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Original Article

Comparison of Patient Profiles of Ventilator-Associated Pneumonia versus Non-Ventilator Associated Pneumonia in Children from Rawalpindi

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ABSTRACT

Objective: To study paediatric patient profiles for comparing demographic and clinical variables between ventilator-associated pneumonia patients and non-ventilator-associated pneumonia patients.

Study Design: Prospective longitudinal study.

Place and Duration of Study: Department of Paediatrics, Combined Military Hospital, Rawalpindi Pakistan, from Feb to Jul 2024.

Methodology: This study included 200 patients aged between 1 month and 15 years who were divided into two groups: Group-A, containing patients diagnosed with ventilator-associated pneumonia (VAP), based on clinical, radiological, and microbiological findings after experiencing more than 48 hours of mechanical ventilation, and Group-B, which included patients not having ventilator-associated pneumonia (non-VAP) after being ventilated for more than 48 hours. Demographic and clinical variables involved duration of paediatric intensive care unit (PICU) stay, body temperature, total leukocyte count (TLC), duration of antibiotic use, frequency of sepsis, shock, altered sensorium, and mortality.

Results: The mean duration of PICU stay (11.12±2.60 days), mean core body temperature (99.35±1.40°C), mean TLC (19.45±2.79 × 10^9/L), mean duration of antibiotic use (8.14±0.91 days), frequency of sepsis and shock (37% & 13%), altered sensorium (8%), steroid use (35%), and mortality (20%) were significantly higher (p<0.05) in Group-A than in Group-B patients.

Conclusion: Ventilator-associated pneumonia patients exhibited significantly higher illness severity and mortality, which highlighted the need for vigilant monitoring and early intervention.

Keywords: Anti-Bacterial Agents, Intensive Care Units, Pneumonia-Ventilator-Associated, Respiratory Tract Infections, Sepsis.

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INTRODUCTION

Ventilator-associated pneumonia (VAP) is a hospital-acquired infection among children on mechanical ventilation, contributing to considerable illness, frequent antibiotic use, extended hospital stays, and increased treatment costs,[1] leading to significant morbidity and mortality.[2] There is substantial variation globally in the prevalence of VAP in paediatric intensive care units (PICUs), ranging from 1 to 63 cases per 1,000 ventilator-days, and the burden of VAP is especially notable in PICUs, ranging from 2% to 35% of ventilated children.[3]

As per the Centre for Disease Control and Prevention, VAP is suspected clinically when a ventilated child develops new or worsening chest infiltrates, fever, purulent secretions, leukocytosis, and supportive microbiological findings after 48 hours on ventilation.[4] These complications can prolong mechanical ventilator support by a week or more and increase antibiotic usage.[5]

A study conducted by Khan *et al.*, at the PICU of a tertiary care hospital in Karachi evaluated the pattern of microorganisms among children with VAP, which highlighted Pseudomonas aeruginosa and Escherichia coli as the leading pathogens, mostly affecting male children aged 6 months to 4 years, and estimated a VAP incidence rate of 1.17 per 1,000 ventilator-days.[6] In another study by Sultan *et al.*, frequency of VAP in the PICU of Allied Hospital, Faisalabad, was found to be 19.8% among 96 studied cases, aged between 1 month and 15 years.[7]

Though limited data is available on paediatric VAP studies in Pakistan, most existing local studies are either cross-sectional or focused on adults, leaving a gap in paediatric comparative cohort data. Therefore, this study aimed to explore the clinical and demographic characteristics of children with VAP admitted to the PICU at Combined Military Hospital Rawalpindi, Pakistan, and compared them with

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ventilated patients who did not develop VAP. The goal was to identify high-risk groups and support early detection and prevention strategies in local settings.

METHODOLOGY

This prospective longitudinal study was conducted at the Department of Paediatrics, Combined Military Hospital Rawalpindi, for duration of 6 months from February 2024 to July 2024 after approval from the Institutional Ethical Review Board (letter no. 519 dated 01 February 2024).

Inclusion Criteria: Paediatric patients aged 1 month to 15 years of both genders receiving mechanical ventilator support for more than 48 hours were included.

Exclusion Criteria: Patients with pre-existing pneumonia or already having lung infiltrates due to pulmonary edema, congestive heart failure, and acute respiratory distress syndrome were excluded.

Using anticipated a mortality rate of 68.2% in patients with VAP versus 48.5% in those without VAP,[8] OpenEpi sample calculator was used to calculate a sample size of 194 (97 in each group).

A signed informed consent was obtained from the parents/guardians of the children, and non-probability consecutive sampling technique was used to enroll patients. We enrolled 200 patients (100 per group), who were divided into Group-A (VAP) and Group-B (non-VAP) according to the presence or absence of new-onset lung infiltrates on chest X-ray along with positive microbiological findings and clinical signs of pneumonia, respectively, after more than 48 hours of mechanical ventilation.

