Doi: 10.32677/IJCH.2017.v04.i04.004

Original Article

Follow-up assessment of pulmonary functions in mechanically ventilated children after discharge from pediatric intensive care unit: A developing country perspective

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Received - 03 August 2017 Initial Review - 03 September 2017 Published Online - 29 October 2017

ABSTRACT

Background: There is a paucity of data on the pulmonary function tests (PFTs) in pediatric mechanically ventilated patients, especially in a developing country setting. **Materials and Methods:** This prospective study was carried out in the pediatric intensive care unit over 15 months. The PFTs were measured using spirometry at discharge, at 3 and 6 months. **Results:** Of 32 eligible children, 20 (mean age 9 ± 2.62 years) completed the 6-month follow-up. The most common indications for mechanical ventilation were respiratory (45%) and neurological (35%) causes. At the end of 6 months, 65% children had abnormal lung function (restrictive pattern). Patients with longer duration of ventilation, high peak pressures, and high fractional inhaled oxygen had a trend toward more abnormality in the lung function. **Conclusions:** Pediatric mechanically ventilated patients developed restrictive pulmonary defects after discharge that gradually improved over time. The majority was asymptomatic and reported no lifestyle limitations. There is a need for longer follow-up studies to assess the lung function and clinical condition postdischarge.

Key words: *Barotrauma, Cohort study, Critical care, Lung function, Spirometry, Volutrauma*

Despite the everyday use of mechanical ventilation for thousands of patients, there are no clear and consistent guidelines for the use of mechanical ventilation for pediatric patients [1]. Children treated with mechanical ventilation consume a sizable chunk of medical resources, and thus, it is both necessary and desirable to be able to continuously evaluate this treatment after discharge from the pediatric intensive care unit (PICU) [2]. It is known that various ventilation strategies can lead to ventilator-associated lung injury [3-5]. Mechanical ventilation thus cannot be considered a harmless support modality which can be employed to keep patients alive while specific treatments are used [6]. Children who survive acute respiratory distress syndrome (ARDS) apparently have long-term normal pulmonary function. Some, however, may develop subclinical dysfunction that persists for many years after the acute episode and is detected only by sophisticated lung tests [7]. There is a distinct lacuna in the data on follow-up and long-term assessment of mechanically ventilated children in terms of complications and quality of life, including their lung function parameters, especially in a developing country setting. The present study was designed to follow-up the lung function parameters of mechanically ventilated children after discharge from PICU.

MATERIALS AND METHODS

This prospective cohort study was carried over a period of 15 months (January 2012 to March 2013) to follow-up the lung function parameters of mechanically ventilated children discharged from the PICU of a tertiary care teaching hospital in North India. The follow-up was done till 6 months postdischarge. The included children were >5 years of age and were mechanically ventilated for >24 h irrespective of underlying chronic condition and indication of mechanical ventilation. Patients discharged against medical advice, being tracheostomized, and those with any contraindication to the use of spirometry were excluded. The study was approved by the Institutional Ethics Committee. Informed written consent was obtained from the parent(s)/guardian(s) of each patient before enrollment.

Baseline and demographic data were recorded when the patient was begun on mechanical ventilation (Table 1). Additional information was recorded subsequently (ventilator settings, complications of mechanical ventilation, extubation or weaning failure, and total duration of oxygen therapy) (Table 1). The body mass index (BMI) of the patients was recorded and

classified according to the WHO standards depending on their Z-score. A BMI of >1 standard deviation (SD) was considered overweight, >2 SD obesity, and <2 SD underweight [8]. Any complication occurring due to mechanical ventilation, including ventilator-associated pneumonia (VAP) and barotrauma, were recorded. VAP was diagnosed as per the clinical pulmonary infection score [9]. A need for reintubation for any reason within 24 h after elective extubation was termed as extubation failure.

