% respectively with p-value 0.545 showing that gender had no effect on the outcome. Severe anemia present in 59.6% cases and increased mortality risk by 10 times compared to non-anemic children(OR-10.67; 95% CI-3.05 to 37.28; p value- 0.0002). Severe acute malnutrition present in 35% cases and increased risk of death by 59 times (OR-59.5; 95%CI- 109.27; p value-0.0054)*
Conclusion: *Comorbid condition like severe anemia and malnutrition significantly increased the mortality that is associated with Acute respiratory distress syndrome.*
Key Word*: **Acute respiratory distress syndrome ; mortality ; anemia ; malnutrition***

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I. Introduction

Acute Respiratory Tract infections are the most common cause of morbidity and mortality among children globally as well as in India.[1] In a scientific paper published in The Lancet by "The India State level disease burden initiative" under the wings of Ministry of Health and Family Welfare, lower respiratory tract infections was the leading cause of mortality in children under the age of 5 years with 17.9 percent.[2] The risk factor for such high mortality in children could be attributed to low birth weight , child and maternal malnutrition and poor sanitation.[3]Acute Respiratory Distress Syndrome (ARDS) is the most dreaded complication of lower respiratory tract infection. It was initially described by Ashbaugh in 1967 in a set of civilian Americans with respiratory conditions.[4] However later many other non-pulmonary conditions like sepsis, aspiration, trauma etc. were identified to result in ARDS.[5] Initially described in adults, the condition has shown to have severe implications in childhood morbidity and mortality. Strategies for effective management of ARDS has been changing and evolving since its first description five decades ago. With the world being plagued by the novel SARS-CoV-2 with its dreaded ARDS complications, more emphasis has been placed on the multimodality management of ARDS to improve survival outcomes. Mortality associated with ARDS has showed a steep decline over the past few decades in many of the first world countries. Mortality rates were

variable across these centres and has been shown to vary from 10-15% with mild cases to as high as 33% in severe disease.[6] However this decline has not been reflected in studies conducted in Asian developing countries with an average mortality of 51% and some centres showing upto 70% death rate. This variability could be attributed to availability of resources, socioeconomic and cultural backgrounds. The aim of this study is therefore to evaluate the mortality associated with ARDS in a tertiary care centre of Western Maharashtra and to assess the risk factors associated with mortality.

II. Material And Methods

This prospective observational study was conducted at the Department of pediatrics, Byramjee Jeejeebhoy medical college, Pune, India from October 2019 to April 2020, in children admitted with Acute respiratory distress syndrome in pediatric intensive care unit. A total of 57 children aged between 1 month to 12 years were enrolled for the study.

Study Design: Prospective observational study

Study Location: This was a tertiary care teaching hospital based study done in Department of pediatrics, Byramjee Jeejeebhoy medical college, Pune, India

Study Duration: October 2019 to April 2020

Sample size: 57 patients.

Sample size calculation: Sample size was calculated using the formula ,$n=Z^2pq/n2$,Where Z is the confidence interval For 99% Confidence interval, Z=2.575.In the study conducted by Bellany G et al, the incidence of ARDS was found to be 10 in 1000 PICU admission.[7] Error was considered to be 5%The sample size was estimated to be n=53

Inclusion criteria: Children between 1month and 12 years of age satisfying the "BERLIN CRITERIA OF ARDS" admitted to PICU requiring ventilator support.

Exclusion criteria:

1. Children with congenital and acquired heart diseases
2. Children with chronic lung diseases
3. Children with methhaemoglobinemia, carboxyhaemoglobinemia

Procedure methodology :

Children admitted to pediatric intensive care unit requiring mechanical ventilation were evaluated for the presence of Acute respiratory distress syndrome. Detailed history was obtained, Chest radiographs taken and PaO2/FiO2 ratio were calculated using arterial blood gas analysis. Children aged between 1 month and 12 years who were satisfying the Berlin Criteria of ARDS based on history, radiograph and arterial blood gas analysis were enrolled into the study after obtaining written informed consent from the parents. Basic dietary history was obtained at admission and anthropometry calculated to assess the nutritional status of the children. Complete hemogram was done to assess the presence and severity of anemia. Children were treated with lung protective ventilation, intravenous antibiotics, judicious fluid administration and other treatment strategies as recommended by PALICC. The children were prospectively observed for outcome. Mortality associated with ARDS were noted. Tbe effects of gender, severe anemia and nutritional status on mortality were assessed.

Statistical analysis:

Data was analyzed using SPSS version 20 (SPSS Inc., Chicago, IL). Student's *t*-test was used to ascertain the significance of differences between mean values of two continuous variables and confirmed by nonparametric Mann-Whitney test Chi-square and Fisher exact tests were performed to test for differences in proportions of categorical variables between two or more groups. The level $P < 0.05$ was considered as the cutoff value or significance.

