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ANTIBIOTIC SENSITIVITY OF ENTEROCOCCUS FAECIUM, STAPHYLOCOCCUS AUREUS, KLEBSIELLA PNEUMONIA, ACINETOBACTER, PSEUDOMONAS AERUGINOSA AND ENTEROBACTER (ESKAPE) ORGANISMS ISOLATED FROM THE ENDOTRACHEAL TUBE ISOLATES FROM A PEDIATRIC ICU OF A TERTIARY CARE HOSPITAL

RESEARCH ARTICLE

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ABSTRACT

Background: *In the recent past, antibiotic resistance observed from the isolates of the intensive care units is one the biggest problems faced by the clinicians. E.coli, Staph.aureus, Klebsiella, Acinetobacter, Pseudomonas and Enterococci (ESKAPE organisms) are the most commonly implicated organisms when multi drug resistant pathogens are discussed. This is an effort to estimate of the problem in our hospital pediatric ICU.*

Methods*: Data was collected from the Microbiology department, J.J.M. Medical College, Davangere, where the culture and sensitivity was done for all the Endotracheal tube tip/aspiration samples received from pediatric ICU. Prevalence of ESKAPE organisms in our hospital and percentage of these isolates that are sensitive to the commonly used antibiotics was analyzed.*

Results: *We found 63 culture and sensitivity reports of endotracheal samples done during the study period that were positive for growth of organisms from the Pediatric Intensive Care Unit (PICU). 58 of them were ESKAPE organisms. 31 samples had Klebsiella isolates (49.20%), 18 samples were positive for Acinetobacter (28.57%), Psuedomonas in 7 (11.11%), Escherichia coli in 3 (4.7%), Staphalococcusaureus was isolated in 2 samples (3.1%) and Citrobacter in 2 (3.1%). After studying the sensitivity pattern, we found that imepenem was the most effective antibiotic against 63.5% of the isolates. Amikacin with 41.26%, ciprofloxacin with 31.74% and tetracycline with 30.15% and gentamicin with 26.98% were the antibiotics that showed activity against the isolates.*

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Conclusion: *Resistance of the ESKAPE organisms is widespread and none of the commonly prescribed antibiotics is ideal for a patient intubated in these ICUs. Imipenem is the only antibiotic that seems ideal which can be administered until the cultures are reported.*

Key words: *ESKAPE, ET tube isolates, pediatric ICU, antibiotic sensitivity.*

Short title: *ESKAPE organisms from ET tube isolates in PICU.*

INTRODUCTION

In 1972, Johanson *et al.* (1) were the first to note an increase in oropharyngeal colonization by microorganisms in patients with increasing severity of illness, and to document thereafter that there was an increased risk of the development of nosocomial pneumonia in patients who had Gram-negative oro-pharyngeal colonization. Subsequent to the findings by these investigators and many others, it has long been recognized that there is a direct relationship between oro-pharyngeal colonization and nosocomial pneumonia. WHO defines a nosocomial infection as "An infection acquired in hospital by a patient who was admitted for a reason other than that infection. An infection occurring in a patient in a hospital or other health care facility in whom the infection was not present or incubating at the time of admission. This includes infections acquired in the hospital but appearing after discharge, and also occupational infections among staff of the facility." Urinary tract infection is the most common nosocomial infection seen followed by pneumonia. Pneumonias are seen in approximately in 3% of the patients in a day who are put on a ventilator. There is a high case-fatality rate associated with ventilator-associated pneumonia, although the attributable risk is difficult to determine because patient comorbidity is so high (2). It has been noted that endotracheal tube colonization and biofilm formation occurs in many patients undergoing mechanical ventilation, from a very early stage. Biofilm formation may in many cases precede the development of nosocomial pneumonia, and perhaps more importantly, represent a persistent source of organisms causing recurrent infections (3, 4). The mortality associated with ventilation associated pneumonia is high occurring in every two of the three patients ventilated (5, 6, 7). Recently, Enterococcus faecium, Staphylococcus aureus, Klebsiella species, Acinetobacter, Pseudomonas aeruginosa, and Enterobacter species (ESKAPE) pathogens have been reported as the top six "bugs" for their wide distribution and ability to escape the effects of antibacterial drugs(8). To treat these multi drug resistant infections, the physicians are forced to use older and more toxic drugs like colistinsulphate whose safety is always questionable(9). This is an effort to observe the common organisms from the ET tube isolates, the prevalence of ESKAPE organisms and their sensitivity pattern to common organisms in the ICU of a tertiary care hospital and help devise a rational antibiotic regimen.

OBJECTIVE OF STUDY

To study the sensitivity pattern of the commonly isolated organisms from the Endotracheal tube samples in from the ICU of a tertiary care hospital.

