Medical Journal of Bakırköy

Med J Bakirkoy 2023;19:287-295
DOI: 10.4274/BMJ.galenos.2023.2023.8-2

Research

Evaluation of Ventilator-associated Pneumonia Approaches in Pediatric Intensive Care Units in Türkiye

Türkiye'de Çocuk Yoğun Bakım Ünitelerinde Ventilatör İlişkili Pnömoni Yaklaşımlarının Değerlendirilmesi

Murat Tanyıldız[1], Furkan Yavuz[1], Karya Şenköylü[1], Ömer Özden[1], Dinçer Yıldızdaş[2]

[1]Koç University Faculty of Medicine, Department of Pediatric Intensive Care, İstanbul, Türkiye
[2]Çukurova University Faculty of Medicine, Department of Pediatric Intensive Care, Adana, Türkiye

ABSTRACT

Objective: The purpose of this study was to collect data on the management of ventilator-associated pneumonia (VAP) in pediatric intensive care units (PICU) in Türkiye and to determine the need for new national pediatric VAP guidelines.

Methods: In this multicenter cross-sectional study, an online questionnaire was disseminated via email to PICUs in various cities across Türkiye. One person at each PICU, namely, the clinician who made the treatment decisions, completed the questionnaire. The VAP diagnosis and treatment algorithms of the PICUs were analyzed using the data obtained from the questionnaires.

Results: Of the initial 32 PICUs, 30 units in 19 cities completed the questionnaire. The average number of beds in the units was 13.13±6.16, and the number of beds per nurse per shift was 2.13±0.57. The mean duration of mechanical ventilation was 5.8±4.2 days. The mean VAP frequency was 2.81% and the mean VAP rate was 5.04 per 1000 ventilator day. Distal airway culture sampling was performed in 86.7% of the units before antibiotic treatment was initiated. The most common agent was *Pseudomonas aeruginosa*, followed by *Klebsiella pneumonia* and *Acinetobacter baumannii*. When the resistance status of the isolates was analyzed, anti-pseudomonal penicillin resistance was 81.2%, anti-pseudomonal cephalosporin resistance was 84.5% for Pseudomonas aeruginosa; cefepime and ceftazidime resistance was 80.5% for *Klebsiella pneumonia*, and carbapenem resistance was 47.5% for *Acinetobacter baumannii*. A nurse-bed ratio >2 made a significant difference in the VAP rates between the PICUs ($p<0.05$).

Conclusion: Consensus exists regarding the need to reduce VAP in PICUs in Türkiye, and up-to-date national guidelines are essential to maximize the efficiency of PICUs.

Keywords: Ventilator-associated pneumonia, multi-center study, pediatric intensive care unit

ÖZ

Amaç: Bu çalışmanın amacı, Türkiye'de çocuk yoğun bakım ünitelerinde (ÇYBÜ) ventilatör ilişkili pnömoni (VİP) yönetimiyle ilgili uygulamalar hakkında veri toplamak ve yeni ulusal pediatrik VİP kılavuzuna olan ihtiyacı belirlemektir.

Gereç ve Yöntem: Bu çok merkezli kesitsel çalışmada, Türkiye'nin çeşitli illerindeki ÇYBÜ'lere e-posta yoluyla çevrimiçi bir anket gönderildi. Her ÇYBÜ'de tedavi kararını veren yalnızca bir klinisyen anketi doldurdu. Anketlerden elde edilen veriler kullanılarak ÇYBÜ'lerin VİP tanı ve tedavi algoritmaları analiz edildi.

Bulgular: On dokuz ilden toplam 32 ÇYBÜ çalışma davetini kabul etti, 30 merkez anketi eksiksiz tamamladı. Birimlerdeki ortalama yatak sayısı 13,13±6,16, vardiyada hemşire başına düşen hasta sayısı ise 2,13±0,57 idi. Ortalama mekanik ventilasyon süresi 5,8±4,2 gündü. Ortalama VİP sıklığı %2,81 ve ortalama VİP oranı 5,04/1000 ventilatör günü idi. Ünitelerin %86,7'sinde antibiyotik tedavisi başlanmadan önce distal hava yolu kültürü alındığı görüldü. En sık etken *Pseudomonas aeruginosa* idi, bunu *Klebsiella pneumonia* ve *Acinetobacter baumannii* izledi. İzolatların direnç durumları incelendiğinde, Pseudomonas aeruginosa'da antipsödomonal penisilin direnci %81,2, antipsödomonal sefalosporin direnci %84,5; *Klebsiella pneumonia* için sefepim ve seftazidim direnci %80,5, *Acinetobacter baumannii* için karbapenem direnci %47,5 olarak bulundu. Hemşire-yatak oranı >2 olması ÇYBÜ'ler arasında VİP oranlarının yükselmesi üzerinde çoklu değişken analizinde istatistiksel olarak anlamlı bir fark yarattı ($p<0,05$).

Address for Correspondence: Murat Tanyıldız, Koç University Faculty of Medicine, Department of Pediatric Intensive Care, İstanbul, Türkiye
Phone: +90 506 240 94 60 E-mail: mtanyildiz@kuh.ku.edu.tr ORCID ID: orcid.org/0000-0001-8804-032X

Cite as: Tanyıldız M, Yavuz F, Şenköylü K, Özden Ö, Yıldızdaş D. Evaluation of Ventilator-associated Pneumonia Approaches in Pediatric Intensive Care Units in Türkiye. Med J Bakirkoy 2023;19:287-295

Received: 07.08.2023
Accepted: 21.08.2023

Sonuç: Türkiye'deki ÇYBÜ'lerde VİP'nin azaltılması gerekliliği konusunda fikir birliği vardır ve ÇYBÜ'lerin etkinliğini en üst düzeye çıkarmak için ulusal güncel kılavuzlar ve uygulamalara ihtiyaç vardır.