III. Result

OUTCOMES:

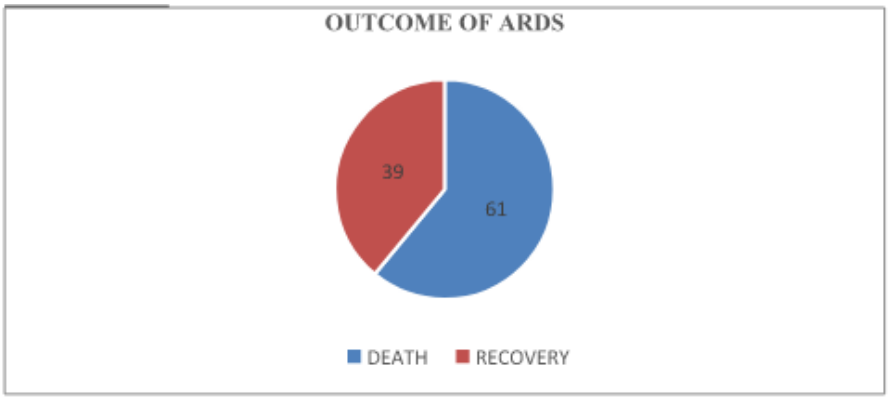

Figure no 1: Outcomes of ARDS

In the present study, of the total 57 children, 61% of the children admitted to PICU expired (n=35) and 39% (n=22) of the patients survived.

1)OUTCOME BASED ON SEVERITY OF ARDS:

Table no 1: Outcome based on ARDS severity

Grade	Death (percent)	Recovery(percent)	95% CI
Mild	20 (n=1)	80 (n=4)	3.56 to 7.04
Moderate	44.8(n=13)	55.2(n=16)	32.98 to 57.29
Severe	91.3(n=21)	8.7(n=2)	73.16 to 97.59

In the study, higher mortality rates were found with worsening severity of acute respiratory distress syndrome. Mortality in the study was 20% for mild (95% CI, 3.56% to 7.04%), 44.8% for moderate(95% CI, 32.98% to 57.29%) and 91.3% for severe (95% CI, 73.16% to 97.59%).

- **GENDER AND MORTALITY:**

Table no 2: Mortality risk assessment based on gender

Gender	Frequency	Mortality	Percent	P value
Male	23	13	56.5	0.545
Female	34	22	64.7	

In our study, male children diagnosed with Acute respiratory distress syndrome had a mortality of 56.5 percent(13 of 23 males) and female children had a mortality of 64.7 percent(22 of 34). Since the p value comparing mortality between male and female patients is 0.545(> 0.05), we infer that the gender of the patient has no effect on mortality.

- **ANEMIA AND MORTALITY:**

Table no 3: Distribution of severe anemia

Severe anemia	Frequency	%
Yes	34	59.6
No	23	40.4

Severe anemia (defined as Haemoglobin < 7g/dl in under 5 age group and Hb < 8g/dl in 5-12 years)[8] was present in 59.6% of patients admitted to intensive care unit with ARDS.

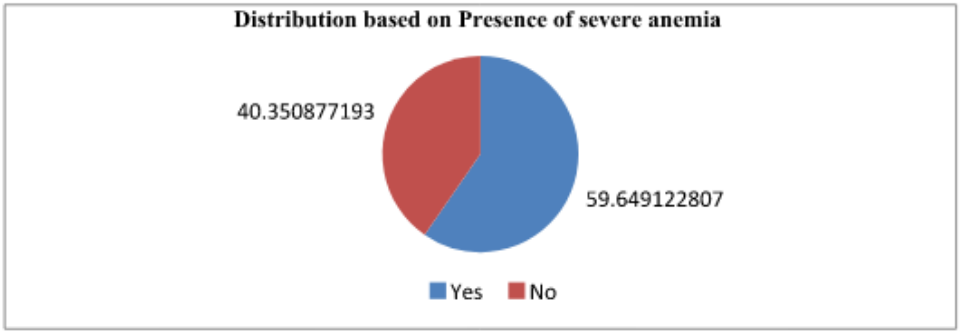

Figure no 2: Pie chart representing distribution of severe anemia

Table no 4: Mortality risk assessment with severe anemia

Risk	Total Cases	Mortality	Odd's ratio	95% CI for OR	P
Anemia	34	28(82%)	10.67	3.0513 to 37.2879	0.0002

Among the 34 patients with ARDS and severe anemia, mortality was 82%(n=28). Odds ratio for the effect of severe anemia on mortality was 10.67 (95% CI, 3.0513 to 37.2879) with a p value of 0.0002. i.e Children with severe anemia who were admitted with ARDS had a 10.67 times increased risk of mortality when compared to non anemic children.

