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Isolated Pattern of Microorganism among Pediatric Patients with Ventilator-associated Pneumonia (VAP) in a Tertiary Care Hospital Karachi

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Background: The Ventilator associated pneumonia (VAP) is a common condition with inflammation of lungs. The patients on mechanical ventilation or artificial breathings for 48 to 72 hours tend to developed this condition., which is a type of Nosocomial Pneumonia.
Objective: To assess the causative agent and treatment pattern among the patients suffering from ventilator associated pneumonia.
Methodology: A cross sectional study was conducted for the period of 8 months at a tertiary health care setup of the Karachi Pakistan among the patient's with VAP. Total of 72 patients with confirmed diagnosis of VAP were included in the study. Data was collected from the children intensive care units on a structed questionnaire. The required variables were obtained from the patients files/Records after the ethical approval was obtained before the collection of data Results were evaluated using the SPSS version 20.0.
Results: The study found out that the VAP is most type of hospital acquired pneumonia form the

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health care system., showed 59.8% (n=61) males and 34.3% (n=35) females' patients with VAP diagnosis. The age group revealed majority of the patients 46.1% (n=47) were 0–1-year-old, 11.8% (n=12) patients were above 2- 3 years old. 18.6% patients (n=19) were >3 years-4years old. The study also assesses ventilators support >48 hours have around 20-30% (Mean 6.9 days CI: 1.16-3.65) chance to develop the VAP. The subsequent effects of VAP shows the two-fold rates of mortality hence requiring the more length of stay at hospital and extra charges.

Conclusion: The VAP occurs among the considerable numbers of patients on the ventilator supports, the findings suggests that an appropriate management, prevention strategies and effective treatment is needed to reduces the mortality and complications of VAP.

Keywords: Ventilator-associated pneumonia; mortality; incidence prevention; nosocomial pneumonia.

1. INTRODUCTION

Pneumonia is a disease of lungs which causes the inflammation, due to any other infection or infective condition. The ventilator associated pneumonia is a condition of inflamed lungs, patients on tracheal intubation or mechanical ventilation for 48 to72 hours tend to developed ventilator associated Pneumonia (VAP) which is a type of Nosocomial Pneumonia [1-2]. The Physiological ventilation is a system which is entirely different from mechanical ventilation that can cause the lungs damage and other complications [3]. The Risk associated with VAP are 3 to 10 folds higher in patients of ICU (Intense care unit) with mechanical ventilation compared to other wards without mechanical ventilation, which increases patient treatment expenses as well mortality rate [3-4] The mechanical support to the lungs increases the chances of infections up to ten folds, since the mechanical support brings the more chances of contamination, the Ventilator contamination is clearly associated with the infections. The Geriatric patients suffers from other health conditions and complications such as renal failure, Diabetic mellitus, chronic liver disease, abdominal surgeries and impaired functional status are at higher risk of developing lungs problems [5]. However, the poor hygiene environment of hospitals or ICU and lack of precautionary measures against infection are the clear target of the VAP [6]. Nosocomial pneumonia is a ventilator-associated pneumonia (VAP) which arises two or more days after a person is admitted to the hospital. It is the most known hospital-associated infection among the geriatric patients indicating 15 to 45% admitted to ICU, in the case of children it indicates about 20% of all types of infection's rate is 2.9 to 21.6 per 1000 ventilator days [7]. Its mortality and morbidity graph are a rise and the patient is hospitalized 7 to 9 days with health care cost Gadappa and Behera, (2018). In ICU, the growth of different nosocomial infections is rising, common in those patients who are requiring ventilator support, and such infection is known as ventilator-associated pneumonia (VAP) [8]. There are two phases of VAP, one is early, and the other is late-onset. The starting 4 days of a ventilator is early onset. And greater mortality has late-onset VAP. During the initial 10 days period of hospital admission, there could be a 90% chance for patients to develop VAP through mechanical ventilators [9] There are several causative agents and many types of bacteria involves in causing the infections, moreover the viruses, fungi and parasites that can be commensals in the patient, can be exogenous source and spread by cross infection are the major cause of Nosocomial infection. No susceptibility of microbial agents to antimicrobial characteristics Pan Drug resistance another major factor for VAP. The VAP occurs among the considerable numbers of patients on the ventilator supports, the findings suggests that an appropriate management, prevention strategies and effective treatment is needed to reduces the mortality and complications of VAP. Microbiological data provides evidences that nosocomial infections are caused by Multi drug resistance [10]. Pathogens that are the major cause of Nosocomial infections are gram Negative Bacteria including Pseudomonas, Klebsiella & and Acinetobacter, and gram-Positive organism like methicillin- resistant staphylococcus aureus (MRSA), coagulase negative staphylococci and Enterococci. Other common Nosocomial organisms are clostridium difficile, vancomycin- resistant Enterococci, anaerobes and Enterobacter Indwelling catheters or contaminates surgical equipment's can also contribute in the increase risk of Nosocomial infection [11].