METHODOLOGY

Source of data: Secondary data will be obtained from the Microbiology department, with due acknowledgement, which routinely does the culture and sensitivity pattern of the required samples. All the samples received by the Microbiology department in the past six months will be studied.

Study Design: Retrospective observational study.

Duration of study: 3 months.

RESULTS

We found 63 culture and sensitivity reports of endotracheal samples done during the study period that were positive for growth of organisms and all the cases were from both the Neonatal Intensive Care Unit (NICU).

In the culture of 63 samples from the pediatric ICU, 31 samples had Klebsiella isolates (49.20%), 18 samples were positive for Acinetobacter (28.57%), Psuedomonas in 7 (11.11%), Escherichia coli in 3 (4.7%), Staphalococcusaureus was isolated in 2 samples (3.1%) and Citrobacter in 2 (3.1%).

Of thesamples cultured, ESKAPE organisms constituted 92.06% of the organisms isolated. Enterococcus and the coliform bacterium, Enterobacter, was not isolated. The other coliform bacterium, Escherichia coli, was isolated in 3 samples (4.7%).2 samples (3.1%) were also positive for another coliform bacterium, citrobacter.

The isolates had been tested for all the commonly prescribed antibiotics. The drugs against which the organism's sensitivity was tested were ampicillin (amp), cotrimoxazole (cot), gentamicin (gen), ciprofloxacin (cip), tetracycline(te), cephalexin (cp), cefazolin (cz), cefuroxime (cu),amikacin (ak), doxycycline (do), ceftriaxone (ci), ceftazidime (ca), cefoperazone (cs), cefotaxime (ce), imepenem (ipm), cefpodoxime (cep), netilmicin (net), cefepime (cpm), cefoperazone + salbactam (cfs), ceftazidime + clavulanic acid (cac), amoxicillin + clavulanic acid (ac), piperacillin + tazobactam (pc), ofloxacin (of), sparfloxacin (spx) and prulifloxacin (pf).

The sensitivity pattern of individual organisms isolated from NICU is given in the **Table 1**.

Table-1: Number of sensitive samples for antibiotics

Drug	Organism (No. of samples)							
	Enterococci (0)	Staph. aureus (2)	Klebsiella (31)	Acinetobacter (18)	Pseudomonas (7)	Enterobacter (0)	E. coli (3)	Citrobacter (2)
Amp		1	0	0	0		0	0
Cot		0	10	3	0		2	0
Gen		1	09	1	5		1	0
Cip		1	14	1	4		0	0
Te		1	11	6	1		0	0
Cp		1	0	0	4		0	0
Cz		0	0	0	0		0	0
Cu		0	0	0	0		0	0
Ak		1	15	3	4		3	0
Do		0	3	0	1		0	0
Ci		0	1	0	0		0	0
Ca		0	2	1	0		0	0
Cs		0	0	0	0		0	0
Ce		1	1	1	5		0	0
Ipm		1	14	14	7		3	1
Cep		0	1	0	0		0	0
Net		0	2	1	3		1	2
Cpm		0	1	0	0		0	0
Cfs		0	1	0	0		0	1
Cac		1	1	1	1		0	0
Ac		1	0	0	0		0	0
Pc		1	10	0	4		0	0
Of		0	2	0	3		0	0
Spx		0	1	0	0		0	0
Pf		0	6	2	1		0	0

In the samples with Staphylococcus aureus, sensitivity was seen for ampicillin, gentamicin, ciprofloxacin, tetracycline, cephalexin, amikacin, cefotaxime, imepenem, ceftazidime in combination with clavulanic acid, amoxyclav, piperacillin in combination with tazobactum showed sensitivity in atleast one sample of the two samples isolated. The resistance of Staphylococcus aureus to other antibiotics was high.

In the samples with Klebsiella, amikacin with sensitivity in 15 samples showed the highest activity. Imepenem, ciprofloxacin were effective in 14 isolates followed by cotrimoxazole in 10 and gentamicin in 9 isolates. Most of the other antibiotics were ineffective.

Acinetobacter, could be maximally inhibited by imepenem, as evidenced in 14 isolates. Tetracycline could inhibit 6 isolates. Most of the other antibiotics were not that effective.

All the pseudomonal isolates were sensitive to imepenem. Cephalexin and gentamicin were effective in 5 isolates each. The resistance of the pseudomonal isolates to the rest of the antibiotics was high.

The isolates of E. coli were all sensitive to amikacin and imepenem. 2 of the 3 isolated organisms were sensitive to cotrimoxazole also. The other coliform, citrobacter was isolated in two samples and both were sensitive to netilmicin.

