Ventilator Associated Common Lung Complications in Pediatric Intensive Care Unit (PICU): Frequency, Risk Factors, and Outcomes

Running Title: Ventilator associated common lung complications in (PICU)

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Abstract

Background*:* Mechanical ventilation (MV) is a common practice in pediatric intensive care units, and more than 20% of patients require invasive ventilator support. Despite the use of lung-protective ventilation modes in the pediatric population, complications of mechanical ventilation are prevalent.

Objectives*:* To determine the risk factors and outcomes of ventilation-associated common lung complications and to analyze the frequencies in PICUs at Assiut University Children's Hospital, Assiut, Upper Egypt.

Methods*:* A retrospective hospital-based case-control study was collected by reviewing and evaluating the medical records data of 154 patients connected to MV for at least 48 hours from April 2022 to April 2023 in the PICU of AUCH, enrolled in the current study. Descriptive statistics, cross-tabulations, and logistic regressions were done to determine risk factors for developing complications.

Results: A total of 154 pediatric patients on mechanical ventilation were included in the study: 75 girls (48.7%) and 79 boys (51.3%). In 38 instances (24.6%), CNS problems were the most prevalent cause of PICU admission; in 22 cases (24.8%), respiratory illnesses came in second. Pneumothorax (17.1%), atelectasis (15.8%), and ventilation-associated pneumonia (VAP) (53.9%) are the most frequent pulmonary problems that were noted.

Conclusion: Despite technological advancements, the incidence of pulmonary problems resulting from mechanical ventilation (MV) in pediatric patients remains elevated.

Keywords*:* Risk factors, outcome, pediatric intensive care unit, ventilation-associated lung complications.

Introduction:

Mechanical ventilation may bring about several negative consequences and issues. Mechanical ventilation's most common adverse consequences are ventilator-induced lung damage, ventilator-associated infections, and hemodynamic compromise from ventilation, leading to acute respiratory distress syndrome (ARDS) (1).

Ventilator-associated pneumonia (VAP) is the term used to describe nosocomial pneumonia that appears 48 hours or longer after the initiation of mechanical ventilation (2).

It is the second most common hospital-acquired infection (HAI) in the pediatric age range, behind bloodstream infection, with a prevalence of 2.9–21.6/1000 ventilator days. About 20% of all HAIs in PICUs are composed of it (3).

The endotracheal tube, the ventilation circuit, and the presence of an orogastric or nasogastric tube are risk factors for ventilator-associated pneumonia (VAP) (4). VAP is associated with higher rates of hospital death, morbidity, and duration of stay (5). Developing nations with few

resources have higher VAP incidence rates (6).

Lung damage brought on by mechanical ventilation that provides either positive or negative pressure to the lung is referred to as ventilator-associated lung injury (VALI) (7). Approximately 10% of kids admitted to the PICU suffer from VALI (8)

Hemodynamic impairment brought on by ventilation results in acute respiratory distress syndrome (ARDS), characterized by a drop in mean arterial pressure of 60 mm Hg or an absolute drop to a systolic blood pressure of less than 80 mm Hg during the first two hours following intubation. Vasopressors are needed to treat this potentially fatal hypotension (9). The frequency of post-intubation hypotension is around 28.6% of intubated patients in the emergency department. There is a statistically significant correlation between hypercarbia (PCO2 > 50 mm) and chronic obstructive pulmonary disease, which can lead to life-threatening hypotension (10).

Thus, the main objective of the current study is to determine the incidence risk factors of ventilation-associated common lung complications in the PICUs at AUCH, as well as their outcome.

Patients and Methods:

This study was a retrospective hospital-based case-control study. The study was approved by the local Ethics Committee at the Faculty of Medicine, Assiut University (IRB No:04-2022- 200022).

(A) Sample Size Calculation:

All children connected to mechanical ventilation meeting our inclusion criteria from the 1st of April 2022 to the end of April 2023 were enrolled in the current study (total coverage).

(B) Patients:

All children aged one month to 16 years admitted to the PICU of AUCH and needed intubation and connected to mechanical ventilation for at least 48 hours from April 2022 to April 2023 were enrolled in the current study. Newborns (aged less than one month) and children connected to MV for less than 48 hours were excluded.