2. METHODOLOGY

A cross sectional study was conducted in the Pediatric Intensive Care Unit of three campuses

of Dr. Ziauddin hospital (Clifton campus, Nazimabad campus, and Kamari campus)

The targeted Patients were the admitted and on mechanical ventilation for >48 hours in Pediatric ICU and diagnosed with VAP admitted to Ziauddin Hospital in different campuses. The duration of the study was 8 months, and data was collected during the period (November 2020 to August 2021) after obtaining approval from Board of advance studies and research. The total Sample size for the current study was 72, calculated by rate of incidence of VAP. The Incidence of VAP was calculated by the total episodes of VAP divided by the total number of mechanically ventilated children. (Vijay ,2018).

By using following formula.

$$n= (1.96)2 \text{ X } P (1-P)/D2;(P=0.25; D=0.10)$$

The incidence (P) of 25%, with precision (D) of 10% at 95% confidence.

However, the patients of one month to 12 years old along with the diagnosing of VAP were included in the study. After the data collection the data was organized and analyzed.

VAP was classified by using four methods which are bedside clinician's diagnosis, positive culture from a tracheal aspirate, changes in chest x-ray, and a raised or low WBC count. For the diagnosis of VAP participants were subjected to the investigation such as differential white blood cells, an x-ray of the chest, tracheal aspirates, and non-bronchoscopy BAL samples were sent to LAB along with the sensitivity pattern of antibiotics. Non-bronchoscopy BAL was subjected to semi-quantitative culture and culture reports with >104 colony-forming units/ mL were considered significant.

3. RESULTS

The results showed 59.8% (n=61) males and 34.3% (n=35) females' patients with VAP diagnosis. The age group revealed majority of the patients 46.1% (n=47) were 0–1-year-old, 11.8% (n=12) patients were above 2- 3 years old. 18.6% patients (n=19) were >3 years-4years old as shown in the Table 1.

The prescription pattern showed different types of drugs combination among the patients. of Amikacin+cefotaxime+tanzo in 3.9% (n=4), Amikacin +Cipro+Azithromycin in 15.7% (n=16), cefotaxime +amikacin+ meropenem+ ciprofloxacin in 19.6% (n=20) patients o VAP. Meropenem+ amikacin+ ciprofloxacin as triple drug combination therapy was observed in 19.6% (n=20) patients shown in the (Table 2).

Table 1. Demographic Detail

Gender	Frequency	Percent	Valid Percent
Female	35	34.3	34.3
Male	61	59.8	59.8
Age ranges in Years			
0- 1 years	47	46.1	46.1
>1 years-2 years	10	9.8	9.8
>2 years-3 years	12	11.8	11.8
>3 years-4years	19	18.6	18.6
>4 years and above	8	7.8	7.8

Table 2. Prescription pattern observed in VAP Patients

Prescription pattern observed in VAP Patients	Frequency	Percent	Cumulative Percent
Amikacin+cefotaxime+tanzo	4	3.9	3.9
Amikacin+Cipro+Azithromycin	16	15.7	15.7
Amikicin+ciprofloxacin	1	1.0	1.0
cefotaxime+amikacin+meropenem+ciprofloxacin	20	19.6	19.6
cefotaxime+ciprofloxacin	15	14.7	14.7
cipro+tanzocin+aztreonam	16	15.7	15.7
Meropenem+amikacin+ciprofloxacin	20	19.6	19.6
vancomycin+flygly	4	3.9	3.9
Total	102	100.0	100.0

The treatment given to the patinets of VAP during their stay at hospital was also observed during the study. The cefotaxime 350mg BD+Phenytoin 10mg BD+Amikicin 30 mg BD+Paracetamol 1000mg BD was prescribed more oftenly to the patinets. However, the use antibiotics in combination with antiviral was observed in majority of the cases as part of treatment. Ciprofloxacin 250 mg BD+Dexamethasone 4mg 8H+Acyclovir 250 BD+Paracetamol 1000 mg BD+Mannitol 100ml 8. The combination of Vancomycin with antiviral was seen in 9.8% of the cases ceftriaxone 150mg BD+Acyclovir 250mg 8H+ Provas 25mg +mannitol 100ml 8H+ Vancomycin 150 mg 8H.