Anahtar Kelimeler: Ventilatör ilişkili pnömoni, çok merkezli çalışma, çocuk yoğun bakım ünitesi

INTRODUCTION

Ventilator-associated pneumonia (VAP) is a nosocomial pneumonia that develops in pediatric intensive care unit (PICU) patients who receive a protocol based on mechanical ventilation (MV) for at least 48 hours (1). VAP is second in line after bloodstream-related infections and constitutes 20% of the extensive number of nosocomial infections encountered in PICUs (2). Although its incidence varies depending on the selected descriptive criteria, it affects 12% of children who receive MV (3). Despite its decreased incidence with the use of bundle applications, mortality in relation to VAP still varies between 20% and 50% by virtue of multidrug resistance (MDR) bacteria development (4). Apart from mortality, one of the most important challenges related to VAP is the prolongation of ICU stay, which directly influences hospitalization costs. It has been shown that VAP prolongs MV therapy by 10 days and the hospital stay by 12 days, and hospital costs are five times higher (5). The most important step in the fight against VAP is to take all necessary measures to reduce the risk factors and administer prompt and appropriate treatment (6). Therefore, VAP prevention and treatment guidelines, supported by current studies, have been established. One of the most important guidelines is that published by the Infectious Diseases Society of America (IDSA) and the American Thoracic Society (ATS), the IDSA/ATS guidelines, in 2016 (7). Additionally, under the leadership of the European Respiratory Society (ERS), the European Society of Clinical Microbiology and Infectious Diseases (ESCMID), the European Society of Intensive Care Medicine (ESICM), and the Latin American Thoracic Societies (ALAT), the ERS/ESICM/ESCMID/ALAT guidelines were developed in 2017 (1). Although there are numerous similarities in the approaches between the two sets of guidelines, some important points can make considerable differences. Both guidelines are designed for adults and are applied to pediatric patients, which has resulted in ambiguous views on current VAP recommendations and their application. In Türkiye, the national pediatric guidelines issued by the Turkish Thoracic Society (TTS) in 2009 under the name "Consensus Report on the Diagnosis and Treatment of Hospital-Developing Pneumonia in Children" have not been updated for more than 10 years (8). Over the past decade, pan-resistant bacteria have developed, which has introduced a new generation of antibiotics to combat these agents. In addition, new concepts have emerged, such as the implementation of inhaled antibiotics and the diagnosis of ventilator-associated tracheobronchitis (VAT) and ventilator-associated events. This period has also seen a rapid increase in the number of centers and PICUs that provide fellowship education programs in Türkiye. Considering these developments, we believe that acknowledging the changes in VAP practices over the past 10 years may open many doors to improving tertiary care services in Türkiye. The aim of this study was to collect data on procedures related to VAP in Turkish PICUs and to assess the need for new national pediatric guidelines. Our study has the unique feature of being the first study on VAP conducted in PICUs in Türkiye, and 30 units from around the country participated.

METHODS

This multicenter descriptive, cross-sectional, and quantitative study was conducted after obtaining approval from the Koç University Institutional Ethics Committee (decision no: 2021.372.IRB2.071, date: 07.10.2021). An online 35-item questionnaire (Qualtrics Survey System, https://koc.ca1.qualtrics.com/jfe/form/SV_9MqUd0i5dig3f6e) was sent directly to PICUs via email, and only the person from each unit who made treatment decisions was allowed to fill in the questionnaire. Only the PICUs that completed the questionnaire were included in the study. After the first email, three reminder emails were sent to the units at one-week intervals. Informed consent was obtained from each unit before responding to the questionnaire. Using the data obtained from the questionnaire, the VAP diagnosis and treatment approaches of the units were analyzed and reported.

Statistical Analysis

The data were analyzed using the Statistical Package for Social Sciences for Windows version 23.0. The number, percentage, mean, standard deviation, and median were used as descriptive statistics to evaluate the data. A chi-square test was used to compare the categorical variables, and multivariate logistic regression was performed to assess the factors related to higher VAP rates. A p-value <0.05 was considered statistically significant.

