

EFFECT OF USING NURSING CARE BUNDLE ON DEVELOPING VENTILATOR ASSOCIATED PNEUMONIA AMONG INFANTS

GEHAN AHMED ELSAMMAN

Professor, Pediatric Nursing, Faculty of Nursing, Cairo-University, Egypt.

AZZA ABDEL MOGHNY ATTIA

Professor, Pediatric Nursing, Faculty of Nursing, Cairo-University, Egypt.

HANAA IBRAHIM RADY

Professor, Pediatric Medicine, Faculty of Medicine, Cairo-University, Egypt.

MOUSA ABDEL FATTAH MOUSA HASSAN

Assistant Lecturer, Pediatric Nursing, Faculty of Nursing, Cairo-University, Egypt.
Email: mousaabdefattah2@gmail.com, mousaabdefattah2@cu.edu.eg

Abstract

Background: Applying nursing care bundle on mechanically ventilated infants play a role in decreasing the incidence of ventilator associated pneumonia and improving their outcomes. Aim: To evaluate the effect of using nursing care bundle on developing ventilator associated pneumonia among infants. Design: A quasi-experimental research pre/post-test design. Sample: A purposive sample of 100 infants on mechanical ventilator in the pediatric intensive care units aged ranges from 1-12 month divided equally into study and control groups. Setting: The study was carried out at pediatric intensive care units of two hospitals; El-Mounira and specialized pediatric hospitals which affiliated to Cairo-University hospitals. **Methods:** Data collected using three tools including personal characteristics and medical history questionnaire, nursing care bundle and ventilator associated pneumonia indicator's record. Results: three-fifths and less of infants in the study and control groups their age ranged from 6 to 12 months and from 1 to less than 6 months respectively, three-fifths and less in both groups were male. The main diagnosis was respiratory distress followed by neurological disorders. Three-fifths and less had oral endotracheal intubation, minority among both groups had unplanned extubation, mechanical ventilation days among the study group were less than the control group with significant difference. One fifth and more than one third of infants developed ventilator associated pneumonia among study and control groups respectively. Highly statistically significant negative correlations were detected between various components of the nursing care bundle and development of ventilator associated pneumonia. **Conclusion:** The current study concluded that application of the nursing care bundle significantly decreases the incidence of ventilator associated pneumonia among infants on mechanical ventilation as well as mean mechanical ventilation days, corticosteroids use and mortality. **Recommendation:** Application of nursing care bundle in pediatric intensive care units should be used as a routine care for infants and replication of the study on larger sample of infants in different settings.

Keywords: Infants, Nursing Care Bundle, Mechanical Ventilation, Ventilator-Associated Pneumonia.

1. INTRODUCTION

Pediatric intensive care units (PICUs) admissions stem from a range of critical conditions requiring intensive monitoring and specialized care. Common causes include severe respiratory illnesses such as acute respiratory distress syndrome and severe pneumonia, which necessitate advanced respiratory support like mechanical ventilation (MV). Furthermore, other significant reasons for pediatric patients to require the high level of care provided [1].

Pediatric intensive care units have the highest incidence of infections because of many causes, including frequent invasive procedures, use of medical devices, and prolonged exposure to multi-drug resistant organisms. Use of medical devices in PICUs is a critical factor in rates of nosocomial infections. Nosocomial infections are a major challenge in critical care medicine worldwide and are associated with significant increases in mortality, morbidity, duration and cost of hospitalization [2].

Mechanically ventilated infants are at risk of many complications as developing ventilator associated pneumonia (VAP), ventilator-induced lung injury, oxygen toxicity, hyperinflation, positional atelectasis and/or consolidation, impaired mucociliary clearance, and decreased functional residual capacity, increasing volume and viscosity of secretions, inadequate humidification of ventilator gases, diseases processes themselves may lead to airway obstruction, infection, atelectasis, and ultimately chronic lung disease. As a result, it necessary to treat all ventilated children in an attempt to reduce the incidence of these squeals [3]. VAP is the most common nosocomial infection in PICUs, and it is a major threat to the recovery of patients receiving MV [4].

VAP rates ranges from 2.7 to 10.9 episodes per 1.000 days of MV in PICUs in high-income countries. Mortality rates associated with VAP ranges between 20% and 70% worldwide [5]. Ventilator associated pneumonia is defined as an episode of pneumonia where the infant is intubated and connected to a ventilator for more than two calendar-days [6].

In studies conducted in Egypt, Iran, China, the United States of America, and Turkey, the VAP rate per 1.000 mechanical ventilator days was found to be 70.3, 21.08, 29.5, 25.3 and 31.2 respectively. Mortality rates associated with VAP range between 20% and 70% worldwide [7]. In an Egyptian study conducted in the PICUs of pediatric Cairo-University hospital titled "Assessment of the effectiveness of a ventilator associated pneumonia prevention bundle" who reported that the overall mortality was 46.15%, VAP mortality rate patients was higher than non VAP patients and recommend for additional studies for application of care bundles and estimating the incidence of VAP in wide sample scale [8]. The critical care nurses play an important role in application of care bundles to decrease incidence and prevention of VAP [9].

Prevention of VAP includes interventions aimed at avoiding aspiration in the lungs, colonization of respiratory tract with pathogenic microorganisms and avoiding contamination of respiratory equipment [10]. A number of evidence-based guidelines was developed and care bundles for VAP prevention which include implementation of a group of evidence-based practices together which should increase conformity to procedures and provide better clinical outcomes [11].

Care bundle is evidence-based guidelines in the PICUs that establish that prevention of VAP is achievable through the application of certain multiple interventions at the same time, implementing care bundles in clinical practice has been widely advocated in mechanically ventilated pediatric patients admitted to PICUs and is associated with a reduced risk of VAP [12].

A care bundle components usually contains list of interventions that should be grouped together into a single quality measure [13]; the key components in the care bundle are proper hand washing, wearing, removing gown and wearing gloves, routine environmental decontamination of the ventilator, head of bed elevation to 30° to 45°, oral care with chlorhexidine, turning the patient at least every 3 hours, ventilator circuit changes when soiled or if not working, changing resuscitation bags every week and hang at bedside rather than left in the bed, chest physiotherapy, closed system suctioning [14]. Also, the application of the care bundle should begin at the time of intubation and continued until extubation [15]. Higher adherence to care bundles correlates with a substantial reduction in VAP rates [12].

There is a significant gap between the recommended application of nursing care bundles and the actual clinical practice, which contributes to the ongoing incidence of VAP in PICUs. Factors of inconsistent implementation by nursing staff including inadequate training, staff shortages, and lack of compliance monitoring contribute to this disparity [16].

In a study titled "Implementation of ventilator bundle for prevention of ventilator associated pneumonia in pediatric intensive care unit" it concluded that VAP is one of the serious complications of MV that significantly increases the length of PICUs stay and mortality and bundle implementation was found effective in decreasing the VAP rate in the PICUs infants [17]. In a study titled "Microbiological pattern of ventilator associated pneumonia" clarified that, VAP rate decreased with compliance with the ventilator bundle from 50 to 14% with significant difference [18].

Nurses in critical care units can make a significant contribution to prevent nosocomial infections as the nurse responsible for applying quality improvement measures [12]. Critical care nurses play an important role in identification of risk factors and prevention of VAP, knowledge on evidence-based practices should bring confidence to intensive care nurses to make appropriate decisions and prevent poor outcomes in the recovery of mechanically ventilated patients [19].