The causative agents were assessed among the patinets of VAP, majority of the patients were found with Pseudomonas aeruginosa, staphylococcus aureus Klebsiella and E.Coli in the order, moreover the days of MV was also noted among the patients the least numbers of days were found 1 day, however the maximum days of MV observed was 7 days. The treatment against the causative agent an the MV total days is expressed in the Table 4.

Table 3. Combination drugs treatment in VAP Patients

Treatment	n	Percentage %	Cumulative Percent %
Amikacin+Cefotaxime+Paracetamole	13	12.7	12.7
Azithromycin 100 mg BD+Provas 4ml BD+Acyclovir 400 mg BD+Paracetamol 1000 mg 8H	1	1.0	1.0
cefotaxime 350 mg BD+Phenytoin 10 mg BD+Amikicin 30 mg BD+Paracetamol 1000 mg BD	1	1.0	1.0
Cefotaxime 375 mgBD+Amikacin 300 mg BD+Phenytoin 20 mg BD+provas 4 ml 8 hrs	13	12.7	12.7
ceftriaxone 150mg BD+Acyclovir 250mg 8H+ Provas 25mg +mannitol 100ml 8H+ Vancomycin 150 mg 8H	4	3.9	3.9
ceftriaxone 30 mg 8H+Paracetamol 500 mg BD+ Provas 4 ml	4	3.9	3.9
ceftriaxone 600 mg/day+amikacin 400 mg BD+Phenytoin 20 mg BD	10	9.8	9.8
cipro 300 mg+Phenytoin 20 mg BD+Provas 4m	26	25.5	25.5
ciprofloxacin 200 mg BD+Phenytoin 20 mg BD + Paracetamol 500 mg BD	1	1.0	1.0
ciprofloxacin 250mg BD + Dexamethasone 4 mg 8H + Acyclovir 250 BD + Paracetamol 1000 mg BD + Mannitol 100 ml 8	2	2.0	2.0
ciprofloxacin 250mg BD+Phenytoin 20 mg BD+Provas 4ml BD+Diazepam 10 mg BD+ Paracetamol 500 mg BD	3	2.9	2.9
gentamycin 20 mg 8H+Provas 200 mg BD+Inj Adrenalin 0.5 ml+paracetamol 100 mg	7	6.9	6.9
tanzo 400 mg 8H, Pracetamol 1000 mg 12H+Amikacin 20 mg BD+Ceftazidine +azithromycin 100 mg/day	7	6.9	6.9
vancomycin 200 BD+Amikicin 200 mg BD+Provas 4 ml BD+Paracetamol 500 mg BD	1	1.0	1.0
vancomycin 200 BD+Provas 4ml 8H+baclofen 10 mg+paracetamol 500 mg BD	3	2.9	2.9
Total	102	100.0	100.0

Table 4. MV duration against causative agents and Treatment

Treatment	MV Duration	E. coli	Klebscilla	Pseudomonas arignosa	staphylococcus aureus
Amikacin+cefotaxime+paracetamole	1-3 days	3		4	4
Azithromycin 100 mg BD+Provas 4 ml BD+Acyclovir 400 mg BD+Paracetamol 1000mg 8H	>7 days		1		
cefotaxime 350 mg BD+Phenytoin 10 mg BD+Amikicin 30 mg BD+Paracetamol 1000mg BD	4-6 days			1	
ceftriaxone 150 mg BD+Acyclovir 250 mg 8H+ Provas 25 mg +mannitol 100ml 8H+ Vancomycin 150 mg 8H	>7 days			4	
ceftriaxone 300 mg 8H+Paracetamol 500 mg BD+ Provas 4ml	1-3 days			3	
ceftriaxone 600mg/day+amikacin 400mg BD+Phenytoin 20mg BD	1-3 days 4-6 days >7 days		0 1 3	0 3 0	3 0 0
ciprofloxacin 200 mg BD+Phenytoin 20 mg BD+Paracetamol 500 mg BD	4-6 days			1	
ciprofloxacin 250 mg BD+Phenytoin 20 mg BD+Provas 4 ml BD+Diazepam 10 mg BD+ Paracetamol 500mg BD	4-6 days			3	
gentamycin 20 mg 8H+Provas 200 mg BD+Inj Adrenalin 0.5ml+paracetamol 100mg	1-3 days 4-6 days	3	0 3		4 0 4
tanzo 400 mg 8H, Pracetamol 1000 mg 12H+Amikacin 20 mg BD+Ceftazidine +azithromycin 100mg/day	1-3 days 4-6 days 7 and above days		0 1 3	1 0 2	

