A Cross -Sectional Study of Bacteriological Profile of Lower Respiratory Tract Infections in Neurosurgery Intensive Care Unit in Central Kerala

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ABSTRACT

BACKGROUND

Lower respiratory tract infections are the most common bacterial infections in neurosurgery intensive care units (NSICU), resulting in high overall mortality. The emergence of antibiotic resistant pathogens poses a challenge to their empiric treatment. Regular surveillance of the prevalent strains and their susceptibility pattern, helps to revise the antibiotic policies and aids in better management of the patient.

METHODS

A cross sectional study was conducted in the Department of Neurosurgery and Microbiology, Government Medical College, Thrissur, over a period of 1 year, using lower respiratory tract specimens of 190 patients with acute respiratory symptoms admitted in neurosurgery intensive care unit. The specimens collected aseptically were processed immediately. Following culture, the bacterial isolates were identified using standard methods and antibiotic susceptibility was done by Kirby Bauer disc diffusion method. The data obtained was coded and entered in Microsoft Excel and expressed as percentage.

RESULTS

Bacterial isolates were obtained from 74 % samples. 82 % isolates were monomicrobial and 18 % were polymicrobial. Majority of the isolates were gram negative bacteria (94 %) followed by gram positive bacteria (6 %). The common gram-negative isolates were *K. pneumoniae* (36 %), *A. baumannii* (29 %), *P. aeruginosa* (20 %). Methicillin-resistant staph (MRSA) (3 %) and methicillin-susceptible staph (MSSA) (3 %) accounted for the gram positive cocci. 61 % isolates were multi drug resistant (MDR). Most common MDR organism was *A. baumannii.* It was observed that 26 % isolates were extended spectrum beta-lactamase (ESBL) producers. A high rate of resistance to cephalosporins, beta lactams, fluoroquinolones, aminoglycosides, and cotrimoxazole was observed. An emerging resistance to carbapenems was observed.

CONCLUSIONS

Proper microbiological work up and antibiotic stewardship programmes can limit spread of resistant organisms, thereby reducing the medical and economic burden of the patient.

KEYWORDS

Lower Respiratory Tract Infection, Neurosurgery ICU, Antimicrobial Susceptibility Tests, Multi Drug Resistant Organisms

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BACKGROUND

Lower respiratory tract infections (LRTI) are the most common bacterial infections among patients in neurological intensive care units. It occurs in 10 - 25 % of all intensive care unit (ICU) patients and results in high overall mortality of 22 % - 71 %.[1] Intubated patients have 7 - 21 times higher rates of pneumonia.[2] Patient on ventilator have 1 - 3 % per day chances of developing pneumonia during first five days of intubation.[3] Patients admitted in neurosurgery intensive care unit with traumatic brain injury, multiple trauma, altered consciousness and impaired protective reflexes have high risk of acquiring respiratory infections.[4]

The important risk factors for infections in NSICU includes mechanical ventilation, presence of indwelling invasive devices, administration of immuno suppressive drugs, long term or repeated use of antibiotics and decreased host defences due to poor health status.[1] Sedatives, feeding tubes and endotracheal tubes attribute to aspiration pneumonia.[3] Host factors include extremes of age, underlying immunosuppression, diabetes and malnutrition. Aspiration pneumonia is more common in patients with stroke and traumatic brain injury due to decreased level of consciousness.[5]

Infections may be acquired by oropharyngeal colonization by the endogenous flora or by pathogens acquired exogenously from the ICU, contaminated respiratory equipment or hospital air. Gram negative infections are usually predominant in NSICU.[4] The aetiological agents may be monomicrobial or polymicrobial. There is an increasing trend of resistance to the conventional antibiotics used for empiric treatment, leading to treatment failure, prolonged hospital-stay, morbidity and death. Infections with extended spectrum beta lactamase Enterobacteriaceae (ESBLE) are emerging.[4]

Hiker and co-workers evaluated patients with acute stroke in a neurological ICU in Germany and found that the incidence of pneumonia was 21 %.[6] Berrouane and colleagues found higher incidence of early-onset pneumonia in patients with neurotrauma.[7] In a study conducted in neuro ICU of a tertiary care centre in central India, bacterial isolates were obtained from 86.08 % lower respiratory tract specimens. A single pathogen was identified in 75.75 % patients and 24.24 % had mixed bacterial aetiology. Gram negative bacteria were predominant.[1] Data on prevalent strains in the ICU and their susceptibility pattern, helps to revise the antibiotic policy and also guides the clinicians for better management of the patient.