2. METHODS

2.1 Aim

To evaluate the effect of using nursing care bundle on developing ventilator associated pneumonia among infants.

2.2 Hypothesis

Infants who will receive the nursing care bundle will have lower incidence of ventilator associated pneumonia than the control group.

2.3 Design

A quasi-experimental research pre-posttest design was utilized.

2.4 Setting

The study was carried out at pediatric intensive care units of two hospitals; El-Mounira and specialized pediatric hospitals which affiliated to Cairo-University hospitals.

2.5 Participants

A purposive sample of 100 infants on MV in the PICUs and were fit with the study's inclusion criteria.

Inclusion criteria

- Infants age from (1-12 months).
- On MV through endotracheal tube (ETT).
- Infants connected to monitor.
- Recently intubated within 48 hours.
- Infants admitted to PICUs for only medical health problems.

Exclusion criteria

- Referred from other hospitals.
- Positive VAP indicator's record.

Sample Size

Sample size was determined based upon the following formula:

$$n = \frac{T^2 \times p(1-p)}{m^2}$$

$$n = (1.96^2) \times 0.04(1-0.04) / (0.05 \times 0.05) = 60.2112.$$

Description

n=required sample size.

t = confidence level at 95% (standard value of 1.96).

p = estimated prevalence of infants on MV at & El-Mounira and specialized pediatric hospitals which affiliated to Cairo-University hospitals (estimated p=0.04) (According to the statistical record (2020) in El-Mounira [20] and specialized pediatric hospitals [21] there were about 280, 120 cases, admitted to PICU on MV for different modalities of therapies) respectively.

m = margin of error at 5% (standard value of 0.05).

(<http://www.ifad.org/gener/tools/hfs/anthropometry>) [22].

- For statistical purposes the sample consists of 100 infants (50 as study group and another 50 will be the control group).

2.6 Data Collection Tools

It was developed by the researcher based on an extensive literature review; the required data were collected through the following tools.

Tool 1: Personal characteristics and medical history questionnaire: it contains two parts as the following:

Part (I). It includes questions related to the personal data of infants: age, gender, rank, weight on admission, current weight, father's education and work, mother's education and work, and residence.

Part (II). It includes questions related to the past and present medical history of infants: initial diagnosis, current diagnosis, date of admission to hospital, place admitted from, level of consciousness, date of MV, type of MV, unplanned extubation and its number, length of stay on MV/days, medication used and respiratory system invasive procedures.

Tool 2: Nursing care bundle record: The bundle content was adapted from Speck et al., (2016) [13] it consists of 16 items, 8 items were omitted (medical care), 8 items were adopted and one item was added (chest physiotherapy). The adapted tool included 9 items as following; universal precautions of infection control that includes (hand washing before and after any procedure, wearing and removing gown, wearing and removing gloves), routine environmental decontamination of the ventilator with germicidal wipes, changing breathing circuits of ventilators only when they are visibly soiled or unclean or if not working, heated ventilator circuits, changing resuscitation bags every week and hang at bedside rather than left in the bed, changing the infant position (semi-fowler's or lateral positioning of infants), scheduled mouth care, chest physiotherapy (percussion, vibration and postural drainage) and accurate, safe comfortable suction (oro-pharyngeal, naso-pharyngeal and endotracheal); the response of this tool was in the form of done and the causes of undo items.

Tool 3: VAP indicator's record: The tool was adopted from National Healthcare Safety Network (NHSN)/Centers for Disease Control (CDC), (2019) [23] to detect VAP among infant less than one year; it consists of three main parts which includes:

Part (I). Radiological signs which include 4 items: 1-new or progressive and persistent infiltrate, 2-consolidation, 3-cavitation and 4-pneumatocoles.

Part (II). Clinical signs and symptoms which includes 8 items: 1-worsening of gas exchange and three of the following items (2-temperature instability with no other recognized cause, 3-leukopenia or leukocytosis and left shift, 4-new onset of purulent sputum, change in the character of sputum or increase in respiratory secretions, or increased suctioning requirements, 5-apnea, tachypnea, nasal flaring with retraction of chest wall or grunting, 6-wheezing, rales, or rhonchi, 7-cough, and 8-bradycardia or tachycardia).

Part (III). Microbiological findings which include 4 items: 1-positive pleural fluid culture, 2-positive quantitative culture, 3- $\geq 5\%$ BAL (Bronchoalveolar lavage)-obtained cells contain intracellular bacteria, and 4-histopathological exam shows abscess formation or foci of

consolidation or positive quantitative culture of lung parenchyma, or evidence of lung parenchyma invasion; the response of this tool was in the form of present, absent and comment.

To detect of VAP requires a combination of radiological signs, clinical signs and symptoms and microbiological findings as following: one or more radiological signs, four or more clinical signs and symptoms and one or more microbiological findings.

2.7 Validity

Content validity of study tools (1, 2) were assured through panel of three experts in the field of pediatric medicine nursing and pediatrics. The tools were examined for content coverage, clarity, relevance, and applicability. The experts agreed on the content of the tools but recommended minor modifications that would make the information clear and more precise, such as rephrasing and rearranging some sentences. VAP indicator's record (tool 3) was adopted from Speck et al., (2016) [13], the construct validity was assured by [24]

2.8 Reliability

Reliability of (tool 2, 3) was performed to confirm tool consistency using Cronbach's alpha, (tool 2) it was 0.79 and (tool 3) it was 0.72– 0.79 which means high internal consistency and high reliability for all tools [24].

2.9 Procedure

The study tools were prepared and then official letters were taken from faculty of nursing to the directors of El-Mounira and specialized pediatric hospitals as well as the heads of PICUs. At first the researcher started with the study group. The researcher met parents of infants eligible for inclusion criteria at the waiting room to introduce him-self to the parents and give them complete description of the purpose and nature of the study to attain their acceptance and co-operation. The researcher fills personal data and medical history of infants from parents and from infant's medical records (tool 1). Before application of the nursing care bundle the researcher filled VAP indicator's record (tool 3) for the study group; it was done as baseline assessment before completion of 48 hours after connection to MV.

If the infant's VAP indicator's record was negative; the researcher applied the nursing care bundle for each infant for 14 days or until the infant extubated for improvement or developed VAP or died. The researcher started application of the nursing care bundle at morning and afternoon shift; for at least 4 times/12 hours that took about 30-45 minutes for each infant, assessed reading of ABG at morning and at the end of afternoon shift if available. The researcher applied the universal precautions of infection control included hand washing, wearing gown and gloves, after that practice routine environmental decontamination of the ventilator with Dettol antibacterial cleansing surface wipes and change the breathing circuits of ventilators if it were visibly soiled or not working, after that operate the heated ventilator circuits and change resuscitation bag if needed and hang it at bedside.

The researcher changed the infant's position every two hours, providing mouth care using sterile water and gauze, after that applied chest physiotherapy (chest percussion, postural drainage and vibration) then applied accurate, safe comfortable suction. After completing the application of the nursing care bundle the researcher remove gloves and gown, provide hand washing and recorded tool 2. The researcher assessed the development of VAP for each infant using the VAP indicator's record (tool 3) daily at the end of afternoon shift for 14 days or until the infant extubated for improvement or developed VAP or died.

The same tools (tool 1 and tool 3) were filled for the control group and done as baseline assessment before completion of 48 hours after connection to MV. If the infant's VAP indicator's record was negative; the researcher assessed the development of VAP for each infant using the VAP indicator's record (tool 3) daily for 14 days or until the infant extubated for improvement or developed VAP or died.

