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ANTIMICROBIAL RESISTANCE PATTERN OF BACTERIAL ISOLATES FROM VENTILATOR ASSOCIATED PNEUMONIA PATIENTS IN ICU ALONG WITH RISK STRATIFICATION

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Abstract:
Background: Ventilator associated pneumonia (VAP) is one of the key challenges for critical care physicians. The study was done to identify the risk factors in patients developing VAP, the bacteriological profile and resistance pattern of the infective bacteria in our intensive care units (ICUs), and formulate empirical antibiotic policy.
Methods: This prospective study was carried out over 1 year period in a Medical College in Kolkata. Out of 60 samples collected from patients admitted to ICU and requiring mechanical ventilation for more than 48 hours and suspected of having Ventilator associated events (VAE). Semi-quantitative culture of Deep tracheal aspirate (DTA) was processed
Results: In the present study of 60 respiratory samples in the form of tracheal aspirate -50(83%) showed growth and 10 (17%) showed no growth. In the study, 98% of isolates were gram negative bacilli and Acinetobacter baumannii was the commonest isolate. Common co-morbidities include Cerebrovascular accident, puerperal sepsis, trauma, diabetic coma, and neurosurgery post-operative complications. Duration of ventilation and history of previous antibiotic use emerged as significant risk factors in the development of VAE in the ICU. **Conclusion:** VAP is associated with significant morbidity and mortality not only due to VAP but the underlying critical illness in the patients. Microbiological data should be used for formulating antibiotic policy of the institution. The pitfall in using empiric antibiotics for suspicion of VAP is the potential for antibiotic overuse, the emergence of resistance, and unnecessary adverse effects.

Key words : Ventilator associated pneumonia, Multi drug resistance , Quantitative culture

INTRODUCTION

Lower respiratory tract infection isone of the commonest bacterial infections among patients admitted in intensive care units(ICUs) being associated with high morbidity, mortality, ranging from 22% to71%(1). In spite of the recent advancements in antimicrobialregimes, VAP continues to be an important cause of death in ICU set up. VAP needs rapid diagnosis and initiation of appropriate antibiotic therapy, as there is adverse effect of inappropriate and inadequate

antibiotictherapy on patients' prognosis. Moreover , there is high risk of emergence of multidrugresistant(MDR) organisms.(2)

Ventilator-associated event (VAE) is common in the intensive care unit (ICU), affecting 8 to 20%of ICU patients and up to 27% of mechanically ventilated patients .(3)Quantitative analysis of TA(tracheal aspirate) has been preferred as a simple and useful procedure in the diagnosis of VAP and has theadded advantages of being a noninvasive and more inexpensivetechnique.(4) Microbial etiology of intensive care unit (ICU)-acquired pneumonia (ICUAP) determines antibiotic treatment andoutcomes. (5)

OBJECTIVES

1. To identify the prevalent bacteriological profile along with determine antimicrobial susceptibility and resistance pattern of respiratory secretion collected by a Deep Tracheal Aspiration(DTA) and Broncho-alveolar lavage.
3. To determine risk factors for development of "ventilator associated events" (VAEs) to VAP

MATERIALS AND METHODS

The study was carried out in Department of Microbiology in collaboration with Department of Critical Care Medicine in a Medical college Hospital of West Bengal.

Study Population

Patients developing clinical signs and symptoms of VAE after 48 hours of admission in the adult CCUs within the time period of August 2018 to July 2019 .

Methods of Data Collection

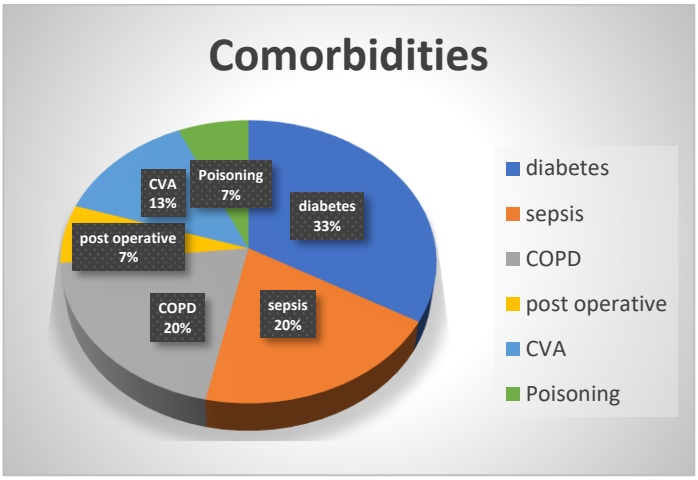
A case record form (pre-tested, semi-structured) with informed consent was used for data collection. Relevant history was takenand important clinical finding was noted. Sample were collectedand processed following standard protocol (as mentioned in Mackie &McCartney). (9)