Lung functions were first measured at the time of discharge and then followed up at 3 months and 6 months. The first spirometry measurement was taken in the inpatient department, and the subsequent (follow-up) measurements were taken in the outpatient department. The equipment used was micro medical gold standard fully computerized portable autospirometer Super Spiro Cat No: SU-6000 (a flow sensing spirometer). The device was calibrated using a 3 L fixed volume calibration syringe following the manufacturer's recommendation. Calibration was verified before every 10th recording. All aseptic precautions were taken. Disposable mouthpieces were used for each patient.

Technique of Spirometry [10,11]

Before the test, inhaled long-acting beta-agonists were stopped for at least 8 h, and short-acting beta-agonists for at least 2 h. Inhaled corticosteroids were continued. Large meals, vigorous exercise, and tight clothing were avoided. The children were asked to bring the inhalers they were using currently. Any child with contraindication to the use of spirometry was excluded at each visit. The procedure was explained and demonstrated to the children before the measurement. Baseline vital capacity (VC) and forced VC (FVC) maneuvers were performed, a minimum of three readings were obtained in each child. The baseline spirometry results were recorded in paper template. Highest values were taken from any one of the three efforts meeting repeatability criteria (not necessarily from the same blow).

The results were compared with the values available for Indian children from a previously published study from our center [12]. Reliable reference values for some parameters such as expiratory volume (EV) and VC could not be obtained. However, these values were measured on follow-up and compared with discharge values. A value <80% of predicted was considered to be abnormal, and test results were predicted for all individuals.

Data were entered into the Microsoft Excel spreadsheet. SPSS software for Windows (version 16.0, Chicago, SPSS Inc.) was used for all the analyses. Continuous variables were expressed in mean and range. Categorical variables were expressed as percentage/proportions and analyzed using the Chi-square test. The absolute lung function values were recorded and analyzed with respect to their expected values. The percentage of expected as well as percentage deficit was calculated. Data at 3 months and 6 months were compared with the discharge data and paired *t*-test was applied to compare them.

RESULTS

During the study period, a total of 32 children were found to be eligible, of which 20 children completed 6-month follow-up (Fig. 1). Baseline characteristics are given in Table 1 and the indications of mechanical ventilation are provided in Table 2. Extubation failure was seen in three children, of them, one had two extubation failures. However, all three were subsequently successfully extubated. After

Table 1: Characteristics of study children

Variables	n (%)
Male	15 (75)
Age (years)	Mean, 9 years (range, 5-16 years)
5-8	9 (45)
9-12	9 (45)
13-16	2 (10)
Urban residence	7 (35)
Nutritional status	
Normal	10 (50)
Undernourished	7 (35)
Overweight	1 (5)
Obese	2 (10)
PRISM III score >10	8 (40)
Duration of ventilation (days)	Mean, 8.3 days (range, 2-17 days)
≤3	3 (15)
≤7	8 (40)
8-14	7 (35)
>14	2 (10)
PICU stay (days)	Mean, 14.2 days (range, 4-23 days)
≤7	4 (20)
8-14	8 (40)
15-21	6 (30)
>21 days	2 (10)
PIP requirement >24 h (cm H_2O)	
<20	11 (55)
21-30	6 (30)
>30	3 (15)
FiO_2 requirement >24 h	
<0.4	10 (50)
0.4-0.6	7 (35)
>0.6	3 (15)
Complications	
VAP	3 (15)
Pneumothorax	1 (5)
Extubation failure	3 (15)
Inotropes	10 (50)
Sedation (<48 h)	5 (25)
Paralytics	3 (15)

PRISM: Pediatric risk of mortality, PIP: Peak inspiratory pressure, FiO_2: Fractional inhaled oxygen, PICU: Pediatric intensive care unit, VAP: Ventilator-associated pneumonia