All paediatric patients in Group-A (VAP) and Group-B (non-VAP) were documented, and their age, weight, and gender were noted. Patients were followed up, and their clinical and microbiological variables were noted. Mean core body temperature was recorded at 6-hour intervals through the duration of admission, measured rectally in children under 2 years of age and axillary in those over 2 years. The endpoint of the study in both Group-A (VAP) and Group-B (Non-VAP) was successful extubation post-treatment or patient demise.

Primary variables measured were mean duration of stay in the paediatric intensive care unit (PICU), mean core body temperature during PICU stay, mean total leucocyte count (TLC), mean duration of antibiotic use, frequency and incidence of sepsis, shock and altered sensorium on admission, use of steroids, and overall mortality. Secondary variables studied were indications for admission in the PICU and causative organisms isolated through microbiological cultures.

Statistical Package for Social Sciences (SPSS) version 26.0 was used to conduct the statistical analysis. Frequencies, percentages, mean and standard deviation were used to statistically characterize demographic data. Means were compared using independent student t-test, while Chi-square test was used to analyse categorical data. Crude odds ratios (OR) with 95% confidence intervals (CI) were calculated to assess the association between ventilator-associated pneumonia (VAP) and mortality. Potential confounding by age was evaluated using the Mantel–Haenszel method, with analysis stratified into predefined age groups. Mantel–Haenszel common odds ratio was compared with the crude odds ratio, and a relative change of ≥10% was considered evidence of confounding. Statistical significance was defined as a *p*-value ≤0.05. Patient flow and methodological steps are illustrated in Figure as given below.

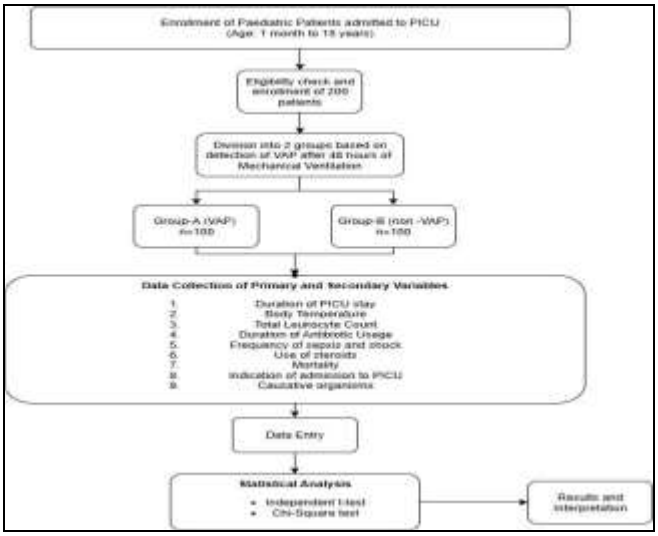

Figure: Diagrammatic Representation of Patient Flow and Various Steps of Study

RESULTS

A total of 200 patients were included in the study protocol and were divided into two groups: Group-A (VAP group, n=100) and Group-B (non-VAP group, n=100).

Table-I shows demographic characteristics of the selected patients. The mean age of patients in Group-A

was 5.65±1.99 years vs 6.10±2.53 years in Group-B (p=0.164). The mean weight of Group-A children was 19.02±3.43 kg versus 19.07±3.38 kg for Group-B (p=0.917). Gender distribution revealed 67% vs 73% males between Group-A and Group-B, respectively, and 33% vs 27% females in Group-A and Group-B, respectively (p=0.139). According to statistical analysis, no significant difference was found between the two groups regarding age, weight, and gender.

Table-I: Demographic Characteristics of Group-A and Group-B (n=200)

Variables		Group-A (VAP) (n=100)	Group-B (non-VAP) (n=100)
Mean age (years)		5.65±1.99	6.10±2.53
Mean weight (kg)		19.02±3.43	19.07±3.38
Gender	Male	67(67%)	73(73%)
	Female	33(33%)	27(27%)

**VAP: Ventilator-Associated Pneumonia,*

Table-II: Comparison of Primary Clinical Variables Between Group-A and Group-B (n=200)

Variables	Group-A (VAP; n=100)	Group-B (non-VAP; n=100)	*p*-value
Mean duration of stay in PICU (Days)	11.12±2.60	4.18±1.03	<0.001*
Mean core body temperature (Fahrenheit)	99.35±1.40	98.73±1.01	<0.001*
Mean leukocyte count (109/L)	19.45±2.79	16.16±1.64	<0.001*
Mean duration of IV antibiotic use (Days)	8.14±0.91	5.11±0.53	<0.001*
Frequency of sepsis	37(37%)	15(15%)	<0.001**
Incidence of shock	13(13%)	01(01%)	<0.001**
Frequency of altered sensorium	08(08%)	03(03%)	0.006**
Use of steroids	35(35%)	09(09%)	<0.001**
Mortality	20(20%)	08(08%)	0.002**