Figure-1: Antibiotic sensitivity of the ET tube isolates

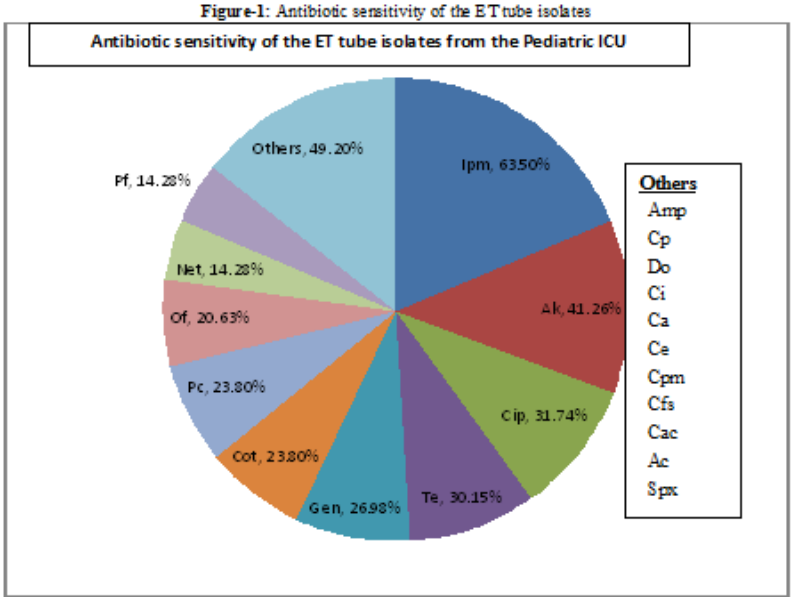

Figure-1: After studying the sensitivity pattern, we found that imepenem was the most effective antibiotic against 63.50% of the isolates. Amikacin with 41.26%, ciprofloxacin with 31.74% and tetracycline with 30.15% and gentamicin with 26.98% were the antibiotics that showed activity against the isolates.

DISCUSSION

The results show that there is a very high prevalence of infections by the ESKAPE organisms in the endotracheal tube isolates of pediatric ICU in the hospital attached to JJM Medical College, Davangere. Of the 63 samples records collected during the study period, 58 were positive for ESKAPE organisms (92.06%). Out of these the highest prevalence was seen with Klebsiella (49.20%) followed by Acinetobacter (28.57%), Pseudomonas (11.11%) and Staphylococcus aureus (3.1%).

A similar study was done in another state of South India by Banda Venkataramana *et al* (10), where the endotracheal tube tips were cultured. The authors found that 35% of the isolated organisms were Pseudomonas aeruginosa, Klebsiella pneumonia was 18%, E. coli was 15%, other enterobacteriacae was 19%, non-fermenting gram negative bacilli was 13% and MRSA was 40%.

Sandiumenge *et al* (11), in their study observed that in a total of 157 microorganisms were isolated in ventilator associated pneumonias (VAP). Gram negative orgainsms were seen in 61.1% (n=96) of the isolates and gram positive rods were seen in 38.8% (n=61) of the isolates. No yeasts were seen in the cultures. Of these isolates, ESKAPE organisms represented 65.6% of isolates (n=103) from patients diagnosed to have VAP and 19.4% of them (n=28) were resistant strains. E.faecium was not isolated in any of the samples from VAP episodes throughout their study period. Staphylococcus aureus was the most commonly isolated organism. They also published in their results an increase in the prevalence of the Acinetobacterbaumanii VAP. They studied the mortality in patients with VAP due to ESKAPE and noted that the mortality in those patients was higher than people with VAP due to non-ESKAPE infections. In patients with VAP due to resistant ESKAPE organisms, the mortality doubled.

In the samples isolated in our study, the prevalence of ESKAPE was high but the diagnosis of VAP was not available in the records. The prevalence doesn't mean an infection. An infection means that germs are in or on the body and make you sick, which results in signs and symptoms such as fever, pus from a wound, a high white blood cell count, or pneumonia. Germs can also be in or on the body, but not make you sick. This is called colonization. People who are colonized will have no signs or symptoms. The organisms that are isolated in the samples in our study may be colonization or an infection.

C. Feldman *et al* (3), in their study have noted that the interior of the E.T tube after intubation was rapidly colonized with gram negative organisms. They observed that colonization started as early as 12 hours and was abundant by 96 hours after intubation and the colonization persisted even after successful treatment of the underlying pneumonia. The same organism in the interior of the E.T. tube was cultured from the secretion of the lower respiratory tract as early as 36 hours of intubation and was prominent by 60-64 hours. They concluded that E.T tube colonization and also production of biofilm production is common in patients with mechanical ventilation from a very early stage. The biofilm production preceeded nosocomial pneumonia in many cases and also prevented the complete eradication of the organism and hence resulted in the recurrence of the infection.