4. DISCUSSION

The study showed the patients of VAP on mechanical support and different combinations of treatment a study conducted on a similar pattern showed around 128 patients with VAP with the distribution as 72% males, which is majority on the gender basis, our study showed 59.8 of the males diagnosed with VAP [12]. The stage of

VAP as per CDC preferred was once 38.4%, on the other hand, 24.4% of microbiologically constant VAP used. The ventilator-associated tracheobronchitis has been studied for the several times to be 11.6%. The most often far away organism actinobacteria is 47%, 28% is Pseudomonas, 15% *Klebsiella*, 5% E. coli, and 5%Enterobacter found in a study however the microorganism distribution in our study showed the pattern *E.coli* cases more than *Klebsiella* and *Pseudomonas arignosamore* than *Staphylococus aureus*[13].

Our study showed that children in ICU had developed VAP (17%). another half (46%) had been fewer than 1 year. the ratio of male to female was 1:2:1. Analyst investigates that less than 1to12 months of incidence of VAP is greater due to the fact of the emergency intubation and use of intravenous sedation [14] A retrospective and cohort study conducted in India showed that children between one month to 12 years have emerged and all children had been MV. The study was arranged in January 2015 to June 2016 on bedded in ICU, the conclusion of VAP was 40% with parenteral diet, the tube of nasogastric including mortality [15]. The Length of stay MV used to be Mean 7.25 days in early VAP, whilst 22.75 days in late VAP. However, our study shows majority of the patients i.e., 46.1% were 0- 1 years, and 18.6% were >3 years-4years, 11.8 % were >2 years-3 years which is supported by the study [16] VAP originated in males and arises in those children who are between 6 months to four years. from 83 patients, 38.6% Pseudomonas aeruginosa ,30.1% E. coli, 9.6% Staphylococcus aureus,9.6% Klebsiella, 7.2% Streptococcus and 4.8% Acinetobacter with VAP [17] Another study showed that 25 patients developed VAP out of 60 patients for more than two days. And remained on antibiotic combination treatment, which is similar to the findings of our study showing MV of 4-6 days against the treatment pattern of ciprofloxacin 250mg BD+Phenytoin 20mg BD+Provas 4ml BD+Diazepam 10mg BD+ Paracetamol 500mg BD. A study showing 26 VAPs per 1000 ventilator days or 25 VAPs per a hundred ventilator days throughout the research period [18]. There used to be a direction with growing mortality in the VAP group, and our study found that more common treatment combination was tanzo 400mg 8H, Paracetamol 1000mg 12H+Amikacin 20mg BD+ Ceftazidine +azithromycin 100mg/day [19] The minimum MV length was found to be 1 day with VAP and maximum of the 7 days. However, the MV length shown in a similar study was 1 week, while the maximum duration was 5 weeks. The minimum course of antibiotics was 5days whereas 35 days were maximum [20] Also supported by another study showing patients diagnosed with VAP were 91%, and before diagnosed antibiotics were provided. 56 cases were diagnosed with VAP,6 cases in early while 50 had late VAP. For 28-day, the 48,68 and 71%of mortality rates in the VAP patients [21].

5. CONCLUSION

The study concluded that ventilator associated pneumonia is one of the common types of Pneumonia acquired from hospitals services or any health care services. Despite advances in antimicrobial therapy, improved supportive care modalities, and the use of preventive measures, ventilator-associated pneumonia (VAP) remains an important cause of morbidity and mortality specifically among children under the age of 12. This study showed that clinicians, policy makers and safety officers can better understand and manage the disease by appropriate planning and strategies to make the treatment the treatment infectious and cost-effective.

CONSENT

As per international standard or university standard, patients' written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

Before research work, an ethical approval was taken from the 'Ethics review committee' of Ziauddin University

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFRENCES

1. Chastre J, Fagon JY. Ventilator-associated pneumonia. American journal of respiratory and critical care medicine. 2002;165(7):867-903.
2. Rello J, Ollendorf DA, Oster G, Vera-Llonch M, Bellm L, Redman R, Kollef MH. Epidemiology and outcomes of ventilator-

associated pneumonia in a large US database. Chest. 2002;122(6):2115-2121.