**Independent student t-test applied; p-value < 0.05 considered significant,*
*** Pearson chi-square test applied; p-value < 0.05 considered significant, Pediatric Intensive Care Unit: PICU, VAP: Ventilator-Associated Pneumonia*

When studying the primary clinical variables, as depicted in Table-II, the mean duration of stay in PICU was significantly extended (p<0.001) in Group-A (11.12±2.60 days) in comparison with 4.18±1.03 days in Group-B. Mean core body temperature measured at intervals in Group-A was 99.35±1.40 degrees Fahrenheit versus 98.73±1.01 degrees Fahrenheit (p<0.001) in Group-B. The mean total leucocyte count on the blood panel was found to be significantly higher in Group-A in comparison with Group-B (19.45±2.79 x109/L vs 16.16±1.64 x109/L; p<0.001). Mean duration of antibiotic use was also assessed to be significantly longer (p<0.001) in Group-A (8.14±0.91 days) as compared to Group-B (5.11±0.53 days). Sepsis as a complication was seen in 37% of patients in Group-A versus 15% of patients in Group-B (p<0.001). Shock occurred in 13% of patients in Group-A compared to 1% in Group-B (p<0.001). The incidence of altered sensorium on admission was seen in 8% of patients in Group-A, while only 3% of patients in Group-B showed this feature (p=0.006). The use of steroids was significantly higher in Group-A (35% of patients) than in Group-B (9% of patients; p<0.001). The overall mortality was also significantly higher in Group-A than in Group-B (20% vs 8%; p=0.002).

Pearson Chi-square test was applied to categorical variables of the present study that showed a significant difference was found among the variables of sepsis (p<0.001), shock (p=0.001), use of steroids (p<0.001), and mortality (p=0.014).

Table-III: Secondary Variables/Admission Indications & Causative Organisms (n=200)

Variables	Group-A (VAP: n=100)	Group-B (non-VAP: n=100)
Indication for admission in PICU		
Respiratory	56(56%)	44(44%)
Abdominal	9(9%)	4(4%)
Neurological	30(30%)	49(49%)
Other	5(5%)	3(3%)
Causative Organisms		
Pseudomonas aeruginosa	38(38%)	51(51%)
Staphylococcus aureus	30(30%)	25(25%)
E. Coli	24(24%)	19(19%)
Klebsiella pneumoniae	6(6%)	4(4%)
Others	2(2%)	1(1%)

**Pediatric Intensive Care Unit: PICU, VAP: Ventilator-Associated Pneumonia*

The study of secondary variables showed the indications for admission in both groups and causative organisms as depicted in Table-III. The major indications for admission to the PICU in Group-A were respiratory causes, being seen in 56% of cases, followed by neurological disorders seen in 30% of cases, with only 9% of cases reported as abdominal ailments along with 5% of cases falling under the category of other causes. In contrast, neurological causes (49%) were the major indication for admission in Group-B, followed by respiratory reasons being seen in 44% of cases, whereas abdominal indications were 4%, and other causes were seen in 3% of cases. Microbiological evidence of causative organisms showed Pseudomonas aeruginosa as the major organism seen in 38% of cases in Group-A patients and Staphylococcus aureus seen in 30% of cases. In Group-B, Pseudomonas aeruginosa (51%) remained the most common organism, followed by *Staphylococcus aureus* (25%) and *E. coli* (19%), showing

a similar but slightly different distribution compared to Group-A. The third most prevalent causative organism was found to be *E. coli* in both Group-A (24%) and Group-B (19%).

Crude odds ratio for mortality in the VAP group compared to the non-VAP group was 2.87.

Table-IV: Crude, Adjusted, and Stratum-Specific Odds Ratios for Mortality Group-A (VAP; n= 100) vs Group-B (Non-VAP; n= 100)

Analysis Type	Odds Ratio (OR)	95% CI	*p*-value
Crude Odds Ratio	2.87	1.15–7.15	0.02
Mantel–Haenszel Adjusted OR (for age)	2.84	1.13–7.10	0.02
Stratum-specific OR (<5 years)	5.77	0.64–52.1	0.12
Stratum-specific OR (≥5 years)	2.46	0.92–6.60	0.07

**Pediatric Intensive Care Unit: PICU, VAP: Ventilator-Associated Pneumonia*

Mantel–Haenszel adjusted odds ratio for age was 2.84, with less than 1% change from the crude estimate, indicating no evidence of confounding by age.

Stratum-specific odds ratios were 5.77 for children under 5 years and 2.46 for those over 5 years.