The researcher assessed reading of ABG at the end of afternoon shift if available after application of routine care by nurses which includes elevation of the head of the bed between 30 to 45 degree, daily oral care with chlorhexidine, turn the infants from back to right and left side every 2 hours. Field work begins from November 2022 to June 2024.

2.10 Statistical Analysis

Data entry and statistical analysis were done using statistical package for the social science (SPSS) 20.0 Data were presented using descriptive statistics in the form of frequencies and percentages for qualitative variables and means and standard deviations for quantitative variables. Qualitative categorical variables were compared using chi-square test. Comparison of means was performed using paired-sample t-test. Correlation among variables was done using Pearson correlation coefficient. One-way repeated measures ANOVA test was done to test the same subjects over time. Fisher exact test was done to test associations between categorical variables. Statistical significance was considered at p-value ≤ 0.05 .

3. RESULTS

Table (1) demonstrated that that three-fifths and less (60% and 58%) their age ranged from 6 to 12 months and from 1 to less than 6 months respectively among study and control group, with mean age 7.5 ± 1.8 and 7.4 ± 1.9 months respectively. Regarding gender, three-fifths and less (60% and 56%) in both groups were males. More than two-fifths and less (44% and 40%) among study and control groups respectively had respiratory distress followed by less than two-thirds (36%) and less than one third (32%) of the infants in both groups had neurological disorders.

Regarding length of stay in PICU by days, more than two-fifths (44%) of infants in the study group stay in PICU for 1-5 day and two-fifths (40%) of infants in the control group stay in PICU for 6-10 days with mean length of stay in PICU 10.5 ± 2.3 and 15.8 ± 3.5 days respectively. Concerning place admitted from, three-fifths and more (60% and 64%) respectively of the infants in the both groups were admitted from the emergency room.

Table (2) presents that three-fifths and less (60% and 58%) of the infants in the study and control groups had oral endotracheal tube (ETT) and two-fifths and more (40% and 42%) had nasal route.

Regarding planned extubation, the vast majority and majority (90% and 88%) of the infants in both groups had planned extubation, minority (10% and 12%) of the infants in both groups had unplanned extubation. All (100%) of infants in both groups were on positive pressure ventilation.

In relation to respiratory system invasive procedures among the study and control groups, less than one third (30%), more than one third (36%) had chest tube insertion and minority (10%); one fifth (20%) had central venous line.

The same table illustrated that two-fifths (40%) of infants in the study group stayed from 1 to 5 days on MV and the same percent of infants in the control group stayed from 6 to 10 days on MV. Concerning the mean days on MV among the study and control groups were 8.2 ± 2.4 and 9.5 ± 3.0 days respectively.

There were no statistically significant differences between both groups regarding the personal characteristics, medical history, history of the MV except for respiratory system invasive procedures, length of MV/days and its mean.

Table (3) delineates that all (100%) of infants of both groups had negative quantitative culture of endotracheal aspirate at the first day of admission to PICU, majority (88%), and less than three-quarters (74%) had negative quantitative of endotracheal aspirate culture at day 7 among the study and control groups, compared to 80% and 64% after disconnection from MV. There was statistically significant difference was detected between both groups regarding microbiological signs of VAP.

Table (4) shows that four-fifths (80%), more than three-fifths (64%) of infants in the study and control groups did not develop VAP, while one fifth (20%) and more than one third (36%) of infants in both groups developed VAP.

In relation to onset of VAP, half and more than two-fifths (50% and 44.44%) of infants with VAP in the study group had early onset (≤ 5 days), half and more (50% and 55.55%) of infants with VAP among the control group had late onset (> 5 days). There were statistically significant differences between the both groups regarding incidence and onset of VAP.

Table (5) clarifies that there were highly statistically significant negative correlations were detected between various components of the nursing care bundle and development of VAP, while positive correlations were detected between application of nursing care bundle and absence of VAP.

Table (6) illustrated that the most significant factors affect the development of VAP were length of MV followed by positive quantitative cultures and diagnosis of neurological disorders. There were highly statistically significant differences between all factors with higher odds ratio and incidence of VAP.

Table 1: Personal Characteristics and Medical History of Infants in the Study and Control Groups (n=100)

Items	Study (n=50)		Control (n=50)		X ² /t	p
	n	%	n	%		
Age /months					3.24	0.82
1 ≤ 6	20	40	29	58		
6-12	30	60	21	42		
Mean ± SD	7.5±1.8		7.4±1.9		t=0.27	0.07
Gender					0.16	0.68
Male	30	60	28	56		
Female	20	40	22	44		
Diagnoses					0.16	0.74
Respiratory distress	22	44	20	40		
Neurological disorders	18	36	16	32		
Gastroenteritis	8	16	9	18		
Sepsis	2	4	5	10		
Length of PICU stay/days					1.4	0.49
1 to 5	22	44	15	30		
6 to 10	18	36	20	40		
11 to 15	7	14	10	20		
> 15	3	6	5	10		
Mean ± SD	10.5±2.3		15.8±3.5		t=0.55	0.21
Place admitted from					0.17	0.67
Emergency Room	30	60	32	64		
Wards	20	40	18	36		

* Significant at p ≤ 0.05 ** Highly significant at p ≤ 0.01

Table 2: History of Mechanical Ventilation and Invasive Procedures of Infants among the Study and Control Group (n=100)

Items	Study (n=50)		Control (n=50)		X ²	p
	n	%	n	%		
Route of intubation:					0.04	0.85
Oral	30	60	29	58		
Nasal	20	40	21	42		
Extubation:					0.10	0.71
Unplanned	5	10	6	12		
Planned	45	90	44	88		
Type of MV:					0.0	1
Positive pressure ventilation	50	100	50	100		
Respiratory system invasive procedures:					10.88	0.02*
Chest tube insertion	15	30	18	36		
Central venous line	5	10	10	20		
Length of using MV/days					15.22	0.01**
1 to 5	20	40	15	30		
6 to 10	15	30	20	40		
11 to 14	15	30	15	30		
Mean ± SD	8.2±2.4		9.5±3.0			

* Significant at p ≤ 0.05 ** Highly significant at p ≤ 0.01

Table 3: Difference of Microbiological Signs of VAP among Infants in the Study and Control Groups at First Day of Admission to PICU, Day 7 and after Disconnection from MV (n=100)

Items		First day		Day 7		Disconnection from MV		F	p
		n	%	n	%	n	%		
Negative quantitative culture of endotracheal aspirate	Study	50	100	44	88	40	80	13.20	0.02*
	Control	50	100	37	74	32	64		
Positive quantitative culture of endotracheal aspirate	Study	0	0	6	12	10	20		
	Control	0	0	13	26	18	36		

* Significant at $p \leq 0.05$ ** Highly significant at $p \leq 0.01$

Table 4: Comparison of VAP Incidence and Onset among Infants in the Study versus Control Groups

Items	Study		Control		X ²	p
	n	%	n	%		
VAP Incidence					12.26	0.01**
Developed	10	20	18	36		
Not developed	40	80	32	64		
Onset of VAP					6.50	0.01**
Early onset (≤ 5 days)	5	50	8	44.44		
Late-onset (> 5 days)	5	50	10	55.55		

* Significant at $p \leq 0.05$ ** Highly significant at $p \leq 0.01$

Table 5: Relation between Application of Nursing Care Bundle Components and Incidence of VAP among Infants in the Study Group (n=50)