RESULTS

We invited 38 PICUs from across Türkiye to participate in this study. Of the 32 units that provided their consent, 30 PICUs from 19 cities completed the questionnaire. Among them, 60% (n=18) were PICUs in university-affiliated hospitals, whereas 40% (n=12) were units in Ministry of Health-affiliated hospitals (Figure 1). All the participating units were third-level mixed ICUs with both medical and surgical patients, and 50% of them provided care for postoperative cardiac patients. The average number of beds in the units was 13.13±6.16 [median 14 (5-32)], and the mean number of nurses was 25.63±13.48 [median =23.5 (10-66)]. The number of beds per nurse per shift was 2.13±0.57. The average number of patients followed per year was 200-400 in 33.3% of the units, 400-600 in 26.7%, and 600-800 in 30%. The corresponding number of patients on MVs followed annually was 50-100 patients in 26.7% of the units, 101-200 patients in 16.7%, 201-300 patients in 30%, and 301-400 patients in 23.3%. The mean duration of MV was 5.8±4.2 days, with 53.3% of PICUs applying MV for between 1 and 7 days (Table 1). In terms of defining VAP, only 26.7% of the PICUs used the IDSA/ATS definition, and the remaining 73.3% used the definition of the Center for Disease Control and Prevention. The mean VAP frequency was 2.81% and the mean VAP rate was 5.04 per 1000 ventilator day. The VAP frequency was between 0% and 5% in 76.67% of the PICUs, and the VAP rate was between 0 and 5 per 1000 ventilator days in 73.3% of the units (Figure 2). *Pseudomonas aeruginosa* (*P. aeruginosa*) was the most common agent (43.3% of cases), followed by *Klebsiella pneumoniae* (*K. pneumoniae*) (33.3%) and *Acinetobacter baumannii* (*A. baumannii)* (16.7%) (Table 2). When the resistance status of the isolates was analyzed, anti-pseudomonal penicillin resistance was 81.2%, anti-pseudomonal cephalosporin resistance was 84.5% for *P. aeruginosa*; cefepime–ceftazidime resistance was 80.5% for *K. pneumoniae*, and carbapenem resistance was 47.5% for *A. baumannii.* Regarding VAP protection, bundle applications were used in all the units, with an average of 14.2±5.6 of the applications listed in Table 3 implemented at each PICU. Before starting antibiotic treatment, 86.7% of the PICUs conducted distal airway culture sampling. Among them, 66.7% of the units used only the non-invasive semiquantitative technique of endotracheal aspiration (ETA) and never used the invasive quantitative culture method of bronchoalveolar lavage (BAL). Of these units, 20% used ETA first, before sending a BAL sample in patients who were unresponsive to treatment. Another 3.3% of the PICUs only used the BAL technique for diagnoses, whereas 6.7% started antibiotic treatment directly without sending any culture samples for analysis. Of the units, 86.6% performed de-escalation after starting antibiotics, and among them, 73.3% obtained cultures and started antibiotics and de-escalated based on the clinical and culture results. Meanwhile, 13.3% obtained cultures only and began antibiotic treatment after 2-3 days, with de-escalation according to the clinical, culture,

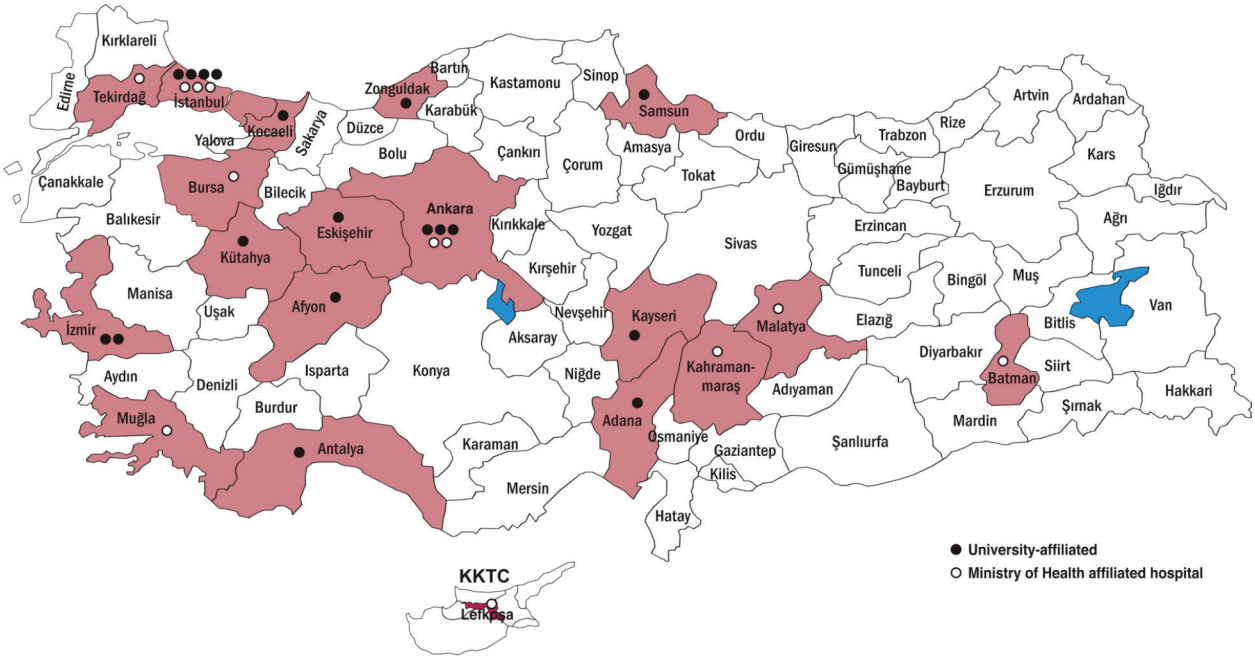

Figure 1. Pediatric intensive care units participating the study in Türkiye

Table 1. General features of pediatric intensive care units

Unit (n=30)	Unit number (n) mean	%
University affiliated	18	60
Ministry of Health affiliated	12	40
Properties of PICU		
Medical + surgical	16	53
Medical + surgical + cardiac	14	47
Number of beds (mean)	13.13±6.16	
Ratio of nurse to bed (mean)	2.13±0.57	
Annual patient range in PICUs		
200-400	10	33.3
400-600	8	26.7
600-800	9	30.0
800-1000	1	3.3
>1000	2	6.7
Annual interval of patient in MV		
0-100	8	26.7
101-200	5	16.7
201-300	9	30.0
301-400	7	23.3
>400	1	3.3
MV duration range in PICUs		
1-7 days	16	53.3
8-10 days	10	33.3
11-14 days	4	13.3