DISCUSSION

Ventilator-associated pneumonia (VAP) is the most prevalent hospital-acquired infection in children, subsequent to bloodstream infections. According to Hernandez-Garcia *et al.,* paediatric patients on mechanical ventilation are in danger of developing VAP, which is assessed to affect about 10 to 20% of ventilated children.[1] Another research study by Sultan *et al.,* witnessed a 19.8% incidence of VAP in the PICU of Allied Hospital, Faisalabad, with reports of higher rates in low- and middle-income countries, largely due to variable infection control standards.[7] The objective of our work was to categorize the clinical variables and related microbial findings to help optimise treatment strategies, ultimately improving patient care and survival outcomes, as no prior investigation has examined the clinical profiles of ventilator-associated pneumonia in our centre or within our local population.

In the present study, a significant difference was present in the mean duration of stay in the PICU for patients diagnosed with VAP as compared to non-VAP patients. The reason behind this is the extended care required due to major complications such as sepsis and shock, which often accompany ventilator-associated pneumonia. Similar results were being reported by Miura *et al.,* Peña-López *et al.,* and Chen *et al.,* who provided substantial data on the association between VAP in children and extension in their PICU stay.[9-11]

Evaluation of clinical parameters showed that there was a significant difference in the mean TLC as well as core body temperatures between both groups: Group-A (VAP) was having significantly higher values than Group-B (non-VAP). The associated inflammatory response due to VAP is known to trigger mechanisms of humoral immunity, resulting in the biochemical profiles mentioned. Accompanying these, the incidence of shock, frequency of sepsis, and frequency of altered sensorium in this research were also statistically significant in Group-A (VAP) compared to Group-B (non-VAP). These results are compatible with the study of Hernandez-Garcia *et al.,* who reported a higher incidence of sepsis in VAP patients.[1] In a study, Atul *et al.,* concluded that the prevalence of VAP with sepsis was 56.67%, which was more than half of the studied population.[12] A comparative study between VAP and non-VAP groups was also performed by Wang *et al.,* to estimate the frequency of shock and sepsis, which determined that sepsis-related mortality was 18.3% in children with respiratory issues.[13] The use of steroids in this study was reported significantly greater in Group-A (VAP) than Group-B (non-VAP): a result that is similar to the findings of Bhattacharya *et al.,* and Amanati *et al.,* who claimed an association of VAP & elevated use of steroids.[14,15] Furthermore, the duration of IV antibiotic use was also longer in Group-A than Group-B, which is proven by the study results of Mustafa *et al.,* who reported increased indications and use of antibiotics in respiratory tract infections.[16]

This investigation demonstrates that mortality in patients due to VAP was significantly greater than in non-VAP patients, which is comparable with the findings of Kalamitsou *et al.,* who claimed prolonged ventilation, a higher length of stay, and mortality in children suffering from ventilator-associated pneumonia.[17] A high mortality rate of 48.3% was also reported by Mokhtar *et al.,* in research conducted in a hospital in Egypt, which stated that VAP was the most common cause of death.[18] It could be partially explained by the use of artificial airways, which circumvent a child's defence against inhaled microbes, and partially by the incorrect application of infection control protocols, which demand immediate attention.[19]

The current analysis revealed that respiratory reasons formed the mainstay of admission indications

in both VAP & non-VAP groups, followed by neurological causes, as confirmed by the reports of Osman *et al.*, and Deraz *et al.*, who documented that chest-related problems were the main reason for PICU admissions, followed by neurological and cardiovascular issues.[19,20] When the isolated causative organisms were studied, Pseudomonas aeruginosa and *Staphylococcus aureus* formed the major bulk of infective organisms, followed by *E. coli* in both groups. These findings were coherent with various studies conducted by Antalová *et al.*, Bhattacharya *et al.*, Ayaz *et al.*, and Mourani *et al.*, who reported that the majority of nosocomial respiratory infections/ ventilator-associated pneumonia were observed by gram-negative organisms, particularly by Pseudomonas aeruginosa.[5,14,21,22]

This study recommends better resources, improved care by trained professionals, and enhanced mechanical ventilatory care in paediatric age groups to decrease morbidity and mortality.

CONCLUSION

Our investigation concluded that patients with ventilator-associated pneumonia had a significantly worse prognosis compared to those without ventilator-associated pneumonia. They required longer durations of mechanical ventilation, prolonged PICU stays, greater inotropic support, and extended use of antibiotics and steroids and showed higher incidences of sepsis and shock, culminating in an increased mortality rate. Thus, focused interventions are crucial to minimize ventilator-associated pneumonia incidence in PICUs.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

DM & SH: Data acquisition, data analysis, critical review, approval of the final version to be published.

ST & BA: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

HA & SM: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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