Items	VAP Present (n=10)		VAP Absent (n=40)	
	r	p	r	p
Universal precautions of infection control	-0.63	< 0.001**	0.66	< 0.001**
Hand washing	-0.68	< 0.001**	0.68	< 0.001**
Routine environmental decontamination	-0.66	< 0.001**	0.65	< 0.001**
Changing breathing circuits when soiled	-0.68	< 0.001**	0.68	< 0.001**
Heated ventilator circuits	-0.64	< 0.001**	0.67	< 0.001**
Changing Infant's position				
Semi-fowler's position	-0.62	< 0.001**	0.62	< 0.001**
Lateral position	-0.62	< 0.001**	0.62	< 0.001**
Changing resuscitation bag (weekly)	-0.45	0.001**	0.68	< 0.001**
Scheduled mouth care	-0.68	< 0.001**	0.64	< 0.001**
Chest physiotherapy	-0.42	0.002**	0.66	< 0.001**
Accurate, safe, comfortable suction	-0.68	< 0.001**	0.65	< 0.001**

* Significant at $p \leq 0.05$ ** Highly significant at $p \leq 0.01$

Table 6: Factors Associated with Development of VAP among Infants in the Study Group (n=50)

Items	Odds Ratio (OR)	95% Confidence Interval (CI)	p
Age (months)			
1 ≤ 6	1.11	0.95 – 1.29	0.15
6-12	1.13		
Weight on admission (kg)	0.98	0.85 – 1.12	0.71
Length of MV (days)	4.25	2.36 – 7.60	0.001**
Not changing breathing circuit	2.45	1.41 – 4.24	0.02*
Use of antibiotics	1.68	0.98 – 2.85	0.06
Multidrug-resistant organisms	2.55	1.44 – 4.49	0.02*
Diagnoses			
Respiratory distress	1.11	0.95 – 1.29	0.15
Neurological disorder	3.55	2.09 – 6.02	0.02*
Gastroenteritis	0.68	0.40 – 1.15	0.13
Sepsis	2.50	1.44 – 4.33	0.01**
Positive quantitative culture	3.81	2.24 – 6.46	0.001**

* Significant at $p \leq 0.05$ ** Highly significant at $p \leq 0.01$

4. DISCUSSION

In relation to infant's age, the current study findings indicated that three-fifths and less, their age ranged from 6 to 12 months and from 1 to less than 6 months respectively among study and control groups. These results were congruent with [25] in study titled "Changing the ventilator breathing circuits to reduce ventilator associated pneumonia" who found that two-thirds and less than three-fifths of infants their age ranged from 6 to 12 months and from 1 to less than 6 months respectively among study and control groups. The mean age of infants in the current study among both groups was 7.5 ± 1.8 and 7.4 ± 1.9 months respectively.

These results agreed with [26] in a study titled "The spectrum of pneumonia among intubated infants in the pediatric intensive care unit" who reported that the mean age of infants in study and control groups was 7.4 ± 1.6 and 7.3 ± 1.8 months respectively. While [27] in a study titled "Exploring risk factors with ventilator-associated pneumonia among infants in intensive care units" who found that the mean age of infants in the study and control groups was 6.3 ± 3.2 and 5.7 ± 3.3 months respectively.

Regarding gender, three-fifths and less, of infants in the study and control groups were males. These results in accordance with [28] a study titled "Effectiveness of educational intervention in preventing ventilator associated pneumonia in neonatal intensive care unit: a cohort study: prevention of ventilator associated pneumonia" who reported that more than two-thirds and more than half of infants in the study and control groups were males. At the same time the present study results were in agreement with [29] in a study titled "Frequency and risk factors of ventilator-associated pneumonia at neonatal intensive care unit of Nishtar Hospital, Multan" who found that less than three-fifths and more than two

fifths of infants in the study and control groups were males. The current study results revealed that there were no statistically significant differences between study and control groups regarding infant's personal characteristics. These results in accordance with [30] in a study titled "Current concepts in assisted mechanical ventilation in the neonate" clarified that there were no statistically significant differences between the study and control groups regarding age and gender.

Concerning diagnoses of infants, the current study results revealed that, more than two-fifths and less, among study and control groups respectively had respiratory distress. These results were in line with [31] in a study titled "Risk factors of respiratory diseases among neonates in neonatal intensive care unit of Qena University hospital, Egypt" who found that less than one half and more of infants among study and control groups admitted to the PICU with respiratory diseases. The researcher's observed that during the clinical practice the main diagnosis of infants still the respiratory problems.

Regarding length of stay in PICU by days, more than two-fifths of infants in the study group stayed in PICU for 1-5 days and two-fifths of infants in the control group stay in PICU for 6-10 days with mean length of stay in PICU 10.5 ± 2.3 and 15.8 ± 3.5 days respectively. These results in agreement with [32] in a study titled "Ventilator-associated pneumonia in pediatric intensive care unit patients: microbiological profile, risk factors, and outcome" who found that less than half of infants in the study group stayed in PICU for 1-5 days and two-fifths of infants in the control group stay in PICU for 6-14 days with mean length of stay 7-15 days. From the researcher's point of view a shorter PICU stay often implies faster recovery, fewer complications, and reduced exposure to hospital-acquired infections.

In spite of there were no statistically significant differences between the study and control groups regarding PICU length of stay but still the study group had less mean length of stay in PICU than the control group and the difference was 5.3 days. These results were contradicted with [33] in a study titled "Impact of nursing guidelines on nurses' knowledge and performance regarding to prevention of ventilator associated pneumonia in neonates" and in another study done by [34] about "Effectiveness of ventilator associated pneumonia care bundle on the pediatric critical care nurses knowledge, practice and critically ill neonates outcome" who stated that there were statistically significant differences between the study and control groups regarding PICU length of stay and the difference was 3.32 days shorter in the study group.

The findings of the present study identified that three-fifths and more respectively of infants in the study and control groups were admitted from the emergency room. These results were in accordance with [27] who reported that less than three-fifths and more than one quarter of infants among both groups respectively were admitted from emergency room followed by ward. From the researcher's point of view infants admitted from emergency room exposed to more invasive procedures such as emergency intubation, cardiopulmonary resuscitation and insertion of central venous line, which may expose infants to infection. The results of the current study clarified that three-fifths and less, of infants in the study and control groups had oral ETT, two-fifths and more had

nasal route. These results supported by [36] who reported that the vast majority and less, of infants in the study and control groups had oral ETT. Also, the current study results in agreement with [35] in a study titled “Ventilator-associated pneumonia in children” who found that four-fifths of infants in the study and control groups had oral ETT and the remaining one fifth were intubated via the nasal ETT.

The current study results showed that the minority of infants in the study and control groups had unplanned extubation. These results were in accordance with [36] in a study titled “Unplanned extubation during pediatric cardiac intensive care: U.S. multicenter registry study of prevalence and outcomes” who reported that one third of infants in both groups had unplanned extubation. Also, [37] in a study titled “Incidence, outcome and determinants of unplanned extubation among pediatric intensive care unit in Addis Ababa, Ethiopia: a nested case–control study” who found that unplanned extubation occurred to more than one quarter of infants in both groups. From the researcher’s point of view unpredictable events such as unplanned extubation might consider as a risk factor of developing VAP.