MV: Mechanical ventilation, PICU: Pediatric intensive care unit

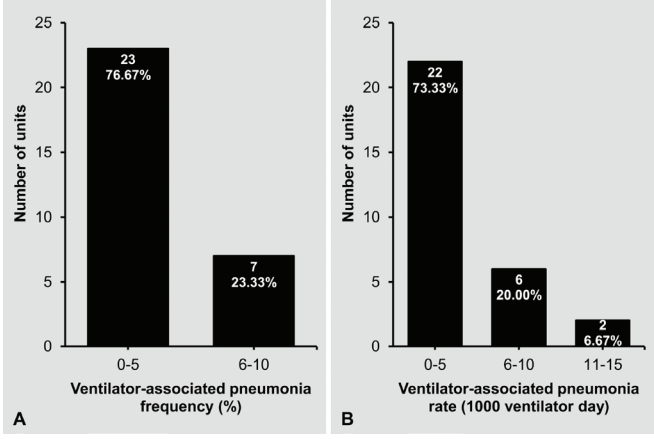

Figure 2. The ventilator-associated pneumonia (VAP) frequency and rates in pediatric intensive care units (PICU) A) The VAP frequency was between 0% and 5% in 76.67% of the PICUs B) the VAP rate was between 0-5 per 1000 ventilator days in 73.3% of the PICUs

and procalcitonin (PCT) results. A few PICUs (6.7%) took cultures and started antibiotics but were not de-escalate. Considering the general duration of antibiotic use for treating VAP (excluding patients with cavitation, necrotizing pneumonia, abscess, and empyema), 23.3% of the PICUs applied treatment against non-resistant Gram-negative bacteria for 7 days and terminated the treatment based on the PCT results. More than half (56.7%) of the units provided 14-day therapy for non-resistant Gram-negative bacteria and terminated the treatment in line with the PCT results. Regardless of the duration, 10% of the units used antibiotics until both a clinical and radiological recovery was achieved, and this treatment was discontinued based on the PCT response. In terms of VAT treatment approaches, 43.3% of the PICUs observed the patients without starting antibiotic treatment, 23.3% started antibiotics immediately, and 33.3% did not start antibiotics but instead followed the clinical and acute phase response. With respect to inhaled antibiotics, 56.7% of the PICUs did not use them, 16.7% used them in patients with VAP with carbapenem-resistant and colistin-sensitive *Acinetobacter* growth, and

Table 2. Microorganism profile of ventilator-associated pneumonia in PICUs in Türkiye

Unit (n=30)	Units (n)	Percent (%)
1st most common VAP agent in PICU		
Pseudomonas aeruginosa	13	43.3
Klebsiella pneumoniae	10	33.3
Acinetobacter baumannii	5	16.7
Stenotrophomonas maltophilia	1	3.3
Staphylococcus aureus	1	3.3
2nd most common VAP agent in PICU		
Klebsiella pneumoniae	15	50.0
Acinetobacter baumannii	9	30.0
Stenotrophomonas maltophilia	3	10.0
Pseudomonas aeruginosa	3	10.0
3rd most common VAP agent in PICU		
Acinetobacter baumannii	11	36.7
Pseudomonas aeruginosa	7	23.3
Klebsiella pneumoniae	5	16.7
Staphylococcus aureus	3	10.0
Stenotrophomonas maltophilia	2	6.7
Enterobacteriaceae	1	3.3
Candida spp.	1	3.3

PICU: Pediatric intensive care unit, VAP: Ventilator-associated pneumonia

Table 3. Bundle component for prevention of ventilator-associated pneumonia

Adherence to hand-hygiene guidelines.
Avoid the use of broad-spectrum and long-term parenteral antibiotic.
Elevation of the head of the bed 30-45° (semi recumbent position).
Regular oral hygiene care methods are applied according to the age of the patient.
Only cuffed tube and orotracheal way preferred for entubation and tube placement is checked frequently to prevent self-extubation.
Non-invasive ventilation offered whenever possible and avoid prolonged mechanical ventilation.
Re-entubation should be prevented. Improve planned extubation with the design of protocols to improve quality.
Unnecessary patient transport is not acceptable.
Endotracheal cuff pressure is routinely checked and maintained between 15-20 mmHg.
Subglottic aspiration yield precedence to oral aspiration.
Ventilator circuit replacement and circuit manipulation are limited. Circuit changes only when visibly soiled or malfunctioning.
Deep sedation is avoided, sedation interruption and spontaneous breathing trials is provided.
Unnecessary peptic ulcer protection [proton pumb inhibitors and histamin receptor 2 (H2) antagonist] are not used.
Disposable one use sterile water is used for in-tube aspiration, avoid saline lavage with suctioning.
Prevent gastric over distention.
Education of the healthcare workers regarding nasocomial infection and VAP prevention.
Deep vein thrombosis prophylaxis is used.