This study was undertaken in a tertiary care teaching hospital at Thrissur, Kerala to isolate the bacterial pathogens causing lower respiratory tract infections in neurosurgery intensive care unit and to determine its antibiotic susceptibility pattern.

METHODS

A hospital based cross-sectional study was done in the Department of Microbiology and Neurosurgery, Government Medical College, Thrissur, Kerala, India. The study was done with the permission of Institutional Research Committee and Institutional Ethics Review Board of the Institution. A total of 190 samples from patients admitted in neurosurgery intensive care unit with acute respiratory symptoms from March 2017 to February 2018 were collected and processed.

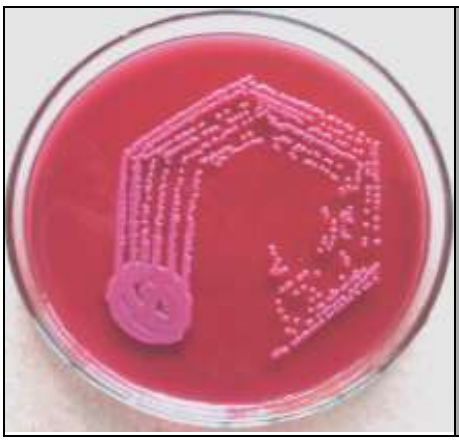

Figure 1. K. Pneumoniae on MA

Figure 2. Double Disc Diffusion Test for ESBL

Figure 3. E-Test for MIC of Colistin

The samples included sputum, endotracheal aspirate and bronchial wash. Blood samples were collected from patients with persisting fever. A smear was made from the homogenized sample and gram staining done. The samples were plated on blood agar (BA), MacConkey Agar (MA), (Fig. 1) and chocolate agar (CA). After overnight incubation at 37 ^{0}C, the bacterial colonies were identified based on colony characteristics, microscopic morphology and biochemical reactions using standard microbiological procedures. American Type Culture Collection (ATCC) strains were used

as controls. The tests done for gram negative bacteria were hanging drop test, catalase test, oxidase test, Hugh Leifson's oxidation fermentation test (OF), nitrate reduction test, indole test, methyl red test (MR), Voges Proskauer test (VP), citrate test, urease test, triple sugar iron test (TSI), sugar fermentation test, Moeller's amino acid decarboxylation media and 10 % lactose. The tests done for gram positive bacteria were catalase and coagulase test.[8] The bacterial isolates were subjected to antibiotic susceptibility testing on Mueller Hinton Agar (MHA) by Kirby Bauer disc diffusion method, following the panel of antimicrobial agents recommended by the Clinical Laboratory Standard Institute (CLSI - 2017).[9] The sensitivity pattern of the antibiotics administered to the patient were also tested. ESBL production was tested by double disc diffusion method.(Fig. 2) Gram negative isolates resistant to Meropenem were tested for sensitivity to colistin by E test. Vancomycin MIC was determined by E - Test (Fig. 3)

Statistical Analysis

After coding, data was entered and analysed in Microsoft Excel version 10 and expressed as percentage.

RESULTS

One hundred ninety samples were collected from neurosurgery ICU during March 2017 to February 2018 and processed in the Central Microbiology Lab of Government Medical College, Thrissur, Kerala, India. Majority of patients in the study were males 144 (76 %) compared to females 46 (24 %). Maximum number of patients 57 (30 %) were in the age group of 60 - 69 years. Majority samples 114 (60 %) were obtained from patients admitted in ICU for 11 - 20 days. Samples 156 (82 %) were mostly obtained from patients diagnosed with traumatic brain injury (TBI). Majority of samples were obtained from patients with tracheostomy (65 %).