Waldemar G *et al* (1) in 1972, in their prospective study of 213 patients admitted to a medical intensive care unit, observed the frequency of colonization of the respiratory tract with Gram negative bacilli and its relation to the nosocomial infection. 95 patients had colonization (45%) and about half of them had colonization on the first day (22%). 23% of these patients had nosocomial pneumonia and the incidence of pneumonia was only 3.3% in patients who had no colonization. So they suggested that interrupting the colonization was an effective method of preventing nosocomial pneumonia. Christophe Delclaux *et al* also emphasized the same in 1997 in their study on patients admitted to the ICU with ARDS (12).

Celis R *et al* (5), have given an opinion that the mortality associated with ventilation associated pneumonia is high occurring in every two of the three patients ventilated. By a logistic regression model, concluded that intubation, depressed level of consciousness, chronic lung disease, thoracic and abdominal surgery, a previous episode of aspiration and age more than 70 years were all independent risk factors for the development of pneumonia. So, we can say that, intubation and hence followed by colonization are risk factors of development of pneumonias.

Langer ML *et al* (6), studied the incidence of pneumonia with respect to the duration of ventilator support. They noted an increase of pneumonia from 5% in individuals receiving ventilator support for one day to 68.8% in individuals receiving support for 30 days. By following a different approach focusing on the onset of infection and not the incidence, the authors have also concluded that highest risk of infection was seen in the first 8 to 10 days of ventilation and later on the acquisition of infection was rare and the risk of VAP was low after 10 days.

With all these studies we can conclude that, the incidence of the VAP was high and increasingly due to the ESKAPE organisms. Intubation, duration of intubation followed by colonization was a risk factor and the treating physicians have to be very careful during the first ten days to prevent the infection.

Klebsiella was the organism that was most commonly isolated (49.20%) from the ET tube samples from the pediatric ICU in our study. The antibiogram shows that the Klebsiella spp. isolated in our study is sensitive to amikacin (48.38% of the isolates) followed by imepenem and ciprofloxacin (45.16%) and 32.25% of the samples to cotrimoxazole. This shows that nearly 50% of samples were resistant to all the antibiotics tested for. The antibiogram of Acinetobacter isolates showed that they were sensitive to imepenem in 77.77% and the other antibiotic that was most effective was tetracycline (33.33%). Acinetobacter also showed a very extensive resistance against many commonly tested antibiotics. Pseudomonas was the next common organism isolated (22.5%) and imepenem was the most effective antibiotic. The other organisms, Staphylococcus aureus, E.coli and citrobacter spp., were isolated in very few samples and so the sensitivity and resistance pattern couldn't be commented upon.

The resistance of the organisms is highly prevalent and alarming. Banda Venkataramana *et al* (10) in their study noted in their study that pseudomonas was the most common organism isolated and maximum resistance was to ceftazidime. Though pseudomonas was isolated in our study, it wasn't the most common organism but the organism isolated was highly resistant to ceftazidime in concordance with their findings. Shashikala R Kanungo, S Sreenivasan and Sheela Devi (13), in their research letter say that the antibiotic resistance is increasing at an alarming rate leading to increasing mortality, morbidity and treatment costs and the key factor in development of drug resistant organisms is inappropriate use of antibiotics.

There are many reasons postulated for the nosocomial respiratory infections. A person's exposure to many microbes during his hospital stay, coupled with patient's susceptibility, diagnostic and therapeutic interventions have increased the chances of a patient acquiring nosocomial infection. By exchange of genetic resistance elements the infecting organisms develop resistance and when antibiotics are used extensively, the susceptible organisms are eradicated and only the resistant strains persist[who]. Kimberly K Jefferson, in her mini review, gave an opinion that biofilm formation is a method of adaptation by the bacteria to survive as a community. This biofilm formed is very resistant to anti-microbial agents tolerating upto 10-100 times the therapeutic doses and such organisms are responsible for many device related infections (4).

Shaaban *et al* (14) observed that of all available antimicrobial agents, carbapenems are the most active and reliable treatment options for infections caused by ESBL isolates. However, overuse of carbapenems may lead to resistance of other Gram-negative organisms. The same has been substantiated in our study as evidenced in the results, carbapenems (imepenem), was probably the most effective antibiotic that could be prescribed until the culture and sensitivity reports of the E.T tube samples were available.

Nosocomial respiratory infections can be prevented by proper disinfection and care of the tubings, respirators and humidifiers, sterile tracheal suctioning, nursing in head-up position, limiting sedation, avoiding oral feeding in comatose patients, pre-operative physiotherapy in patients with chronic respiratory disease. To prevent treatment emergent resistance appropriate antibiotic policies must be framed and followed in the ICUs.

If proper preventive measures are not taken then the incidence of "Super Bugs" like the carbapenemase producing Klebsiella pneumonia, New Delhi Metallo-beta-lactamase-1 (NDM-1), will increase and with it the mortality and morbidity will also increase.

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