VAP: Ventilator-associated pneumonia

13.3% used them for patients with VAP with carbapenem-resistant, colistin-susceptible all Gram-negative bacteria growth. In our questionnaire, we enquired about the approach toward acute phase reactant responses in the routine practices of the PICUs and found that 43.3% of the units used the acute phase reactant levels at the time of diagnosis, when evaluating the treatment response, and when deciding whether to discontinue treatment. Furthermore, 33.3% of the units used these at both the time of diagnosis and the evaluation of the 72-hour treatment response, 13.3% followed the acute phase reactant levels at the time of diagnosis and daily, whereas 6.7% applied them in their practice only at the time of diagnosis. When the VAP protocols used by the PICUs were queried, 26.7% of the units indicated that they used their own protocols, 26.7% used the IDSA/ATS guidelines, 3.3% used the ERS/ESCMID/ALAT guidelines, and 10% used the TTS national guidelines. In contrast, 33.3% did not use any VAP protocols. When factors such as patient profile (medical + surgery versus medical + surgery + cardiac), nurse-to-bed ratio, MV time, bundle application, culture method, antibiotic duration, and the VAP protocol used by the PICUs were compared between the units with a VAP rate of >5 to ≤5 per 1000 ventilator days, only having a nurse-patient ratio >2 made a significant difference to the VAP ratio between the units [odds ratio (OR), 1.22; 95% confidence interval (CI), 1.15-1.28; p<0.01].

DISCUSSION

Our study included 30 tertiary-level PICUs in Türkiye that had completed our online questionnaire (Figure 1). Although the distribution of the units included in the study was not homogeneous across the country (19 cities), the inclusion of the provinces with the highest populations and patient densities was very important when evaluating the general situation in Türkiye. When the average number of patients followed up in the PICUs per year was examined, we observed that most of the units had a very intensive patient follow-up schedule of over 400 patients per year. Accordingly, the number of patients receiving MV treatment exceeded 200 per year in most of the units. When the VAP frequency and VAP rates of the units were evaluated, the mean VAP frequency was 2.81% and the VAP rate was 5.04 per 1000 ventilator days. The International Nasocomial Infection Control Consortium (INICC) study was conducted in 36 countries between 2004 and 2009, and the results showed that the average VAP frequency observed in the 45 PICUs participating in the study was 2.5%, with a VAP rate of 6.5 per 1000 ventilator days (9). In recent prospective studies conducted in PICUs, the VAP rate was found to vary between 5.4 and 41 per 1000 ventilator days (10-12). In a study conducted in a cardiac ICU where only postoperative pediatric cardiac patients were followed up, the VAP rate was 29 per 1000 ventilator days, which was considerably higher than the general average VAP rate seen in PICUs (13). In our study, no significant difference was found in the VAP rate between the PICUs where postoperative cardiac patients were followed up and those where such patients were not. With the widespread introduction of bundle measures in PICUs, a significant decrease in VAP rates has been observed. Kunzman et al. (14) showed that the VAP rate decreased from 55 to 19 per 1000 ventilator days in 5 months with five bundle practices, namely, 1) 30° head elevation, 2) age-appropriate oral care, 3) inspection of the location of the oro/nasogastric tubes every 3-4 hours by marking them with a marker after the location of the

tubes was confirmed, 4) avoiding the routine use of saline before endotracheal tube aspiration, and 5) positioning the set to prevent water accumulation in the ventilator set and directing water to the water trap reservoir. In the same study, when a coordinator supervised these practices and provided one-to-one training, the VAP rate decreased to 4 per 1000 ventilator days (14). The use of the INICC Multidimensional Approach and INICC Surveillance Online System applications, i.e., 1) bundle applications, 2) training, 3) outcome surveillance, 4) process surveillance, 5) VAP rate feedback, and 6) performance feedback, led to a decrease in the VAP rate from 7.84 to 4.74 per 1000 ventilator days (15). In our study, we observed that bundle practices were performed in all PICUs. An average of 14.2±5.6 measures from the bundle practices (Table 3) were implemented, and compliance with the bundle practices was supervised by the respective infection control committees and coordinators. All PICUs demonstrated the following common practices: 1) adherence to hand hygiene; 2) avoidance of the use of long-term and broad-spectrum antibiotics; 3) bed head-level elevation by 30°-45°; 4) age-appropriate oral hygiene; 5) preference for only a cuffed tube and the orotracheal method for intubation, and the oro/nasogastric tube was checked frequently; and 6) preference for non-invasive ventilation whenever possible with an avoidance of prolonged MV.

One of the most important ways to decrease the VAP rate is to shorten the duration of MV and the length of ICU stay. In a recent study, Rosenthal et al. (16) showed that a longer length of ICU stay, which increased the VAP risk by 7% per day (OR, 1.07; 95% CI, 1.07-1.08; $p<0.0001$), and longer MV duration (OR, 0.96; 95% CI, 0.95-0.96; $p<0.0001$) were independent risk factors for VAP. In a single-center study, Chompton et al. (12) showed that patients with VAP had a longer MV duration and ICU stay than those without VAP (15 days vs. 6 days, and 19 days vs. 9 days, respectively). In our study, the mean duration of MV was 5.8±4.2 days, which supports the rate of VAP found in our study. However, when the PICUs with VAP rates below and above 5 per 1000 ventilator days were compared, no significant difference was found in terms of MV duration (MV, <7 vs. >7 days, respectively). We performed a multivariate logistic regression analysis to determine the factors affecting VAP incidence; the nurse-patient ratio was found to be significantly related. When we compared the units with VAP rates below 5 per 1000 ventilator days with the units with VAP rates above 5 per 1000 ventilator days, a nurse-patient ratio >2 significantly increased the VAP rate ($p<0.05$). A recent study showed that the incidence of VAP was closely related to nursing services, especially the number of patients per nurse during night shifts, and the level of experience of the nurses directly affected the incidence of VAP (17).