(C) Data Collection:

The following data were collected from medical records: full history taking including name, age, sex, causes of PICU admission, developed complications, duration of hospital stay (days), and outcome (discharged or died), vital signs, systematic physical examination and routine investigations, and acute phase reactants was also recorded. In addition, a blood culture to identify the causative organism was also collected for all studied participants' medical records before and after M.V.

(D) Statistical Analysis:

All statistical calculations were done using SPSS (statistical package for the social science; SPSS Inc., Chicago, IL, USA) version 22. Data were statistically described in terms of mean±standard deviation (±SD) median (range) and compared by Mann Whitney U test, or presented as numbers (percentages) and compared by Chi-square ($\chi 2$) or Fisher Exact test. The odds ratio (OR) with a 95% Confidence Interval (CI) and Logistic Regression was calculated to predict the development of complications among the studied participants. P-value set significant at 0.05 level.

Results:

Table (1): Demographic and Clinical data of the studied cases

Variable name	**Total cases (n=154)**	
Age (years), median (range)	years (one month–15 years) 4	
Males sex, n (%)	79	(51.3)
Causes of PICU admission, n (%)		
CNS causes	38	(24.6)
GIT causes	21	(13.6)
Pulmonary causes	22	(14.8)
Metabolic causes	14	(9.1)
Renal problems	9	(5.8)
Cardic causes	8	(5.2)
Post-surgical	11	(7.0)
Inherited disease	6	(3.9)
Hematological causes	5	(3.2)
Other*	20	(12.2)
Complication, n (%)		(49.4) 76
VAP		40 (53.9)
Pneumothorax		13 (17.1)
Atelectasis		12 (15.8)
ARDS		8 (9.3)
Bronchopleural fistula		1 (1.3)
Pneumonitis		1 (1.3)
Lobe collapse		1 (1.3)
Mode of ventilation, n (%)		
PCV	76	(49.4)
SIMV	68	(44.2)
CPAP	10	(6.5)
Duration of hospitalization (days), median (range)	(60 – 2) 7	
Outcome, n (%)		
Died	38	(24.7)
Improved	116	(75.3)

* Others include: Accident, toxicity, corrosive inhalation, chylus abdomen, Neman pick type c, charge syndrome, carbo monoxide, and alm phosphide, child abuse, choanal atresia. SIMV: Synchronized Intermittent Mandatory Ventilation; PCV: pressure-controlled ventilation; CPAP: continuous positive airway pressure.

Table (1) A total of 154 children were enrolled in the current study with a median (range) age of 4 years (one month up to 16 years), and 51.3% were boys. CNS disorders were the most common cause of PICU admission (24.6%), followed by chest infections in 14.8%. 49.4% develop complications; VAP was the most common complication in 53.9%. The median duration of hospitalization was seven days (range 2-60 days). PCV mode was the most used in 49.4 %. Regarding patient outcomes, 75.3% were improved and discharged home in good health, with an overall mortality rate of 24.7%.

Table (2): The relationship between Demographic and clinical data to complications

Variable name	Not complicated (n=78)		Complicated (n=76)		P value
Age (years), median (range)	5 years (3 months–15 years)		years (one 2 month–15 years)		**0.001 >**
Sex, n (%)					0.744
Male	39	(50.0)	40	(52.6)	
Female	39	(50.0)	36	(47.4)	
System affection					**0.001 >**
Single system affection	60	(76.9)	28	(36.8)	
Multisystem affection	18	(23.1)	48	(63.2)	
Days on MV, n (%)					**0.001 >**
< 7 days	61	(78.2)	8	(10.5)	
≥ 7 days	17	(21.8)	68	(89.5)	
Hemodynamic status					0.077
- Stable	46	(59.0)	34	(44.7)	
- Unstable	32	(41.0)	42	(55.3)	
Respiratory rate					**0.035**
- Normal	68	(87.2)	56	(73.7)	
- Tachypnea	10	(12.8)	20	(26.3)	
Blood pressure					0.225
- Normal	62	(79.5)	54	(71.1)	
- Hypotension	16	(20.5)	22	(28.9)	
Heart rate					0.235
- Normal	59	(75.6)	48	(63.2)	
- Tachycardia	16	(20.5)	22	(28.9)	
- Bradycardia	3	(3.8)	6	(7.9)	
Body temperature					0.395
- Normal	62	(79.5)	56	(73.7)	
- Feverish	16	(20.5)	20	(26.3)	
Need inotropes					**0.015**
- No	55	(70.5)	39	(51.3)	
- Yes	23	(29.5)	37	(48.7)	