The current study results found that less than one third and more than one third of infants in the study and control groups had chest tube insertion. These results were contradicted with [38] who found that the majority and less than one quarter of infants both groups had chest tube.

These study results were inconsistent with [37] who reported that more than three-fifths of infants in the study and control groups had chest tube. In a study titled “Epidemiology and outcomes of ventilator-associated pneumonia in a large US database” who found that more than three-quarters and majority of infants in both groups had chest tube [39]. From the researcher’s point of view increase the frequency of using invasive procedures especially to the respiratory system may increase susceptibility of VAP.

The findings of the present study identified that the minority and one fifth of infants in the study and control groups had central venous line. These results supported by [40] in a study titled “Risk factors for neonatal ventilator-associated pneumonia: a retrospective cohort study” who found that nearly one quarter and one fifth of infants in both groups had central venous line. Also, the current study finding disagree with [41] in a study titled “Prevalence of ventilator-associated pneumonia in children admitted to pediatric intensive care units in the Middle East: a systematic review” who found that two-thirds and three-fifths of infants in the study and control groups had central venous line.

The present study results concerning MV showed that there were statistically significant differences between the study and control groups regarding total days of MV with means score 8.2 ± 2.4 and 9.5 ± 3.0 days respectively among the both groups. These results go in line with [42] in a study titled “Ventilator-associated pneumonia in infants at a pediatric intensive care unit: a retrospective observational study” who reported that there were statistically significant differences between the study and control groups regarding total days of MV and infants with VAP had longer duration of MV with mean of days was 8.7 ± 3.6 days and 9.3 ± 2.6 days respectively in both groups.

Also, the current study results were in contrast with [31] who found that the mean duration of MV among infants in the study and control groups was 8.9 ± 2.5 days and 9.0 ± 3.7 days with statistically significant differences. Also, the study results were inconsistently with [43] in a study titled “Ventilator-associated pneumonia in neonates admitted to a tertiary care NICU in Bulgaria: a prospective cohort study” who mentioned that the mean duration of MV among infants in both groups was 5.4 ± 4.5 days and 6.2 ± 1.2 days respectively with statistically significant differences. From the researcher’s point of view duration of MV in the current study may be due to the main diagnosis was respiratory distress.

Concerning microbiological signs, the present study findings indicated that all infants in the study and control groups had negative quantitative culture of endotracheal aspirate (ETA) at the first day of admission to PICU, 88% and 74% of infants in both groups had negative quantitative of ETA culture at day 7. These results in line with [44] in a study titled “Endotracheal aspirate and ventilator-associated pneumonia in neonates: revisiting an age-old debate” who reported that all infants in the study and control groups had negative culture of ETA at the first day of admission to PICU, 86% and 71% of infants in both groups had negative culture of ETA at day 7 of MV. Also, the current study findings agree with [45] in a study titled “Endotracheal aspirate microscopy, cultures and endotracheal tube tip cultures for early prediction of ventilator-associated pneumonia in neonates” who found that 83% and 70% of infants in the study and control groups had negative quantitative culture of ETA at day 7 of MV. From the researcher’s point of view nosocomial infections in the PICU are a major concern due to the vulnerability of critically ill children and the frequent use of invasive procedures.

The current study results revealed that there was statistically significant difference was detected between the study and control groups regarding results of quantitative culture of ETA after disconnection from MV. These findings in agreement with [46] in a study titled “Evaluation of microbiological signs in infants in PICU” who found that there were statistically significant differences between both groups regarding results of quantitative culture of ETA after disconnection from MV. Regarding development of VAP, the current study findings showed that four-fifths, more than three-fifths of infants in the study and control groups did not develop VAP after disconnection from MV. These findings in accordance with [47] in a study titled “Non-invasive high-frequency oscillatory ventilation in preterm infants after extubation: a randomized, controlled trial” who found that majority and more than three-fifths of infants in both groups did not develop VAP after disconnection from MV.

Also, these findings in line with [48] in a study titled “Prevention of ventilator-associated pneumonia in European standards of care for newborn health” who reported that four-fifths of infants in the study group and three-fifths of infants in the control group did not develop VAP. From the researcher’s point of view application of nursing care bundle in the study group and routine care for the control group was effective in reducing the incidence of VAP. The current study findings showed that one fifth and more than one third of infants in the study and control groups developed VAP after disconnection from MV.

The current study results in agreement with [49] in a study titled “Ventilator-associated pneumonia in a pediatric intensive care unit: incidence, risk factors and etiological agent” who showed that less than one quarter and more than one third of mechanically ventilated infants in the study and control groups developed VAP after disconnection from MV. The present study results in line with [50] in a study titled “Healthcare-associated infections in Iranian pediatric and adult intensive care units: a comprehensive review of risk factors, etiology, molecular epidemiology, antimicrobial sensitivity, and prevention strategies” who reported that more than one fifth and more than one third of mechanically ventilated infants in the study and control groups developed VAP after disconnection from MV. The current study findings were contradicted with [46] and with [48] who reported that more than two-quarters and more than two-thirds of infants in both groups developed VAP after disconnection from MV.

In relation to the onset of VAP, it was found that early onset of VAP (≤ 5 days) was 50% (5 out of 10 infants with VAP) and 44.44% (8 out of 18 infants with VAP) in the study and control groups respectively, while 50% (5 out of 10 infants with VAP) and 55.55% (10 out of 18 infants with VAP) developed late onset of VAP (> 5 days) among the two groups respectively. These results agree with [31] and [37] who found that 33 infants out of 60 developed VAP in the study and control groups after 2 days from initiation of MV.

These findings were in line with [51] in a study titled “Prevalence of ventilator-associated pneumonia in neonates in a tertiary care hospital in Western Nepal” who reported that 18 infants with VAP out of 30 infants in both groups had early onset of VAP (≤ 5 days), 12 infants with VAP out of 30 infants in both groups had late onset (> 5 days). Also, the present study results agree with [52] in a study titled “Ventilator-associated pneumonia in an academic intensive care unit in Johannesburg, South Africa” who found that 8 and 10 infants with VAP out of 50 infants in both groups had early onset of VAP (≤ 5 days), 6 and 15 infants with VAP out of 50 infants in both groups had late (> 5 days).

The present study findings were disagreed with [53] in a study titled “Incidence and risk factors of ventilator associated pneumonia in neonatal intensive care unit in AL-Ahrar teaching hospital, Egypt” who reported that 7.9 and 8.5 infants with VAP out of 60 infants developed VAP in both groups after 48 hours of MV. The current study results illustrated that there were highly statistically significant negative correlations were detected between various components of the nursing care bundle and development of VAP. These findings supported by [54] in a study titled “What are the effects of care bundles on the incidence of ventilator-associated pneumonia in pediatric and neonatal intensive care units? A systematic review” who found that there was a strong negative relationship between care bundle adherence and VAP incidence.

These findings in agreement with [55] in a study titled “Relationship between ventilator bundle compliance and the occurrence of ventilator-associated events: a prospective cohort study” who reported that the VAP incidence rate demonstrating a significant strong negative correlation between the care bundle application and VAP occurrence. Also, the present study findings in accordance with [56] in a study titled “Multifaceted interventions are likely to be more effective to increase adherence to the ventilator care bundle: a

systematic review of strategies to improve care bundle compliance” who found that a statistically significant strong negative correlations were detected between various components of the nursing care bundle and VAP rates. These results prove the study hypothesis that assumed infants who will receive the nursing care bundle will have lower incidence of VAP than the control group.