When we examined the frequency ranking of the VAP agents seen in the PICUs in our study, we observed that *P. aeruginosa* had the highest ranking, followed by *K. pneumoniae* and *A. baumannii*. All three types showed resistance to at least two drugs. VAP caused by MDR Gram-negative bacteria is a major global problem. In studies conducted in Europe and the USA on VAP, it was observed that the prevalence of Gram-negative bacteria had increased to 76.13%-95.3% since 2010, and *P. aeruginosa* and *A. baumannii* were the leading agents (18-20). In the USA, carbapenem resistance in *P. aeruginosa* has been shown to reach 16.1%-28.4%, resistance to anti-pseudomonal penicillins (piperacillin-tazobactam) 15.6%-19.1%, and resistance to anti-pseudomonal cephalosporins (e.g., ceftazidime or cefepime) 9.5%-29.4%, and these figures are gradually increasing. While colistin resistance in *P. aeruginosa* is approximately 2% in the USA, resistance is increasing in Europe and the Mediterranean region (21). In our study, anti-pseudomonal penicillin resistance and anti-pseudomonal cephalosporin resistance were found in >80% of the patients with *P. aeruginosa*, 80.5% of those with *K. pneumonia*, and 47.5% of the patients with *A. baumannii*, which indicates a serious issue in PICUs in Türkiye.

Both the IDSA/ATS and ERS/ESICM/ESCMID/ALAT guidelines recommend distal airway sampling and cultures before providing treatment, whereas the IDSA/ATS guidelines recommend a non-invasive semiquantitative ETA culture method. In meta-analyses and Cochrane data, it has been shown that the culture technique does not change clinical outcomes, such as mortality, length of ICU stay, and mean MV duration (22). In general, semiquantitative ETA cultures have a higher sensitivity and lower specificity (23). However, because no evidence has been provided to show that invasive quantitative cultures will lead to better clinical outcomes, non-invasive semiquantitative cultures are recommended because non-invasive sampling is easier and faster and causes fewer complications (7). The ERS/ESICM/ESCMID/ALAT guidelines recommend that invasive quantitative (BAL, mini-BAL) methods should be used in stable patients, if possible, when taking cultures. However, due to problems such as the increased oxygen requirements of patients during this method and the risks associated with the procedure, such as bleeding, bronchospasm, and technical impossibilities, this recommendation is considered to have low evidence value and has been classified as a weak

recommendation because of insufficient supporting data. The mini-BAL application has also been recommended as an alternative to the BAL application because it is a less invasive technique (1). In our study, the majority of PICUs used non-invasive semiquantitative methods (in line with the IDSA/ATS guidelines), as invasive methods are more difficult to apply in the pediatric age group.

A diagnosis of VAP should be made very rapidly. Inappropriate and late initiation of antibiotic therapy significantly increases the risk of morbidity and mortality in patients with VAP. The diagnosis is based on radiological and clinical findings. The Clinical Pulmonary Infection score, C-reactive protein (CRP), and PCT are not included in the IDSA/ATS or ERS/ESICM/ESCMID/ALAT guidelines for the diagnosis of VAP and antibiotic initiation. The IDSA/ATS guidelines strongly discourage the use of biomarkers, CRP, and PCT at the time of diagnosis and emphasize that daily serial CRP and PCT monitoring is a highly unnecessary and cost-increasing practice. In our study, we found that most PICUs performed CRP and PCT control at diagnosis, evaluated the treatment response, and discontinued treatment, which is not recommended in the guidelines. Performed daily serial CRP and PCT monitoring, which is undoubtedly a remarkable finding in terms of practice, as it may increase both the cost and duration of antibiotic use.

The IDSA/ATS and ERS/ESICM/ESCMID/ALAT guidelines agree that 7-8 days of antibiotic treatment is sufficient for VAP (1,7). However, the ERS/ESICM/ESCMID/ALAT guidelines also emphasize that treatment should be tailored to the patient, and longer antibiotic use may be required in patients with immunodeficiency, cystic fibrosis, empyema, lung abscess, cavitation, or necrotizing pneumonia and in those in whom inappropriate treatment was previously started (1). In our study, when the duration of antibiotic use in VAP in the absence of immunodeficiency, cystic fibrosis, empyema, lung abscess, cavitation, and necrotizing pneumonia was examined, we found that most of the PICUs (56.7%) preferred long-term (14 days') treatment, and 23.3% discontinued treatment if PCT was negative after 7 days (short-term) treatment.

De-escalation is recommended in many international and national guidelines to prevent the high costs, side effects, and possible development of resistance that may be caused by the overuse of antibiotics. When studies on the subject were examined, it was noted that most of the studies were observational studies, randomized controlled studies were few in number, the studies were not blinded, and they had a high risk of bias (7,24). Moreover, no difference was found between the de-escalation and continuous antibiotic treatment groups in terms of mortality and duration of ICU stay. However, when all these studies and clinical observations were evaluated together, the beneficial aspects of the de-escalation approach in VAP outweighed the risks, and de-escalation has thus been recommended in both the IDSA/ATS and ERS/ESICM/ESCMID/ALAT guidelines (1,7). When the de-escalation approach of the PICUs in our study was evaluated, we observed that 73.3% of cases were de-escalated based on culture growth.