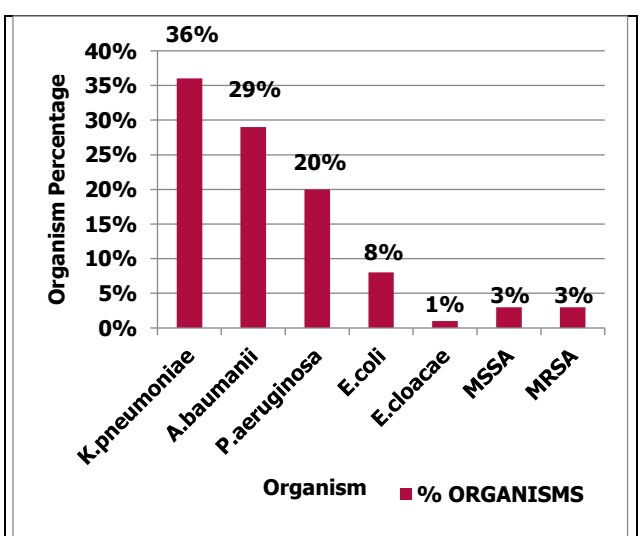

Figure 4. Bacteriological Profile of Organisms Isolated from NSICU

The major co-morbidity found in the study population was diabetes mellitus (40 %). Of the 190 lower respiratory tract specimens processed, bacterial isolates were obtained from 140 (74 %) samples, 21 (11 %) showed normal upper respiratory tract flora and 29 (15 %) showed no growth. Out of the total culture positive cases (140), 115 (82 %) were monomicrobial and 25 (18 %) were polymicrobial (mixed pathogens). *P. aeruginosa* and *K. pneumoniae* were most commonly isolated from mixed infections. Majority of the bacterial isolates in this study were gram negative bacilli 108 (94 %) followed by gram positive cocci 7 (6 %). The most common isolate was *K. pneumoniae* followed by *A. baumannii.* (Fig. 4). Among GNB, 66 (61 %) isolates were multi drug resistant and 42 (39 %) were non multidrug resistant isolates (Table-1).

Organism	Total Number of Isolates	Number of MDR Organisms	Percentage
A. baumannii	33	29	88 %
K. pneumoniae	41	26	63 %
P. aeruginosa	23	7	30 %
E. coli	9	4	44 %

Table 1. Multidrug Resistant Gram-Negative Bacteria

Antimicrobial susceptibility testing of P. aeruginosa showed that 60 % isolates were resistant to Ceftazidime, Ciprofloxacin and Gentamicin. Resistance was low against Amikacin (26 %), Cefepime (21 %) and Imipenem (16 %). Resistance to Piperacillin-Tazobactam was shown by 8 (35 %) isolates. Out of 66 (61 %) MDR organisms, 17 (26 %) isolates were ESBL producers. Out of 26 MDR *K. pneumoniae* isolates, 7 were ESBL producers and of the 29 MDR *A. baumannii* isolates6 were ESBL producers.

All MSSA isolates were resistant to Penicillin. 2 (50 %) isolates were resistant to Erythromycin. 1 (25 %) resistance towards Clindamycin and Cotrimoxazole. All MRSA isolates were resistant to Penicillin, Erythromycin and Cotrimoxazole and all were sensitive to Vancomycin. 2 (67 %) isolates were resistant to Clindamycin. (Figure 5 & 6)