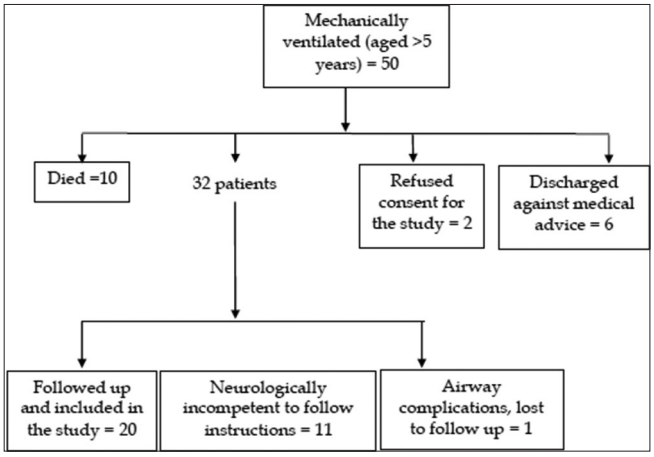

Figure 1: Total number of mechanically ventilated patients in pediatric intensive care unit above 5 years of age and their eligibility for the present study

Table 2: Indications of mechanical ventilation

Indications	n (%)
Neurological causes	7 (35)
Traumatic brain injury	3 (15)
Meningoencephalitis	2 (10)
Guillain-Barre syndrome	2 (10)
Pulmonary causes	9 (45)
ARDS	3 (15)
Pneumonia	2 (10)
Chest trauma	2 (10)
Pulmonary hemosiderosis	1 (5)
Organophosphorus poisoning	1 (5)
Multisystem/others	4 (20)
Septic shock	1 (5)
Post-operative major vascular repair (elective)	1 (5)
Polytrauma	2 (10)

ARDS: Acute respiratory distress syndrome

3 months of follow-up, 15 (75%) children demonstrated abnormal lung function (restrictive pattern), while 25% had normal lung function. None exhibited an obstructive pattern of abnormality. At 6 months, the percentage of children with normal lung functions had increased to 35%. Distribution of characteristics of children in relation to their pulmonary function tests (PFTs) at 3 and 6 months is described in Table 3. Although female patients, urban patients, underweight children, and adolescents had worse lung function, there was no statistically significant difference ($p > 0.1$). Similarly, children with primary neurological involvement or elective ventilation showed better lung functions on follow-up compared to those with primary respiratory involvement, but the difference was not statistically significant.

Children with longer duration of PICU stay, longer duration of mechanical ventilation, and those suffering from complications had a trend toward more abnormality in lung function. Extubation failure was not found to influence long-term pulmonary function. Patients who required lesser sedation and no paralytics did better, while those requiring high peak inspiratory pressure (>30 cm of H_2O) and high fractional inhaled oxygen (FiO_2) (>0.60) had a trend toward more abnormality in lung function. Most of the patients demonstrated significant deficit in the measured values of inspiratory volumes (IVs), inspiratory capacity (IC), FVC, and forced EV in the first second (FEV1) at 3 and 6 months (Table 4), but the deficit decreased as compared to the discharge values. Only five children at 3 months (25%) and eight children at 6 months (40%), postdischarge had normal FEV1 values. Six children (32%) had IC values within normal range after 6 months. All children had normal tidal volumes (TVs) at 6 months, and only 3 (14%) had a significant deficit in peak expiratory flow rate (PEFR). No child, at either 3 months or 6 months, showed any abnormality in the FEV1/FVC. PFT values at 6 months (% of expected values) have been shown in the figure (Fig. 2). Although majority (65%) of the children demonstrated restrictive lung function defects, most of them were asymptomatic, reported no lifestyle limitations and were attending school regularly.

DISCUSSION

On pulmonary function testing at 3 months and 6 months PICU postdischarge, we found predominantly restrictive abnormality in our population. None of the children had an obstructive pattern defect. Our findings are supported by Golder et al. [13], who studied five children with acute hypoxemic respiratory failure and found the occurrence of restrictive defect in four of these patients at 6-10 months postdischarge. Ben-Abraham et al. [7] followed up seven children with ARDS, six had normal pulmonary function, and one had restrictive abnormality. However, they followed up at a longer interval, shortest being 3 years. Lyrene and Truog [14] reported two survivors of pediatric ARDS who developed restrictive abnormality at 1 year of follow-up. Weiss et al. [15] performed spirometry in 11 patients with respiratory failure at an average of 23-month follow-up postdischarge. Eight had normal lung function, one had obstructive, and two had mixed pattern, but the obstructive element in last two children was elucidated on giving bronchodilators and noting the improvement in mid-maximal expiratory flow. They also evaluated patients at a longer follow-up period than the present study.