Microbiological Methods

Deep Tracheal aspirate(DTA) samples and Broncho-alveolar lavage were processed through semi-quantitative method of bacteriological culture on blood agar,chocolate agar , MacConkeyagar, nutrient agar and colony count of 10^4bacterial colonies per ml in case of BAL fluid and 10^5CFU/ mL for DTA were considered significant except for the sample collected from patient who was on previousantibiotic .Aerobic isolates were identified by Gram stain and Microscopy, routine biochemical tests as per standard protocol(9). Antimicrobial susceptibility of isolates was tested by modified KirbyBauer disk diffusion method as per the recommendations of Clinical and Laboratory Standards Institute (CLSI guidelines).(10)

RESULT AND ANALYSIS

Total 60 respiratory samples from patients admitted in CCU wereprocessed in the laboratory. Out of the total 60 samples from patients having sign and/ symptoms of Lower respiratory infection, 55(92%) showed culture to be positive and 5(8%) samples showed no growth. Acinetobacter (48%) was the commonest isolate recovered from respiratory secretion samples followed by Klebsiella(29%)and Pseudomonas(19%). Only Polymixin B showed 100 % sensitivity against all these isolates



The comorbidities most commonly associated with were generalized sepsis(n=20%) , Cerebrovascular disease (n=13.%),Diabetes(n=33%),COPD(n=20%).Post operative patients Neurosurgery department requiring ventilator support.

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TABLE 3 :Resistant pattern of bacteriological isolates.

Organism	Polymixin B	carbapenems	3rdgen cephalosporin	aminoglycosides	Pip-tazo	quinolones
Acinetobacter	0%	77%	100%	76%	90%	98%
Klebsiella	0%	67%	96%	77%	76%	100%
Pseudomonas	0%	54%	90%	60%	45%	95%
E.coli	0%	30%	86%	28%	31%	86%

Association of culture positivity was significantly associated withprevious use of Antimicrobial ($p<0.0005$) Out of 55 culture positive samples 15 samples(27%) showed more than one bacterial isolate .Generalized sepsis was commonest associated co-morbidity in patients with polymicrobial infection..

DISCUSSION

ICU associated lower respiratory infection and antimicrobialresistance is regarded as agrave problem worldwide and it is associated with significantupsurge in morbidity, mortality and associated healthcare expenditure (11)(12).The present study was undertaken to understand the bacteriological profile and the pattern of drug sensitivity and resistance of the bacterial isolates. The rate of development of VAP in ICU of our set-up was 31% . Out of 172 patients 55 developed VAP(31%). Pneumonia is a frequent complication in patients admitted to the ICU.It is frequently polymicrobial with predominantly multi drug resistant GNB, such as Acinetobacter, Pseudomonas, Klebsiella, E.coli.(14–16).In our study 98% isolates were gram negative bacilli and Acinetobacter spp was the commonest isolate which is similar to study by Rajasekhar et al(17) and Dey et al(18)and Ranjan et al.(19)

In the present study total 60 respiratory samples in the form of BAL fluid and deep tracheal secretions were collected and processed in our Microbiology laboratory. Out of the total 60 samples 55(92%) showed growth and 5 (8%) showed no growth.

15 (25%) samples yielded growth of 2 organisms, so total 65 isolates were processed and their results were analyzed. Ferrer, Miquel et al found about 14%polymicrobial isolates from respiratory samples of ICU patients suffering from pneumonia. (5) In Indian scenario, Goel et al had found similar rate of polymicrobial infection in her research In a four year study from Kashmir. (20)

Age of the study subjects were considered as a factor associated with infection. The lowest age of patient was 9 years and highest age was 84 years in this study. Mean age was 37.33years which is similar to study by Gadaniet al.(21)

In the present study subjects were distributed according to gender .81% of males and 86% of females showed culture positive infectionamong whom the samples were collected. But this association was notstatistically significant.