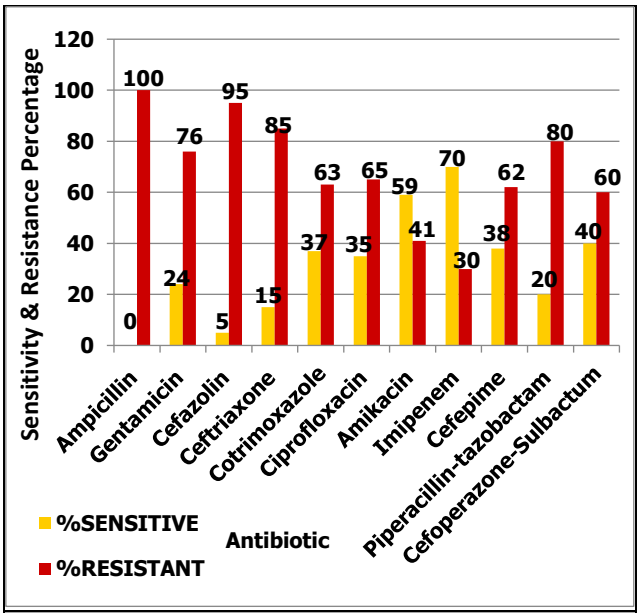

Figure 5. Antimicrobial Susceptibility Pattern of K. pneumoniae

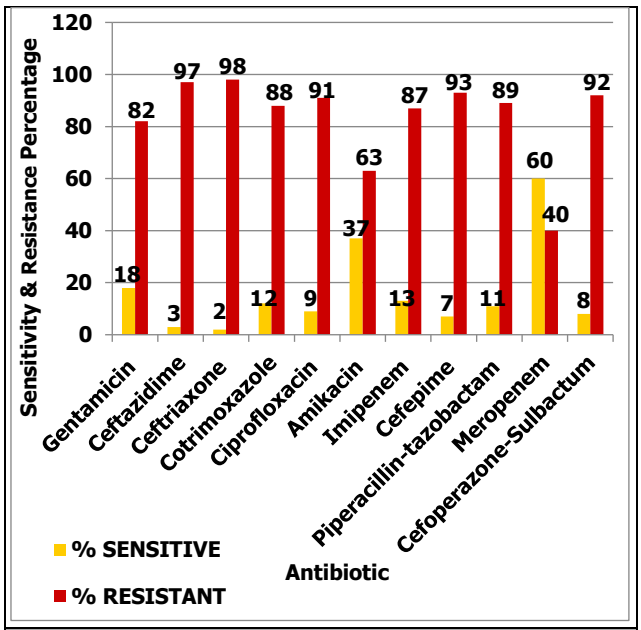

Figure 6. Antimicrobial Susceptibility Pattern of A. baumannii

DISCUSSION

The flora of the oral tract rapidly shifts on admission from typical community respiratory organisms (Streptococci, *Haemophilus influenzae*) towards "hospital-associated" pathogens such as *S. aureus*, Enterobacteriaceae, Pseudomonas and Acinetobacter species. Analysis of the samples in this study revealed that the majority of patients were between 60 – 69 years (30 %). In a study conducted by Zorana et al. in a neurological centre in Serbia, infections were more common in the elderly.[10] This could be due to the abnormal elastic recoil, poor ciliary motility and mucociliary clearance in the elderly, leading to decreased coughing and clearing of the upper airways. 76 % of the study population were males and 24 % were females. Male patients accounted for 58 % cases in a study conducted in NSICU in New Delhi by Mehndiratta et al.[11] and could be due to males being commonly involved in outdoor activities. Most common sample received was tracheal aspirate (80 %), followed by sputum (14 %). Mehndiratta et al. reported that bacterial isolation was more from respiratory secretions than from blood and therefore blood culture is less sensitive and also the ease of collecting respiratory specimens.[11]

Infection rate was high among patients hospitalized for 11 - 20 days (60 %). Brittney et al. reported that patients with longer hospital stay had more adverse out comes than those admitted for a short duration.[10] This could be due to the poor health status, mechanical ventilation, cross infections, lack of hand hygiene during patient care and the use of contaminated respiratory equipment. In this study, infection rate was high in patients with traumatic brain injury (82 %). Berrouane and colleagues found higher incidence rates of pneumonia in patients with neurotrauma than without neurotrauma.[7] Trauma disrupts the integrity of skin and tissues and compromises the host's natural protective barriers leading to immunosuppression. Infection rate was found to be high in patients with tracheostomy (65 %). The presence of an endotracheal device disrupts the normal ciliary clearance of bronchial secretions and impairs patient's capacity to cough. Secretions pool around the endotracheal cuff and serve as the primary route of bacterial entry into the lower respiratory tract. Impaired glottis closure due to tracheostomy or nasogastric tubes, permits aspiration of the commensal oropharyngeal flora and alimentary tract contents. Biofilm formed inside and outside the endotracheal tube serves as a bacterial reservoir.