In this study, on pulmonary volume studies, a number of children with normal spirometry emerged to have restrictive abnormality. All patients recovered normal TV at the end of follow-up period. Significant improvement in IV as compared to discharge value was found both at 3 and 6 months; although the values remained below expected in a large number of children. Both the values were statistically significant, demonstrating significant improvement in IC on follow-up. Significant improvement in VC values was found at 3 months and 6 months as compared to discharge values. Only a few adult studies have reported on VC deficits in survivors of ARDS, and no corresponding pediatric studies were found [16-18]. Children with ARDS in our study also appeared to have greater VC deficits. PEFR values showed significant improvement over their discharge values with only three children having abnormal values at 6 months. Our findings are supported by other studies [13,15]. Golder et al. [13] reported 2

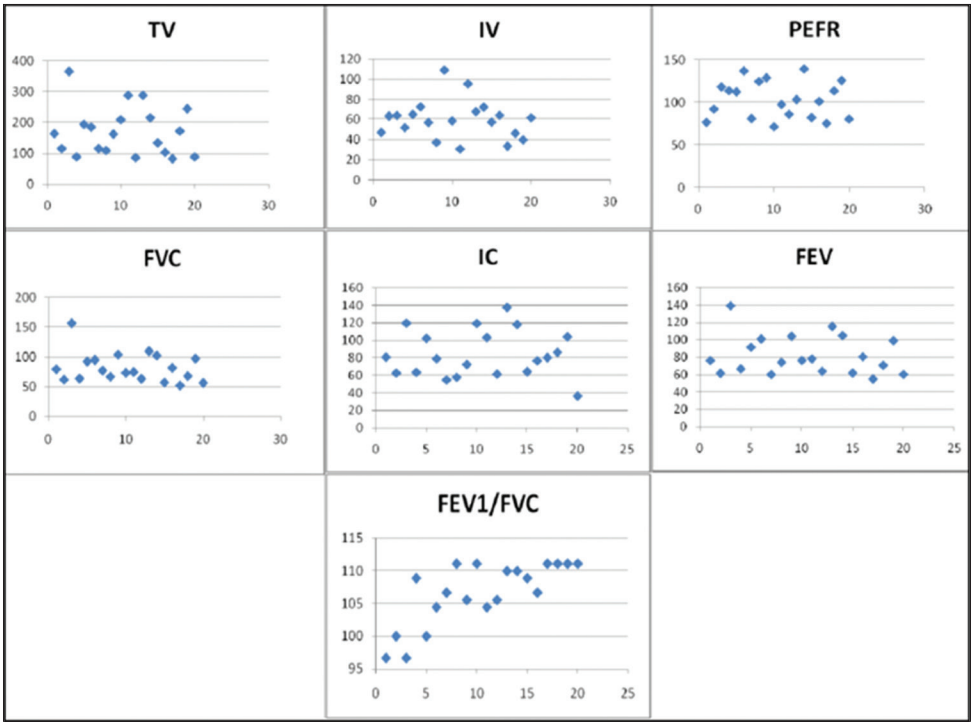

Figure 2: Pulmonary function test values at 6 months expressed as percentage of expected values

Table 3: Distribution of characteristics of children in relation to their PFTs at 3 and 6 months