Out of 55 patients who developed VAP – 8 cases of cerebrovascularaccident(13%),11 cases with COPD (20%), ,4post operative cases including 3 neurosurgery cases (7%),18 cases diabetes withmetabolic or other complication (33%)and 4 cases of poisoning,druganaphylaxis and connective tissue disorder . Study by Dey et al andVora et al alsorevealed similar disease profile.(18) .(22)Comorbidities associated with VAP In our study which is associated with development of pneumoniain ICU were mainly Diabetes mellitus with or without metabolic complication, Sepsis, COPD .Other comorbidities include CNS diseases like Encephalopathy, Strokes, comatose patients ,postoperative complication. Association of these comorbidities were similar to other studies by Dey et al (23)and Sujatha et al (24)

Risk Factors

Mechanical ventilator,duration of hospital stay,history of previous antibiotic abuse, misuse ,overuse emerged as important risk factors in development of LRTI in ICU in our study.Prior use of antibiotic has also statistically significant association with development of LRTI caused multi drug resistant isolates in our study (p value<.001),prolonged antibiotic administration to ICU patients for primary infection helps in selection and subsequent colonization with resistant organism responsible for superinfection. A sentinel study of VAP in a French ICU noted that priveous antimicrobial therapy significantly increased the rate of VAP associated with infection by P.aeruginosa and Acinetobacter spp.(25)

Acinetobacter spp.(43.75%) was found to be one of the commonest organism causing pneumonia in our CCU set-up. Other organisms were Klebsiella pneumoniae (25%),Pseudomonas aeruginosa (23.4%), Escherichia coli (4.6%) and Staphylococcusaureus (1.5%) The finding of Acinetobacter as commonest isolate issimilar to other recent studies.Saravu et al in 2013 (26) ,Dey et al(18) in 2007 and Manchanda V et al(27)in 2010 in Indian study and Meduri in 1991(28) in American studyhad similar isolates.Ranjan N et al found (29) that the mostcommon pathogens causing VAP were Acinetobacter spp andPseudomonas aeruginosa.Most of the other studies had detected prevalence of gram negativeisolates from respiratory samples collected in ICU similar to our study.Pseudomonas spp and Klebsiella were reported as commonest isolate in many Indian and International studies .(29–31)Multidrug resistance (MDR) is defined as insensitivity or resistance against more than .(32,33)In the present study isolates of Acinetobacter spp. causing VAP were highly resistant to Ciprofoxacin, 3rdgeneration Cephalosporins and even to Meropenem.The only drug having a good in-vitro activity against Acinetobacter isolates were Polymyxin B with a sensitivity rate being almost 100%.

Klebsiella spp showed almost 100% resistance against Amoxycillin clavulanic acid, Quinolones and cotrimoxazole . The resistance of some GNB to aminoglycosides has been well-recognized in many hospitals. Klebsiella showed 81% resistance against Amikacin in our investigation.

Carbapenems are frequently used as a last option in treating grave infections caused by GNB's. in our present study Klebsiella showed 31.25% resistance towards carbapenem in accordance to observations made by other studies like Akhtar et al 2010 (34)that showed 26.1% resistance and Fatima et al2012(35) , that showed 24% resistance. This was in contrast to observations made by Gonluguret al.(36) and Gladstone et al.2005(37) that comparatively showed lower rates of resistance toward carbapenems, whereas study done by Kucukates and Kocazeybek showed high sensitivity to carbapenem.(38).

Pseudomonas in the present study showed maximum resistance against 3rd generations Cepholosporins, Quinolones and Aminoglycoside 93%,86% and 80% respectively.Carbapenems

like Imipenem and Meropenem and Piperacillin-Tazobactum combination were somewhat effective against Pseudomonas with sensitivity rate of 47% and 53% respectively. Only Polymixin B showed 100% sensitivity against all the isolates .Results was in accordance with other studies.(39,40).Another past study that evaluated the in vitro activity of colistin in isolates of Gram-negative bacteria reported that all MDR P.aeruginosa isolates were susceptible to colistin. These data support a role for colistin in the treatment of infections caused by MDR P. aeruginosa.(39).
However, ceftazidime showed poor activity against Pseudomonas in the present study, which yield similar result in study done by Yayan et al 2015.(40) There has been renewed interest in colistin despite concerns over its nephrotoxicity and neurotoxicity in light of the increasing numbers of infections caused by multi-drug-resistant (MDR) pathogens, particularly P aeruginosa and Acinetobacter baumannii.(40)

CONCLUSION

Acinetobacter spp is considered as the most common bacteria causing life threatening infections in the ICUs. Most of the gram negative isolates specially Acinetobacter spp showed resistance to most of the commonly prescribed antibiotics . Outcome in case LRTI in ICU depends not only on drug resistance organism but also on the presence of other comorbid conditions like sepsis ,CNS diseases and diabetes. Worrisome increase in the resistance to antibiotics including Polymixin-B as the only useful antimicrobial against most of the gram negative isolates from respiratory samples calls for urgent intervention to prevent their continued upsurge. It is recommended that hospital antibiotic policies be based on, and regularly reviewed and modified in accordance with hospital antibiogram results by hospital infection control committee. Therefore, we can conclude that for effective management of LRTI's,an ultimate and detailed bacteriological diagnosis and susceptible testing is required to overcome global problem of antibiotic resistance.

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