In studies and meta-analyses on the use of inhaled antibiotic therapy for treating VAP, inhaled antibiotics used in addition to systemic antibiotic therapy, especially in VAP caused by gram-negative bacteria with MDR characteristics, were found to increase the rate of recovery and shorten the duration of intravenous antibiotic use and MV time (7,25,26). The IDSA/ATS guidelines recommend the use of inhaled antibiotics in addition to systemic treatment in VAP caused by Gram-negative bacilli susceptible only to aminoglycosides or polymyxin (colistin or polymyxin B) because it shortens the duration of intravenous antibiotic use and recovery time and reduces costs (7). In our study, the majority of PICUs did not use inhaled antibiotics; however, considering the high incidence of carbapenem-resistant, colistin-sensitive *A. baumannii*, the use of inhaler antibiotics should be included in the national VAP guidelines.

The most important limitation of our study was that the data were obtained via a questionnaire. However, to increase the reliability of the data, only one person, namely, the person who made the treatment decision (department director or assistant director), from each PICU completed the questionnaire.

CONCLUSION

We found a general consensus on the diagnosis, treatment, and prevention of VAP in PICUs in Türkiye. Furthermore, there has been considerable rational progress in the fight against VAP. However, there is a need for updated national guidelines given the differences in international guidelines. The study's findings were critical in determining where a developing country stood in terms of addressing VAP in PICUs in accordance with current guidelines.

Acknowledgements

The authors gratefully acknowledge the statistical assistance of Canser Boz, Phd from İstanbul University, Faculty of Health Science. This study conducted with the collaboration of the members of "Ventilator-Associated Pneumonia in Pediatric Intensive Care Units in Türkiye (VAPPICT) Study

Group". VAPPICT Study Group: Gazi Aslan, Yasemin Çoban, Muhammed Üdürgücü, Nagehan Aslan, Mehmet Çeleğen, Serkan Özsoylu, Faruk Ekinci, Zeynel Abidin Ozturk, Mutlu Uysal Yazici, Tahir Dalkıran, Hakan Tekguc, Ayhan Yaman, Eylem Kıral, Serhat Emeksiz, Esra Şevketoğlu, Demet Demirkol, Tanıl Kendirli, Muhterem Duyu, Pınar Yazıcı Özkaya, Nurettin Onur Kutlu, Alper Köker, Oğuz Dursun, Sinan Yavuz, Feyza İncekoy Girgin, Ayşe Filiz Yetimakman, İbrahim Ethem Pişkin, Özlem Sarıtaş Nakip, Arzu Oto, Başak Yıldız, Ahmet Yöntem, Selman Kesici.

ETHICS

Ethics Committee Approval: This multicenter descriptive, cross-sectional, and quantitative study was conducted after obtaining approval from the Koç University Institutional Ethics Committee (decision no: 2021.372.IRB2.071).

Informed Consent: Informed consent was obtained from each participant before responding to the questionnaire.

Authorship Contributions

Concept: M.T., F.Y., D.Y., Design: M.T., F.Y., Data Collection or Processing: M.T., F.Y., K.Ş., Ö.Ö., D.Y., Analysis or Interpretation: M.T., F.Y., Ö.Ö., D.Y., Literature Search: M.T., K.Ş., Ö.Ö., Writing: M.T., F.Y., K.Ş.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declare that this study received no financial support.