Table (2) shows that patients who developed complications were younger age, suffered from multisystem affection, and had a longer duration on MV. Also, complicated cases had a higher need for inotropes (23 cases (29.5%) vs. 37 cases (48.7%), P=0.015) and also suffered from higher respiratory rates 10 cases (12.8%) vs. 20 cases (26.3%), P=0.035). Other clinical assessments were comparable between both groups with no significant difference (P > 0.05).

Table (3): Logistic regression analysis for prediction of developing complications

Variables	Univariate analysis			Multivariate analysis		
	OR	**95% CI**	**P value**	**OR**	**95% CI**	**P value**
Age						
< 4 years	4.971	9.908 – 2.495	**0.001>**	3.038	14.493 – 0.637	0.163
≥ 4 years	ref			ref		
WBCs				Not included in the final model		
Normal	ref					
Leukocytosis	3.200	6.798 – 1.506	**0.002**			
Leucopenia	NA	NA – 0.0	0.999			
System affection						
Single	ref			ref		
Multiple	5.714	11.545 – 2.828	**0.001>**	130.278	2532.471 – 6.702	**0.001**
CRP						
Negative	ref			ref		
Positive	32.857	84.037 – 12.847	**0.001>**	142.670	1897.22 – 10.729	**0.001>**
Need inotropes						
No	ref			ref		
Yes	2.269	4.401 – 1.169	**0.015**	2.355	17.036 – 0.326	0.396
Respiratory rate						
Normal	ref			ref		
Tachypnea	2.429	5.611 – 1.051	**0.038**	6.105	52.146 – 0.715	0.070
ABG						
Normal	ref			ref		
Compensated	0.694	2.049 – 0.235	0.508	0.223	2.061 – 0.024	0.220
Metabolic acidosis	2.352	4.698 – 1.177	**0.015**	6.891	60.549 – 0.784	0.082
Days on MV, n (%)						
< 7 days	ref			ref		
≥ 7 days	30.500	75.668 – 12.294	**0.001>**	84.566	765.128 – 9.347	**0.001>**

MV: mechanical ventilation; CI: Confidence interval; OR: Odds ratio. * P value is significant □0.05

Table (3) Univariate logistic regression analysis for predicting developing complications among the studied cases was confirmed on multivariace logistic regression analysis which showed that multiple system affection, positive CRP, and those needing MV for ≥ 7 days are still significant predictors for developing complications.

Discussion

In the PICU, mechanical ventilation is often utilized, and more than 20% of patients need invasive ventilator support. Although lung-protective ventilation techniques are widely used in the pediatric population, problems from mechanical ventilation still happen often, and pediatric doctors must be skilled in recognizing, avoiding, and managing these difficulties (11).

The study included 154 children aged one month up to 16 years who were all intubated and connected to MV for at least 48 hours; the median age of the studied participants was 4 years and ranged from one month up to 16 years in a study conducted by Vijayakumary et al. (2012) the median age of patients was 3 years (12).

In the present study, there was no sex predilection (male-to-female ratio of 1.1:1). The same ratio was reported by Amanati A. et al. (2017) (13).

In the presented study regarding the cause of PICU admission and connection to M.V., CNS disorders were the commonest cause accounted for (24.6%), followed by chest infections documented (14.8%). This agreed with a study done by Mukhtar et al. (2014), who showed that the indications for MV in PICU were divided into four major categories, including acute neurological illness (35.8%), respiratory illness (20.8%), cardiac failure (13%) and miscellaneous group (30.3%) (14). Meanwhile, the present study was contrary to a study done in EL-Mahalla Chest Hospital in 2015 in which the indications for MV were acute on top of chronic respiratory failure (77.7%), followed by acute hypoxemic respiratory failure (11.54%), post-arrest (10%) and coma (0.77%) (15). The most likely explanation for this could be due to the differences in diseases prevalent at the time and region of the study and the variation in patient populations in different studies.