In the present study, 186 (98 %) patients had received empiric therapy with antibiotics and only 4 patients did not receive any treatment. In spite of empiric treatment, the majority of patients developed infection (Fig. 6, 7). Hirsh et al. explains that trauma patients usually tend to be under dosed since antibiotics are lost through haemorrhage and fluid shifts from volume resuscitation.[12] Inappropriate initial antibiotic therapy is a modifiable risk factor that has been associated with increased mortality in patients with serious infections.

In the present study, bacterial isolates were obtained from 140 (74 %) samples. 21 (11 %) showed normal upper respiratory tract flora and 29 (15 %) showed no growth. The specimens remained sterile on culture probably due to previous antibiotic therapy or atypical bacterial infection. In a study conducted by Bajpai et al. in the neuro ICU of a tertiary care centre in central India, bacterial isolates were obtained from 86.08 % lower respiratory tract specimens and 13.91 % specimens were sterile.[1] The present study's findings also correlates with studies conducted by Veenakumari et al. in an ICU of a neuro centre in South India, where 74 % lower respiratory tract specimens were culture positive, 10.5 % showed normal upper respiratory tract flora and 15.4 % showed no growth.[13] Out of the total culture positive (140) cases, 115 (82 %) were monomicrobial and 25 (18 %) were polymicrobial. *P. aeruginosa* and *K. pneumoniae* were most commonly isolated from mixed infections. These results were comparable to a study conducted by de Roux et al. where a mixed aetiology was found in 13 % of hospitalised patients with pneumonia.[14] AO. Okesola and O.M. Ige, reported that the most prevalent bacterial combination were Klebsiella and Pseudomonas species.[15] Mixed infections are associated with a more severe and longer hospital stay and an increased rate of antibiotic treatment failures.

Majority of the bacterial isolates in the present study were gram negative bacilli (94 %) followed by gram positive cocci (6 %). The most common gram negative isolate was *K. pneumoniae* (36 %) (Fig. 4). Gonlugur et al. conducted a study in Turkish university hospital and reported that the most common organisms were Klebsiella spp. and *A. baumannii* (27 %).[16] The most common isolates reported in a study conducted by G.B Orsi et al. in NSICU of a clinic in Rome were *P. aeruginosa* and *S. aureus*.[4] In a study conducted by Reethadevi et al. in Medical College Hospital, Calicut, Acinetobacter spp. was predominantly isolated from patients with neurosurgical interventions.[17] According to the NNIS system report by CDC, MRSA accounts for 52.3 % of *S. aureus* nosocomial infections and is one of the leading causes of nosocomial pneumonia.[18] Hence in USA as per CDC commonest etiological organism is *S. aureus* followed

by GNB while in Asian and European studies it is GNB which are commoner than *S. aureus*.[19] *K. pneumoniae* causes a classic form of primary pneumonia. It tends to be destructive, with extensive necrosis and haemorrhage, resulting in the production of thick, mucoid and brick red or thin and "currant-jelly like" sputum. There is an evolving antibiotic resistance against this pathogen.

Out of the 94 % GNB isolates in our study, 66 (61 %) were multi drug resistant and 42 (39 %) were non multidrug resistant isolates (Fig.6). According to Rosenthal et al. MDR organisms are far higher in ICUs in Latin America, Asia, Africa, and Europe than in U.S.[20] In a study conducted by Vishwanath et al. 37 % gram negative organisms were found to be multidrug resistant. *K. pneumoniae* 85 (48.6 %) and Acinetobacter spp. 59 (33.7 %) were the predominant MDR gram-negative bacilli isolated.[21]

A. baumannii has emerged as a lower respiratory tract pathogen, especially in critically ill patients. Multi drug resistance is the hallmark of *A. baumannii* infections (Fig.7). It is capable of incorporating genes coding for resistance against multiple classes of antibiotics. The hardiness of the organism and resistance to commonly used antiseptics and disinfectants have promoted its survival in the hospital environment.