REFERENCES

1. Torres A, Niederman MS, Chastre J, Ewig S, Fernandez-Vandellos P, Hanberger H, et al. International ERS/ESICM/ESCMID/ALAT guidelines for the management of hospital-acquired pneumonia and ventilator-associated pneumonia: Guidelines for the management of hospital-acquired pneumonia (HAP)/ventilator-associated pneumonia (VAP) of the European Respiratory Society (ERS), European Society of Intensive Care Medicine (ESICM), European Society of Clinical Microbiology and Infectious Diseases (ESCMID) and Asociación Latinoamericana del Tórax (ALAT). Eur Respir J 2017;50:1700582.
2. Foglia E, Meier MD, Elward A. Ventilator-associated pneumonia in neonatal and pediatric intensive care unit patients. Clin Microbiol Rev 2007;20:409-25.
3. Chang I, Schibler A. Ventilator Associated Pneumonia in Children. Paediatr Respir Rev 2016;20:10-6.
4. Metersky ML, Wang Y, Klompas M, Eckenrode S, Bakullari A, Eldridge N. Trend in Ventilator-Associated Pneumonia Rates Between 2005 and 2013. JAMA 2016;316:2427-9.
5. Karaoglan H, Yalcin AN, Cengiz M, Ramazanoglu A, Ogunc D, Hakan R, et al. Cost analysis of ventilator-associated pneumonia in Turkish medical-surgical intensive care units. Infez Med 2010;18:248-55.
6. Martin-Loeches I, Torres A, Rinaudo M, Terraneo S, de Rosa F, Ramirez P, et al. Resistance patterns and outcomes in intensive care unit (ICU)-acquired pneumonia. Validation of European Centre for Disease Prevention and Control (ECDC) and the Centers for Disease Control and Prevention (CDC) classification of multidrug resistant organisms. J Infect 2015;70:213-22.
7. Kalil AC, Metersky ML, Klompas M, Muscedere J, Sweeney DA, Palmer LB, et al. Management of Adults With Hospital-acquired and Ventilator-associated Pneumonia: 2016 Clinical Practice Guidelines by the Infectious Diseases Society of America and the American Thoracic Society. Clin Infect Dis 2016;63:e61-111. Erratum in: Clin Infect Dis 2017;64:1298. Erratum in: Clin Infect Dis 2017;65:1435. Erratum in: Clin Infect Dis 2017;65:2161.
8. Demir E, Kara A, Ince E, Kiper N, Kuyucu N, Karabocuoglu M, et al. Turk Toraks Dernegi cocuklarda hastanede gelisen pnomoni tanı ve tedavi uzlaşı raporu. Thorac Res Pract 2009;10: Supplement 3-16.
9. Rosenthal VD, Bijie H, Maki DG, Mehta Y, Apisarnthanarak A, Medeiros EA, et al. International Nosocomial Infection Control Consortium (INICC) report, data summary of 36 countries, for 2004-2009. Am J Infect Control 2012;40:396-407.
10. van Wyk L, Applegate JT, Salie S. Ventilator-associated pneumonia in PICU - how are we doing? South Afr J Crit Care 2022;38:10.7196/SAJCC.2022.v38i2.536.
11. Vijay G, Mandal A, Sankar J, Kapil A, Lodha R, Kabra SK. Ventilator Associated Pneumonia in Pediatric Intensive Care Unit: Incidence, Risk Factors and Etiological Agents. Indian J Pediatr 2018;85:861-6.
12. Chomton M, Brossier D, Sauthier M, Vallières E, Dubois J, Emeriaud G, et al. Ventilator-Associated Pneumonia and Events in Pediatric Intensive Care: A Single Center Study. Pediatr Crit Care Med 2018;19:1106-13.
13. Shaath GA, Jijeh A, Faruqui F, Bullard L, Mehmood A, Kabbani MS. Ventilator-associated pneumonia in children after cardiac surgery. Pediatr Cardiol 2014;35:627-31.
14. Kunzmann H, Dimitriades K, Morrow B, Argent A. Reducing paediatric ventilator-associated pneumonia – a South African challenge! South Afr Crit Care 2016;32:17-20.
15. Al-Abdely HM, Khidir Mohammed Y, Rosenthal VD, Orellano PW, ALazhary M, Kaid E, et al. Impact of the International Nosocomial Infection Control Consortium (INICC)'s multidimensional approach on rates of ventilator-associated pneumonia in intensive care units in 22 hospitals of 14 cities of the Kingdom of Saudi Arabia. J Infect Public Health 2018;11:677-84.
16. Rosenthal VD, Jin Z, Memish ZA, Rodrigues C, Myatra SN, Kharbanda M, et al. Multinational prospective cohort study of rates and risk factors for ventilator-associated pneumonia over 24 years in 42 countries of Asia, Africa, Eastern Europe, Latin America, and the Middle East: Findings of the International Nosocomial Infection Control Consortium (INICC). Antimicrob Steward Healthc Epidemiol 2023;3:e6.
17. Yin Y, Sun M, Li Z, Bu J, Chen Y, Zhang K, et al. Exploring the Nursing Factors Related to Ventilator-Associated Pneumonia in the Intensive Care Unit. Front Public Health 2022;10:715566.
18. Assefa M. Multi-drug resistant gram-negative bacterial pneumonia: etiology, risk factors, and drug resistance patterns. Pneumonia (Nathan) 2022;14:4.
19. Sader HS, Farrell DJ, Flamm RK, Jones RN. Antimicrobial susceptibility of Gram-negative organisms isolated from patients hospitalised with pneumonia in US and European hospitals: results from the SENTRY Antimicrobial Surveillance Program, 2009-2012. Int J Antimicrob Agents 2014;43:328-34.
20. Weiner LM, Webb AK, Limbago B, Dudeck MA, Patel J, Kallen AJ, et al. Antimicrobial-Resistant Pathogens Associated With Healthcare-Associated Infections: Summary of Data Reported to the National Healthcare Safety Network at the Centers for Disease Control and Prevention, 2011-2014. Infect Control Hosp Epidemiol 2016;37:1288-301.
21. Rhodes NJ, Cruce CE, O'Donnell JN, Wunderink RG, Hauser AR. Resistance Trends and Treatment Options in Gram-Negative Ventilator-Associated Pneumonia. Curr Infect Dis Rep 2018;20:3.
22. Berton DC, Kalil AC, Teixeira PJ. Quantitative versus qualitative cultures of respiratory secretions for clinical outcomes in patients with ventilator-associated pneumonia. Cochrane Database Syst Rev 2014:CD006482.

23. Solé Violán J, Fernández JA, Benítez AB, Cardeñosa Cendrero JA, Rodríguez de Castro F. Impact of quantitative invasive diagnostic techniques in the management and outcome of mechanically ventilated patients with suspected pneumonia. Crit Care Med 2000;28:2737-41.
24. Khan RA, Aziz Z. A retrospective study of antibiotic de-escalation in patients with ventilator-associated pneumonia in Malaysia. Int J Clin Pharm 2017;39:906-12.
25. Tumbarello M, De Pascale G, Trecarichi EM, De Martino S, Bello G, Maviglia R, et al. Effect of aerosolized colistin as adjunctive treatment on the outcomes of microbiologically documented ventilator-associated pneumonia caused by colistin-only susceptible gram-negative bacteria. Chest 2013;144:1768-75.
26. Doshi NM, Cook CH, Mount KL, Stawicki SP, Frazee EN, Personett HA, et al. Adjunctive aerosolized colistin for multi-drug resistant gram-negative pneumonia in the critically ill: a retrospective study. BMC Anesthesiol 2013;13:45.