In the current study, the median duration of MV was seven days (range: 2-60 days). This, in agreement with the PICU of Pakistan (2014), showed that the duration of MV was 4-6 days (14). In a study by Vijayakumary et al. in Sri Lanka, the intubation duration was 6 days (12). Also, studies were done in Italian (16), Latin America (17), and Cairo (18); the median duration of MV was 3.1, 4.5, 5, and 9 days, respectively.

This variation could be due to hospital differences, cases, mixed health provider staffing, and technologies.

In the present study, the most used mode of MV was PCV in 49.4%, SIMV in 44.2%, and CPAP in 6.5%. This is in agreement with the study by Farias et al. (2012), which showed that the ventilatory modes preferred at the beginning of MV were A/C (assistant/control) (17). But this is against the study done by Esteban et al. (2002) (19) and Kübler et al. (2013) (20) that showed different modes of MV; the modes were BiPAP (84.9%) followed by CPAP (15.2%).

In the current study, [76(49.4%)] cases developed pulmonary complications; it has been shown in a similar study that the percentage of complications was 42.8% (21). The most frequent pulmonary complications in the presented study were VAP in [40(53.9%)], pneumothorax in [13(17.1%)], and atelectasis in [12(15.8%)]. This finding agrees with the Egyptian study of Meligy et al. (2017) (18). In a study by Mukhtar et al., atelectasis was documented in only 4.6% of the patients, although it was still the most common complication (14).

This finding supports the fact that the incidence of VAP in our country is still very high. However, clinicians are trying to endorse a VAP bundle. Still, there is a missing link between low-staffed units and the absence of infection control personnel monitoring during night shifts, which may partially explain this high rate of VAP among the studied participants.

In this study, an estimation of the risk of developing complications was assessed by calculating odds ratios (OR) and logistic regression analysis, which reflected predictors of mortalities. Shows that multiple system affection, positive CRP, and those needing MV for $\geq$ 7 days are still significant predictors for developing complications. This is in agreement with (14).

Our study showed that the length of hospitalization and time of connecting to MV had a significant influence on the occurrence of complications. In 2005, Fontela et al. first showed that MV $\geq$ 15 days was associated with a low extubation success rate (4.5%), which significantly prolonged MV connection time and, subsequently, the occurrence of complications (22); this finding suggests that knowledge advancements about weaning, and support care can improve the extubation success rate over time, so lower time of hospitalization.

In our study, there was a relation between the reason for patient PICU admission and the occurrence of complications, as we noted that patients admitted to PICU with multi-organ failure more often suffered from complications in 74 % of complicated cases. The results, like

studies done by Rajnan et al. (2014), showed that the % of complications in patients with surgical causes of PICU admission was 76% (23).

Regarding the outcome of studied cases, 75.3% were improved and discharged home in good health, with an overall mortality rate of 24.7%. This agrees with previous reports stating that the survival rate was 63% and 58.3% in Pakistan (24) and Turkey (21). This was against a study by Saleh et al. (2019), in which the survival rate of mechanically ventilated cases was 23% while the mortality rate was 77% (25).

The mortality rate in our study was quite not high. There could be several reasons for the low mortality rate. Firstly, the patients presented to our hospital at an early stage of the disease, and hence, more efficient treatment was provided as per uniform protocol. Secondly, most of our patients belong to rural areas; hence, the chances of cross-infection were much less. Thirdly, most of the patients we presented to were primarily treated by us and were not referred from other health care centers.

Study limitations: A relatively small sample size and conducted in a single center could limit the generalizability of the current findings.

Conclusion

This study determined that the frequency of pulmonary complications secondary to MV in pediatric patients is similar to that reported in developing countries and has not varied significantly with time despite technological improvements in MV devices.

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