The present study results showed that there were positive correlations were detected between application of nursing care bundle and absence of VAP. These results in accordance with [57] in a study titled “Prevention of ventilator-associated pneumonia through care bundles: a systematic review and meta-analysis” who found that higher nursing care bundle compliance is positively correlated with lower VAP rates. Also, the current study findings in agree with [58] in a study titled “Efficacy of compliance with ventilator-associated pneumonia care bundle: a 24-month longitudinal study at Bach Mai Hospital, Vietnam” who found that there were positive correlations were detected between full compliance with care bundle and VAP reduction. From the researcher’s point of view VAP reduction may be related to application of all component of the bundle until extubation from MV.

The current study results delineates that the most significant factors affect the development of VAP were length of MV followed by positive quantitative cultures and diagnosis of neurological disorders. These results in agreement with [59] in a study titled “Incidence, risk factors, short-term outcomes, and microbiome of ventilator-associated pneumonia in very-low-birth-weight infants: experience at a single level III neonatal intensive care unit” who found that the main risk factors of VAP development was duration of MV.

Also, the present study findings in accordance with [60] who mentioned that the strong independent factor for VAP development was prolonged MV and positive quantitative cultures. The current study findings in agree with [61] in a study titled “Risk factors of ventilator-associated pneumonia in a pediatric intensive care unit” who found that MV duration and neurological disorders were significant risk factors for VAP development. The current study findings were contradicted with [57] who found that neurological disorders were factor for VAP development. The current study findings showed that there were highly statistically significant differences between all factors with higher odds ratio and incidence of VAP. These results in accordance with [51] who reported that there were strong statistically significant differences between all risk factors and the occurrence of VAP, supported by high odds ratios.

5. CONCLUSION AND RECOMMENDATIONS

The current study concluded that application of the nursing care bundle significantly decreases the incidence of VAP among infants on mechanical ventilation as well as mean mechanical ventilation days, corticosteroids use and mortality. It was recommended that application of nursing care bundle in pediatric intensive care units should be used as a routine care for infants and replication of the study on larger sample of infants in different settings.

6. LIMITATIONS

- The age group of infants from 6 to 12 months according to inclusion criteria mentioned in study protocol not available for early 6 months of data collection. Therefore, the age group changed to 1 to 12 months.
- Infants who were died in the study and control groups were excluded from the study sample and replaced with another infants.

7. ABBREVIATIONS

PICUs	Pediatric intensive care units
MV	Mechanical ventilation
VAP	Ventilator associated pneumonia
ABG	Arterial blood gases
BAL	Bronchoalveolar lavage
SPSS	Statistical package for the social science
ETT	Endotracheal tube
ETA	Endotracheal aspirate

8. DECLARATIONS

8.1 Ethical Considerations

This study was part of a doctorate thesis; a primary approval was attained from the scientific research ethics committee in the faculty of nursing, Cairo-University. All parents who participated in the study were informed about the aim, procedure, benefits, and nature of the study and the written consent was obtained by the researcher from parents. The researcher emphasized that participation in the study was voluntary and parents can withdraw from the study at any time without any effect on the care provided to their infants and collected data was only used for the research purpose. The confidentiality of information was assured by coding.

8.2 Availability of data and materials

The data that support the findings of this trial are available from the corresponding author upon reasonable request.

8.3 Competing Interests

The authors declare that they have no competing interests.

8.4 Funding

This study received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Acknowledgment

The authors would like to extend their sincerest gratitude and appreciation to the parents of infants. We also express our gratitude to nursing and medical staff at the PICUs of El-Mounira and specialized pediatric hospitals which affiliated to Cairo-University hospitals for their flexibility and great cooperation. We are most grateful to the editor and the anonymous referees for their most helpful and constructive comment on earlier versions of this article.

References

- 1) Biban, S., Boville, B., Blanton, R., Lukaszewicz, G., Wincek, J., Bai, C., & Forbes, M. (2022). A multicentered prospective analysis of diagnosis, risk factors, and outcomes associated with pediatric ventilator-associated pneumonia. *Pediatric Critical Care Medicine*; 16(3): 65-73. <https://doi.org/10.1097/PCC.0000000000000338>.
- 2) Venkatachalam, V., Hendley, O., & Willson, D. (2017). The diagnostic dilemma of ventilator-associated pneumonia in critically ill children, *Pediatric Critical Care Medicine*; 12(3): 286-296. <https://doi.org/10.22038/PCC.41838.3524>.
- 3) Vedavathy, N., & Sangamesh, F. (2019). Predictors of mortality in ventilated infants in intensive care unit. *Bangladesh Journal of Child Health*; 33(3): 77-82. <http://dx.doi.org/10.3329/bjch.v33i3.5687>.
- 4) Zhou, C. (2018). Correlation of ventilator-associated pneumonia with mortality in pediatrics, *Journal of Hainan Medical University*; 22(2): 41-43. <https://doi.org/10.3390/ijerph17155452>.
- 5) Isguder, R., Ceylan, G., Agin, H., Gulfidan, G., Ayhan, U., & Devrim, L. (2017). New parameters for childhood ventilator associated pneumonia diagnosis. *Pediatric pulmonology*; 52: 119–128. <https://doi.org/10.1177/2374373519869156>.
- 6) National Healthcare Safety Network (NHSN)/Centers for Disease Control (CDC), (2020). Manual patient safety component protocol, division of healthcare quality promotion. http://www.cdc.gov/ncidod/dhqp/pdf/nhsn/NHSN_Manual_PatientSafetyProtocol_CURRENT.pdf.
- 7) Beraldo, A., & Andrade, B. (2021). The incidence of ventilator-associated infections in children determined using bronchoalveolar lavage, brief report. *Global Pediatric Health*; 1-4. <https://doi.org/10.3109/08860228309076044>.
- 8) Hassnean, A. (2018). Assessment of the effectiveness of a ventilator associated pneumonia prevention bundle, published master Thesis, Faculty of Medicine, Cairo-University, Egypt, 63.
- 9) Cooper, B., & Haut, C. (2019). Protocol preventing ventilator associated pneumonia in children: an evidence-based. *American Association of Critical-Care Nurses*; 33: 21-29. <https://doi.org/10.1089/neu.2019.4004>.
- 10) Kusahara, D., Enz, C., Avelar, A., Peterlini, M., & Pedreira, M. (2020). Risk factors for ventilator associated pneumonia in infants and children: a cross section cohort study. *American Journal of Critical Care*; 23(6): 469-478. <http://dx.doi.org/10.4037/ajcc2014127>.
- 11) American Thoracic Society, (2021). Recommendations on prevention of ventilator-associated pneumonia, 1-21. <http://www.ATS.gov.hk/files>.
- 12) Vandijck, D., Labeau, S., Vogelaers, D., & Blot, S. (2017). Prevention of nosocomial infection in pediatric intensive care units, *Pediatric Critical Care Medicine*; 15(5): 251-256. <https://doi.org/10.1177/0193945914533158>.