3. Kollef MH, Hamilton CW, Ernst FR. Economic impact of ventilator-associated pneumonia in a large matched cohort. Infection Control & Hospital Epidemiology. 2012;33(3):250-256.
4. Garnacho-Montero J, Ortiz-Leyba C, Jimenez-Jimenez FJ, Barrero-Almodovar AE, Garcia-Garmendia JL, Bernabeu-Wittell M, Madrazo-Osuna JJCID. Treatment of multidrug-resistant Acinetobacter baumannii ventilator-associated pneumonia (VAP) with intravenous colistin: a comparison with imipenem-susceptible VAP. Clinical Infectious Diseases. 2003;36(9):1111-1118.
5. Blonz G, Kouatchet A, Chudeau N, Pontis E, Lorber J, Lemeur A, Colin G. Epidemiology and microbiology of ventilator-associated pneumonia in COVID-19 patients: A multicenter retrospective study in 188 patients in an un-inundated French region. Critical Care. 2021;25(1):1-12.
6. Emonet S, Lazarevic V, Leemann Refondini C, Gaïa N, Leo S, Girard M, Pugin J. Identification of respiratory microbiota markers in ventilator-associated pneumonia. Intensive care medicine. 2019; 45(8):1082-1092.
7. Godin JA, Chahla J, Moatshe G, Kruckeberg BM, Muckenhirn KJ, Vap AR, LaPrade RF. A comprehensive reanalysis of the distal iliotibial band: quantitative anatomy, radiographic markers, and biomechanical properties. The American Journal of Sports Medicine. 2017; 45(11):2595-2603.
8. Joseph NM, Sistla S, Dutta TK, Badhe AS, Parija SC. Ventilator-associated pneumonia: a review. European journal of internal medicine. 2010;21(5):360-368.
9. Park DR. The microbiology of ventilator-associated pneumonia. Respiratory care. 2005;50(6):742-765.
10. Ippolito M, Misseri G, Catalisano G, Marino C, Ingoglia G, Alessi M, .Cortegiani A. Ventilator-associated pneumonia in patients with covid-19: A systematic review and meta-analysis. Antibiotics. 2021; 10(5):545.
11. Luyt CE, Sahnoun T, Gautier M, Vidal P, Burrel S, Pineton de Chambrun M, Chastre J. Ventilator-associated pneumonia in patients with SARS-CoV-2-associated acute respiratory distress syndrome requiring ECMO: A retrospective cohort study. Annals of Intensive Care. 2020; 10(1):1-10.
12. Wu D, Wu C, Zhang S, Zhong Y. Risk factors of ventilator-associated pneumonia in critically III patients. Frontiers in pharmacology. 2019;10:482.
13. Giacobbe DR, Battaglini D, Enrile EM, Dentone C, Vena A, Robba C, Bassetti M. Incidence and prognosis of ventilator-associated pneumonia in critically ill patients with COVID-19: A multicenter study. Journal of clinical medicine. 2021; 10(4):555.
14. Kalanuria AA, Mirski M, Ziai W. Ventilator-associated pneumonia in the ICU. Annual Update in Intensive Care and Emergency Medicine. 2014;65-77.
15. Craven DE. Epidemiology of ventilator-associated pneumonia. Chest. 2000; 117(4):186S-187S.
16. Sen A. An observational study on incidence, etiology, and risk factors of ventilator associated pneumonia in our intensive care unit (Doctoral dissertation, Government Dharmapuri Medical College, Dharmapuri).
17. Zack JE, Garrison T, Trovillion E, Clinkscale D, Coopersmith CM, Fraser VJ, Kollef MH. Effect of an education program aimed at reducing the occurrence of ventilator-associated pneumonia. Critical care medicine. 2002;30(11):2407-2412.
18. Kollef MH. Prevention of hospital-associated pneumonia and ventilator-associated pneumonia. Critical care medicine. 2004;32(6):1396-1405.
19. Godin JA, Chahla J, Moatshe G, Kruckeberg BM, Muckenhirn KJ, Vap AR, LaPrade RF. A comprehensive reanalysis of the distal iliotibial band: Quantitative anatomy, radiographic markers, and biomechanical properties. The American Journal of Sports Medicine. 2017; 45(11):2595-2603.
20. Rajalakshmi E. A study on incidence and etiology of ventilator associated pneumonia (Doctoral dissertation, Madras Medical College, Chennai); 2010.

21. Steen J, Vansteelandt S, De Bus L, Depuydt P, Gadeyne B, Benoit DD, Decruyenaere J. Attributable mortality of ventilator-associated pneumonia. Replicating findings, revisiting methods. Annals of the American Thoracic Society. 2021;18(5):830-837.

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