- **MALNUTRITION AND MORTALITY:**

Table no 5: Distribution of malnutrition

Nutritional status	Frequency	%
Normal	17	29.8
Moderate malnutrition	19	33.3
Severe malnutrtion	20	35.1
Obese	1	1.8

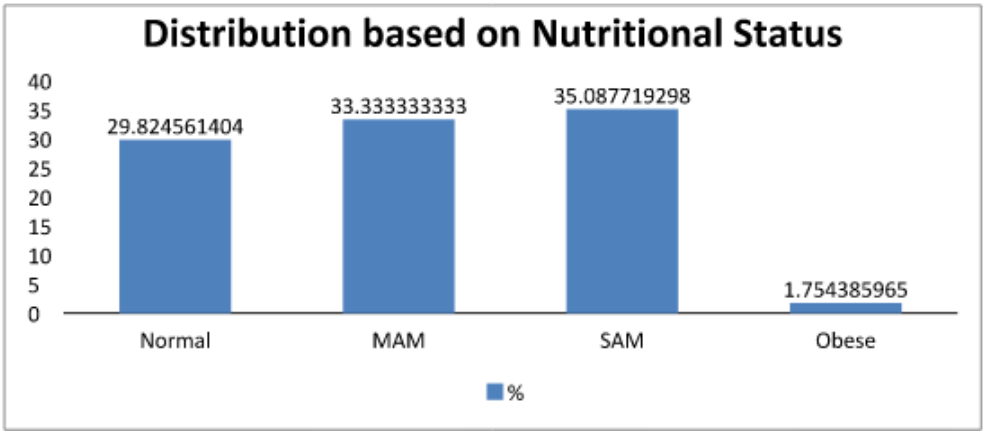

Figure no 3: Bar chart representing the nutritional status of patients

In the current study, nutritional status was adequate in 30% of the study subjects while 70% had some form of malnutrition as defined by the WHO guidelines. 33.3% of children (n=19) had moderate acute malnutrition and 35%(n=20) were suffering from severe acute malnutrition at the time of their admission.

Table no 6: Mortality risk assessment with malnutrition

Risk	Cases	Mortality	OR	95% CI for OR	P
Normal	17	6	0.3013	0.0947 to 1.0137	0.0386
MAM	19	8	0.2963	0.0939 to 0.9351	0.0380
SAM	20	20	59.5161	3.3440 to 109.2757	0.0054
Obese	1	1	1.9565	0.0763 to 50.1793	0.6851

In the study group, 6 of 17 children with normal nutritional status died with an odds ratio of 0.3013(p=0.0386) and 8 of 19 children with moderate malnutrition died with an odds ratio of 0.2963(p=0.0380).
All children with severe malnutrition died with an odds ratio of 59.5(p=0.0054).
While the presence of a relatively better nutritional status (normal and moderate malnutrition) increased the chances of survival, risk of mortality was 59.5 times higher in children with severe malnutrition.

IV. Discussion

Acute Respiratory Distress Syndrome (ARDS) is the most dreaded complication arising in a child requiring intensive care. Although its implication on mortality and morbidity is overwhelming and familiar, the condition is largely under- diagnosed because of the huge financial burden the diagnostic test places on resource limited facilities. Over the past five decades since ARDS was first described massive improvements have been made in the treatment strategies. Mortality associated with ARDS has showed a steep decline over the past few decades in many of the first world countries. Mortality rates were variable across these centres and has been shown to vary from 10-15% with mild cases to as high as 33% in severe disease.[6] However this decline has not been reflected in studies conducted in Asian developing countries with an average mortality of 51% and some centres showing upto 70% death rate.

The current study demonstrated a high mortality rate of 61% which was consistent with study conducted by Goh et al(62% mortality)[9] and Costil et al(60% mortality).[10] The mortality in our study was relatable to the findings of the LUNG SAFE trial. The mortality rate in mild and moderate grades of ARDS in our study was 20% and 44.8% and that of the LUNG SAFE trial was 34.9% and 40.3% respectively.[7] However the death in severe ARDS group is much higher in the current study, 91.3% against the 46.1% in the LUNG SAFE study. This could be explained by the comparatively higher proportion of co-existing comorbidities in our community and study population than the first-world countries.

Malnutrition and anemia were found to have a significant bearing on the severity of ARDS and the outcome.

Anemia was present in 59.6% of the study population and was found to increase the risk of mortality 10 times than non anemic children(OR-10.67; 95% CI for OR-3.05 to 37.28; pvalue- 0.0002).

Nutritional status was adequate in 30% of the study subjects while 70% had some form of malnutrition as defined by the WHO guidelines. 33.3% of children (n=19) had moderate acute malnutrition and 35%(n=20) were suffering from severe acute malnutrition at the time of their admission. Children with adequate nutritional status and moderate malnutrition had better chances of survival, whereas the presence of severe malnutrition on admission significantly raised the risk of death. (OR-59.5; 95%CI for OR- 109.27; p value-0.0054).
Gender was not found to have any bearing on the mortality rate.

V. Conclusion

The high mortality rate associated with acute respiratory distress syndrome in many Asian and other third world countries could be due to the high incidence of co-existing comorbidities like anemia and severe acute malnutrition.

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