- 13) Speck, M., Rawat, M., Weiner, B., Tujuba, B., Farley, M., & Berenholtz, M. (2016). Structural measures for prevention of ventilator associated pneumonia. *Folia Medical Journal*; 54(1): 12-18. <https://doi.org/10.2478/v10153-011-0072-z>.
- 14) Center for Disease Control and Prevention, (2020). Ventilator-associated pneumonia (VAP) event, device associated module, 6:11. <http://www.cdc.gov/nhsn/pdfs/pscmanual/6pscvapcurrent.com>.
- 15) Bockhim, E., & Twibell, K. (2018). Effect of a nursing educational intervention on the prevention of ventilator associated pneumonia in the pediatric intensive care unit. A research paper submitted to the graduate school in partial fulfillment of the requirements for the degree masters of Science. Ball State University Muncie, Indiana. <https://doi.org/10.1111/jan.13106>.
- 16) American Thoracic Society, (2021). Recommendations on prevention of ventilator-associated pneumonia, 1-21. <http://www.ATS.gov.hk/files>.
- 17) Alcan, M. (2019). Implementation of ventilator bundle for prevention of ventilator associated pneumonia in pediatric intensive care unit, *Journal of Pediatric Neonatal Care*. 12(5):118–129. <https://doi.org/10.1080/14767058.2018.1465550>.
- 18) Ali, S., Waheed, K., & Iqbal, Z. (2019). Microbiological pattern of ventilator associated pneumonia. *Journal of Ayub Medical College Abbottabad- Pakistan*; 27(1): 117–119. <https://doi.org/10.1016/j.amcap.2019.08.030>.
- 19) Ahmed, G., & AboSamra, O. (2017). Knowledge of pediatric critical care nurses regarding evidence-based guidelines for prevention of ventilator associated pneumonia, *Journal of Education and Practice*. 6(9): 94-101. <https://doi.org/jep/s43045-020-00041-0>.
- 20) Statistic office of El-Mounira pediatric hospital, Cairo University (2020): Egypt.
- 21) Statistic office of specialized pediatric hospital, Cairo-University (2020): Egypt.
- 22) <http://www.ifad.org/gener/tools/hfs/anthropometry>.
- 23) National Healthcare Safety Network (NHSN)/Centers for Disease Control CDC, (2019). Criteria for defining ventilator-associated pneumonia among infants. <https://www.cdc.gov/nhsn/faqs/faq-vae.html#q28/>.
- 24) Al-Alaiyan, S. & Binmanee, A. (2017). Neonatal ventilator-associated pneumonia: An underdiagnosed problem in the neonatal intensive care units, *Journal of Pediatric Neonatal Care*. 7(3):119–122. <https://doi.org/10.1016/j.ijnurstu.2011.09>.
- 25) Selamat, N., Aung, K., & Soe, M. (2024). Changing the ventilator breathing circuits to reduce ventilator associated pneumonia, *Int Arch Nurs Health Care*, 7(3), 1-5. <https://doi.org/10.5005/jp-journals-10071-24854>.
- 26) Varnell, V., Raschetti, R., Centorrino, R., Montane, A., Tissieres, P., Yousef, N., & De Luca, D. (2019). The spectrum of pneumonia among intubated infants in the pediatric intensive care unit. *Pediatr Pulmonol.*, 54(12), 1982–1988. <https://doi.org/10.1007/s00431-020-03710-8>.
- 27) Dagher, F. E., Attia, A. A., Mahmoud, N. F., & Badr, A. M. (2018). Exploring risk factors with ventilator-associated pneumonia among infants in intensive care units. *Medical Journal of Cairo University*, 86(December), 3505–3518. https://mjcu.journals.ekb.eg/article_60591.html.
- 28) Jahan, I., Shaon, S. N. U., Saha, D., Moni, S. C., Dey, S. K., & Shahidullah, M. (2022). Effectiveness of educational intervention in preventing ventilator associated pneumonia in neonatal intensive care unit: a Cohort Study: Prevention of ventilator associated pneumonia. *Bangladesh Medical Research Council Bulletin*, 47(2), 143–150. <https://doi.org/10.3329/bmrcb.v47i2.57772>.

- 29) Hussain, A., Anwar, M., Sheikh, A.A., & Khan, A. (2024). Frequency and risk factors of ventilator-associated pneumonia at neonatal intensive care unit of Nishtar hospital, Multan. *The Professional Medical Journal*, 31(2), 259–263. <https://doi.org/10.29309/TPMJ/2024.31.02.7955>.
- 30) Chakkarapani, A. A., Adappa, R., Mohammad Ali, S. K., Gupta, S., Soni, N. B., Chicoine, L., & Hummler, H. D. (2020). Current concepts in assisted mechanical ventilation in the neonate. *International Journal of Pediatrics & Adolescent Medicine*, 7(4), 201–208. <https://doi.org/10.1016/j.ijpam.2020.11.002>.
- 31) Abdel Baseer, K. A., Mohamed, M., & Abd-Elmawgood, E. A. (2020). Risk factors of respiratory diseases among neonates in neonatal intensive care unit of Qena University hospital, Egypt. *Annals of Global Health*, 86(1), 22. <https://doi.org/10.5334/aogh.2739>.
- 32) Bhattacharya, P., Kumar, A., Kumar Ghosh, S., & Kumar, S. (2023). Ventilator-associated pneumonia in pediatric intensive care unit patients: microbiological profile, risk factors, and outcome. *Cureus*, 15(4), e38189. <https://doi.org/10.7759/cureus.38189>.
- 33) Abou Zed, F., & Mohammed, A. (2019). Impact of nursing guidelines on nurses' knowledge and performance regarding to prevention of ventilator associated pneumonia in neonates. *Journal of Nursing Education and practice*, 9 (10), 1-14. <https://doi.org/10.5430/jnep.v9n10p15>.
- 34) Akl, B., Saadon, M., & Sayed, A. (2020). Effectiveness of ventilator associated pneumonia care bundle on the pediatric critical care nurse's knowledge, practice and critically ill neonates' outcome. *Journal of Nursing and Health Science*, 9(3), 57-68. <https://doi.org/10.9790/1959-0903125768>.
- 35) Chang, I., & Schilber, A. (2016). Ventilator-associated pneumonia in children. *Pediatric Respiratory Review*; 20: 10-16. <https://doi.org/10.1016/j.prrv.2015.09.005>.
- 36) Pasquali, S. K., Klugman, P. T., Schumacher, K., Banerjee, M., Zhang, W., Bertrandt, R., Wolovits, J. S., Murphy, L. D., Misfeldt, A. M., Alten, J., & Cooper, D. S. (2023). Unplanned extubation during pediatric cardiac intensive care: U.S. multicenter registry study of prevalence and outcomes. *Pediatric Critical Care Medicine*, 24(7), 551–562. <https://doi.org/10.1097/PCC.0000000000003235>.
- 37) Issa, H. G., Tefera, M. A., & Mengesha, A. T. (2023). Incidence, outcome and determinants of unplanned extubation among pediatric intensive care unit in Addis Ababa, Ethiopia: A nested case–control study. *Pediatric Health, Medicine and Therapeutics*, 14, 213–223. <https://doi.org/10.2147/PHMT.S594325>.
- 38) Chakkarapani, A. A., Adappa, R., Mohammad Ali, S. K., Gupta, S., Soni, N. B., Chicoine, L., & Hummler, H. D. (2020). Current concepts in assisted mechanical ventilation in the neonate. *International Journal of Pediatrics & Adolescent Medicine*, 7(4), 201–208. <https://doi.org/10.1016/j.ijpam.2020.11.002>.
- 39) Rello, J., Ollendorf, D. A., Oster, G., Vera-Llonch, M., Bellm, L., Redman, R., & Kollef, M. H. (2022). Epidemiology and outcomes of ventilator-associated pneumonia in a large US database. *Chest*, 129(5), 1210–1218. <https://doi.org/10.1378/chest.122.6.2115>.
- 40) Dang, J., He, L., & Li, C. (2023). Risk factors for neonatal ventilator-associated pneumonia: a retrospective cohort study. *Experimental Biology and Medicine*, 248(23), 2473–2480. <https://doi.org/10.1177/15353702231220673>.
- 41) Mohamed, A., Abdelraheem, M. B., Alsubaie, M. A., & Omar, M. A. (2023). Prevalence of ventilator-associated pneumonia in children admitted to pediatric intensive care units in the Middle East: a systematic review. *Pediatric Pulmonology*, 58(6), e3661. <https://doi.org/10.1002/ppul.2661>.
- 42) Lee, P., & Chen, H. (2017). Ventilator-associated pneumonia in infants at a pediatric intensive care unit: a retrospective observational study. *Pediatric and Neonatology*; 58: 16-22. <https://doi.org/10.1016/j.pedneo.2017.10.014>.