Variables	At 3 months		p	At 6 months		p
	Normal (%)	Restrictive (%)		Normal (%)	Restrictive (%)	
Gender						
Male	5 (33)	10 (67)	0.14	6 (40)	9 (60)	0.42
Female	-	5 (100)		1 20	4 (80)	
Age (years)						
5-8	3 (33)	6 (67)	0.59	4 (44)	5 (56)	0.49
9-12	2 (22)	7 (88)		3 (33)	6 (67)	
13-16	-	2 (100)		-	2 (100)	
Residence						
Rural	4 (31)	9 (69)	0.42	5 (38)	8 (62)	0.66
Urban	1 (14)	6 (86)		2 (29)	5 (71)	
Nutritional status						
Underweight	1 (14)	6 (86)	0.24	1 (14)	6	0.07
Normal	2 (20)	8 (80)		3 (30)	7	
Overweight	1 (100)	-		1 (100)	-	
Obese	1 (50)	1 (50)		2 (100)	-	
Primary system involvement						
Neurological	4 (57)	3 (43)	0.06	4 (57)	3 (43)	0.13
Respiratory	-	9 (100)		1 (11)	8 (89)	
Multisystem	1 (33)	2 (66)		1 (33)	2 (66)	
Others/elective	-	1 (100)		1 (100)	-	
PRISM III score						
≤10	3 (25)	9 (75)	1.0	5 (42)	7 (58)	0.44
>10	2 (25)	6 (75)		2 (25)	6 (75)	
Duration of ventilation (days)						

(*Contd...*)

Table 3: (Continued)

Variables	At 3 months		p	At 6 months		p
	Normal (%)	Restrictive (%)		Normal (%)	Restrictive (%)	
≤7	4 (36)	7 (64)	0.32	6 (55)	5 (45)	0.4
8-14	-	7 (100)		1 (14)	6 (84)	
>14	1 (50)	1 (50)		1 (50)	1 (50)	
PICU stay (days)						
≤7	2 (50)	2 (50)	0.26	3 (75)	1 (25)	0.09
8-14	2 (25)	6 (75)		3 (37)	5 (63)	
15-21	-	6 (100)		-	6 (100)	
>21	1 (50)	1 (50)		1 (50)	1 (50)	
Extubation failure						
Yes	1 (33)	2 (67)	0.72	2 (67)	1 (33)	0.21
No	4 (24)	13 (76)		5 (29)	12 (71)	
PIP (cm H_2O) for >24 h						
<20	3 (27)	8 (73)	0.83	5 (45)	6 (54)	0.49
21-30	1 (16)	5 (84)		1 (16)	5 (84)	
>30	1 (33)	2 (67)		1 (33)	2 (67)	
FiO_2 (%) for >24 h						
<0.4	2 (20)	8 (80)	0.86	4 (40)	6 (60)	0.88
0.4-0.6	2 (28)	5 (72)		2 (28)	5 (72)	
>0.6	1 (33)	2 (67)		1 (33)	2 (67)	
Complications						
VAP	-	3 (100)	0.27	-	3 (100)	0.07
Pneumothorax	-	1 (100)		-	1 (100)	
None	5 (31)	11 (69)		9 (56)	7 (44)	
Sedation						
None	-	2 (100)	0.62	-	2 (100)	0.55
48 h	1 (20)	4 (80)		2 (40)	3 (60)	
>48 h	4 (31)	9 (69)		5 (38)	8 (62)	
Paralysis						
None	5 (29)	12 (71)	0.83	7 (41)	10 (59)	0.49
≤48 h	-	3 (100)		-	3 (100)	
>48 h	-	-		-	-	

PFTs: Pulmonary function tests, PRISM: Pediatric risk of mortality, PIP: Peak inspiratory pressure, FiO_2: Fractional inhaled oxygen, PICU: Pediatric intensive care unit, VAP: Ventilator-associated pneumonia

Table 4: PFTs mean values at discharge and 6 months with corresponding change

Parameters	Mean±SD value at discharge (%)	Mean±SD value at 3 months (%)	Mean change over 3 months (%)	p	Mean±SD value at 6 months (%)	Mean change over 6 months (%)	p
TV	125.43±41.49	139.50±58.17	+14.13	0.34*	171.57±79.42	+46.13	0.02
IV	34.18±15.2	49.48±29.65	+15.3	0.03	59.70±19.33	+25.52	<0.001
PEFR	61.29±37.38	88.41±22.69	+27.12	0.02	103.12±21.96	+41.83	<0.001
FVC	60.99±22.41	68.38±28.01	+7.38	0.81*	81.58±24.72	+20.59	0.01
FEV1	57.18±21.41	68.35±27.13	+11.34	0.01	81.91±24.72	+24.72	<0.001
FEV1/FVC	93.75±14.50	99.97±5.91	+6.22	0.053*	100.25±4.87	+6.50	0.052*
IC	62.65±19.11	79.91±29.26	+17.25	0.01	85.88±26.21	+23.22	0.002
VC	0.96±0.54 L	1.23±0.58 L	+0.267 L	0.01	1.43±0.57 L	+0.473 L	<0.001