In this study, a high rate of resistance to Cephalosporins and lower resistance towards Carbapenems were noticed among the various gram negative isolates. The resistance of some GNB to Aminoglycosides especially Gentamicin was more than Amikacin. Colistin was highly sensitive against Acinetobacter spp. while Piperacillin-Tazobactam, Cefoperazone-Sulbactam and Imipenem had good activity against Pseudomonas spp. The high rate of resistance to Cephalosporins could be due to the selective influence of extensive usage of third generation Cephalosporins. Lower resistance rate was observed towards Carbapenems.

In a study conducted by Goel et al. *K. pneumoniae* showed high rate of resistance to Ciprofloxacin, Amikacin, and Cotrimoxazole. The resistance rate towards Amikacin, implies emerging resistance towards the drug.[22] Mehndiratta et al. reported 100 % sensitivity of *K. pneumoniae* to Imipenem and Gentamicin resistance was more compared to Amikacin resistance.[11] In our study, 100 % Colistin sensitivity was observed for the meropenem resistant *A. baumannii* isolates (Fig7). Among *A. baumannii*, Datta et al. observed very high resistance to third generation Cephalosporins, beta lactam and beta lactamase inhibitor (Piperacillin + Tazobactam) combination and Carbapenems (Imipenem).[23] Goel et al. concluded that meropenem was the most effective in vitro drug (77 %) against *A. baumannii*.[22]

Antimicrobial susceptibility testing of *P. aeruginosa* showed that resistance was low against Amikacin (26 %), Cefepime (21 %) and Imipenem (16 %). In his study, Gonlugur et al. observed lower resistance rates were reported for Imipenem (21.6 %) and Amikacin (25.4 %).[16]A higher prevalence of Carbapenem resistance (42.8 %) was reported by Gladstone et al.[24]

All MRSA isolates were sensitive to Vancomycin. In a study conducted by Harikrishna et al. 72.1 % MRSA isolates were found to be multi drug resistant.[25] Therefore, MRSA surveillance and strict drug policy are of utmost importance.

In our study, 17 (26 %) isolates were ESBL producers. A prospective survey of occurrence of ESBLE was conducted by Arpin et al. in a neurosurgical intensive care unit in France. They reported 27 % ESBL producing *K. pneumoniae* exhibiting a similar antibiotype and producing an SHV - 4 type beta lactamase.[26] ESBLs have been reported from all parts of the world. The true incidence is not estimated owing to the difficulty in testing and inconsistencies in reporting. The risk of acquiring ESBLE increased post operatively and with the length of ICU stay.

Though most of the gram negative organisms show susceptibility to Carbapenem, the resistance to Imipenem is on a rise, all over the world. Colistin, Polymyxin, and Aminoglycosides may be considered as potentially beneficial drugs in patients with infections due to multi drug resistant gram-negative bacilli.

In our study, most of the isolates were resistant to Cefoperazone-sulbactam, used empirically in our centre. Antimicrobial resistance monitoring therefore helps in optimization of antimicrobial therapy. It is important in ICU's, since infection and antimicrobial consumptions are significantly higher in this area

Studies have identified antimicrobial exposure as a risk factor for these infections. The inadvertent use of broad-spectrum antibiotics should be discouraged.

Nursing procedures like hand washing, single use equipment, isolation of infected or colonized patients, should be emphasized. Aetiological agents in respiratory infections and their antibiotic susceptibility pattern varies from country to country and even between different ICUs of the same hospital. It also differs according to the population of the patients in the intensive care unit, duration of hospital-stay and prior antimicrobial therapy.

CONCLUSIONS

Preventive strategies for hospital acquired pneumonia should be directed at reducing the bacterial burden colonizing the aerodigestive tract and measures to decrease the risk of aspiration. Isolation policies should be adopted while handling colonized or infected patients with drug resistant organisms. Patients transferred from local nursing homes and community hospitals should be screened as a source of resistant bacilli and appropriate measures should be taken while attending these patients. Molecular diagnosis can help in rapid and improved management of severe infections with resistant organisms. Infection is a major contributor to adverse patient outcome. Antibiotic stewardship programmes should be implemented to limit emergence and spread of resistant organisms. Regular surveillance that directs appropriate empirical therapy, good microbiological workup and strict infection control practices help to reduce the morbidity and mortality associated with infections in critically ill patients in the ICU.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.

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