- 43) Ivanova, M., Petrova, P., Dimitrova, I., & Nikolov, S. (2022). Ventilator-associated pneumonia in neonates admitted to a tertiary care NICU in Bulgaria: a prospective cohort study. *Frontiers in Pediatrics*, 10, Article 909217. <https://doi.org/10.3389/fped.2022.909217>.
- 44) Tuteja, A., Pournami, F., Nandakumar, A., Prabhakar, J., & Jain, N. (2022). Endotracheal aspirate and ventilator-associated pneumonia in neonates: revisiting an age-old debate. *Indian Journal of Pediatrics*, 89(12), 1202–1208. <https://doi.org/10.1007/s12098-022-04142-y>.
- 45) Gupta, M. K., Mondkar, J., Swami, A., Hegde, D., & Goel, S. (2017). Endotracheal aspirate microscopy, cultures and endotracheal tube tip cultures for early prediction of ventilator-associated pneumonia in neonates. *Indian Pediatrics*, 54(3), 211–214. <https://doi.org/10.1007/s13312-017-1033-2>.
- 46) Kopač, M. (2018). Evaluation of microbiological signs in infants in PICU. *Journal of Pediatric Intensive Care*, 8(2), 51–56. <https://doi.org/10.1016/j.jhin.2018.09.017>.
- 47) Li, Y., Wei, Q., Zhao, D., Mo, Y., Yao, L., Li, L., Dai, W. (2021). Non-invasive high-frequency oscillatory ventilation in preterm infants after extubation: A randomized, controlled trial, *Journal of International Medical Research*, 49(5). <https://doi.org/10.1177/0300060520984915>.
- 48) Dubois, C., Tissières, P., Helder, O., Mader, S., & Borghesi, A. (2023). Prevention of ventilator-associated pneumonia in European standards of care for newborn health. European Foundation for the care of newborn infants. <https://newborn-health-standards.org/standards/standards-english/patient-safety-hygiene-practice/prevention-of-ventilator-associated-pneumonia/>.
- 49) Vijay, G., Mandal, A., Sankar, J., Kapil, A., Lodha, R., & Kabra, S. K. (2018). Ventilator-associated pneumonia in a pediatric intensive care unit: incidence, risk factors and etiological agent, *Indian Journal of Pediatrics*, 85(10), 861-866. <https://doi.org/10.1007/s12098-018-2662-8>.
- 50) Safarabadi, M., Motallebirad, T., Azadi, D., & Jadidi, A. (2024). Healthcare-associated infections in Iranian pediatric and adult intensive care units: a comprehensive review of risk factors, etiology, molecular epidemiology, antimicrobial sensitivity, and prevention strategies. *Journal of Intensive Care Medicine*, 59(9): 1–15. <https://doi.org/10.1177/08850666241249162>.
- 51) Lamichhane, A., & Mishra, A. (2019). Prevalence of ventilator-associated pneumonia in neonates in a tertiary care hospital in Western Nepal. *JNMA Journal of the Nepal Medical Association*, 57(216), 84–87. <https://doi.org/10.31729/jnma.4295>.
- 52) Mazwi, S., van Blydenstein, S. A., & Mukansi, M. (2023). Ventilator-associated pneumonia in an academic intensive care unit in Johannesburg, South Africa, *African Journal of Thoracic and Critical Care Medicine*, 29(4), 10.7196/AJTCCM.2023.v29i4.154. <https://doi.org/10.7196/AJTCCM.2023.v29i4.154>.
- 53) Elsayed, W., Attia, T. H., & Arafa, M. A. (2024). Incidence and risk factors of ventilator associated pneumonia in neonatal intensive care unit in AL-Ahrar teaching hospital, Egypt. *Zagazig University Medical Journal*, 30(1), 1-5. <https://doi.org/10.21608/ZUMJ.2021.15553.1387>.
- 54) Niedzwiecka, T., Patton, D., Walsh, S., Moore, Z., O'Connor, T., & Nugent, L. (2019). What are the effects of care bundles on the incidence of ventilator-associated pneumonia in pediatric and neonatal intensive care units? A systematic review. *Journal for Specialists in Pediatric Nursing*, 24(4), e12264. <https://doi.org/10.1111/jspn.12264>.
- 55) Hassan, E. A., & Elsamani, S. E. A. (2022). Relationship between ventilator bundle compliance and the occurrence of ventilator-associated events: a prospective cohort study. *BMC nursing*, 21(1), 207. <https://doi.org/10.1186/s12912-022-00997-w>.

- 56) Thapa, D., Liu, T., & Chair, S. Y. (2023). Multifaceted interventions are likely to be more effective to increase adherence to the ventilator care bundle: A systematic review of strategies to improve care bundle compliance. *Intensive and Critical Care Nursing*, 74, 103310. <https://doi.org/10.1016/j.iccn.2022.103310>.
- 57) Rello, J., Povoas, P., Salluh, J., & Rodríguez, A. (2023). Prevention of ventilator-associated pneumonia through care bundles: a systematic review and meta-analysis. *Journal of Intensive Medicine*, 3(4), 352–364. <https://doi.org/10.1016/j.jointm.2023.04.004>.
- 58) Hoang, H. M., Dao, C. X., Ngo, H. H., Nguyen, T. T., & Le, M. Q. (2024). Efficacy of compliance with ventilator-associated pneumonia care bundle: A 24-month longitudinal study at Bach Mai Hospital, Vietnam. *SAGE Open Medicine*. <https://doi.org/10.1177/20503121231223467>.
- 59) Van der linden, E. J., Smith, A. L., Garcia, R. M., Zhang, Q., & Lee, C. (2024). Incidence, risk factors, short-term outcomes, and microbiome of ventilator-associated pneumonia in very-low-birth-weight infants: experience at a single Level III neonatal intensive care unit, *Journal of Neonatal-Perinatal Medicine*. <https://doi.org/10.1159/000000000>.
- 60) Rangelova, V. R., Raycheva, R. D., Kevorkyan, A. K., Krasteva, M. B., & Kalchev, Y. I. (2022). Ventilator-associated pneumonia in neonates admitted to a tertiary care NICU in Bulgaria. *Frontiers in Pediatrics*, 10, Article 909217. <https://doi.org/10.3389/fped.2022.909217>.
- 61) Noaman, A. (2021). Risk factors of ventilator-associated pneumonia in a pediatric intensive care unit. *Alexandria Journal of Pediatrics*, 34(1), 18–22. <https://doi.org/10.4103/ajop.ajop321>.