***p value >0.05, TV: Tidal volume, IV: Inspiratory volume, PEFR: Peak expiratory flow rate, FVC: Forced vital capacity, FEV1: Forced expiratory volume in the first second, IC: Inspiratory capacity, VC: Vital capacity. SD: Standard deviation, PFTs: Pulmonary function tests**

(of 6) children with abnormal PEFR values at 6 months; however, Weiss et al. [15] reported 2 (of 11) children with abnormal values of PEFR at a longer follow-up.

At 6 months, 12 children (60%) demonstrated residual deficit in their FVC. This is consistent with the findings of Golder et al. [13] where 4 (of 5) children had abnormal

FVC values at 6 months of follow-up. However, Weiss et al. reported that only 3 (of 11) children demonstrated a deficit in FVC. Ben-Abraham et al. [7] also had similar findings, where 1 (of 7) children demonstrated a deficit in FVC value. In both these studies, the follow-up was done at a longer duration of ≥1 year. It is possible that with a longer duration of follow-up, we might have found improvement in the FVC values as the 6 months mean values showed a significant improvement over the discharge values. Similar results in adults were recorded with notable improvement seen in longer follow-up [16,19-21]. Similar observations could be made regarding FEV1. Only eight children had normal values at 6 months. The improvements in FEV1/FVC ratio are also supported by pediatric studies, all of whom reported normal FEV1/FVC ratios on follow-up [7,13,15]. It appears that pediatric mechanically ventilated patients infrequently suffer from obstructive airway defects. In contrast, adults with ARDS have a high incidence of deficit in FEV1/FVC ratio; thus, signifying an obstructive pattern of pulmonary function [17,22-24].

Although we found many children (65%) with restrictive PFT pattern, the majority of them was asymptomatic and was attending school regularly. This means, whatever problem developed in the lung mechanics did not manifest clinically under routine circumstances. However, this limited pulmonary reserve as shown by the restrictive PFT pattern could probably become clinically relevant under stressful situations including another lower respiratory tract infection or excessive physical activity. Hence, there is the importance of monitoring PFT in these children. A longer follow-up could have answered this issue better. There is a possibility that children with primary respiratory causes for ventilation may have reduced lung function due to underlying respiratory condition in addition to any ventilator-associated damage. However, we did not find any difference between the two conditions.

Our study has some limitations. The need for cooperation required for pulmonary function testing eliminated many children limiting the sample size and power of the study. Most of the children were asymptomatic at follow-up, and the diagnosis of pulmonary disease in asymptomatic patients using PFT remains to be validated. The study group was heterogeneous in respect to the baseline characteristics and underlying etiologies of the respiratory failure. The inclusion of such a varied population may not have yielded uniform results applicable to other populations. Another limitation was the time period for follow-up, a longer follow-up may yield better results and may tell the time period by which normal lung function is attained. Nevertheless, our study is unique of its kind due to reporting data from a developing country setting.

CONCLUSION

Pediatric mechanically ventilated patients developed restrictive pulmonary defects after discharge that gradually improved over time. The majority were asymptomatic, reported no lifestyle limitations and were attending school regularly. There is a need for longer follow-up studies to assess the lung function and clinical parameters postdischarge.

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Funding: None; Conflict of Interest: None Stated.

How to cite this article: Garg M, Bhargava S, Pooni PA, Das RR, Mishra NR. Follow-up assessment of pulmonary functions in mechanically ventilated children after discharge from pediatric intensive care unit: A developing country perspective. Indian J Child Health. 2017; 4(4):471-477.