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Micro-Organism Profile and Antibiotic Susceptibility Patterns in General ICU of Tertiary Care Hospital Situated in Hills

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Abstract

Introduction: This study was undertaken in Indira Gandhi Medical College, Shimla to evaluate antibiotic sensitivity patterns of various microbes isolated from patients in general Intensive Care Unit. Thus it would serve as a guide to institute empirical antibiotic therapy.

Materials and methods: All patients admitted to general ICU with Endotracheal tube (ETT) *in situ* were included in this observational study. Those with ETT in place for more than 24 h were excluded from the study. ETT culture samples were collected at 36-48 h and on seventh day of intubation. Culture report and antibiotic susceptibility profile were observed and data hence collected were evaluated.

Results: Out of the total 946 ET culture samples studied 533 (56.3%) showed growth of microorganisms. The number of ET culture isolates increased as the days of intubation increased, i.e., from 45.33% on second day to 70.07% on seventh day. NFG, *Klebsiella* spp. and *Pseudomonas* spp. contributed to more than 70% of the ET culture isolates. The ET culture isolates demonstrated high degree of resistance to most of the antibiotics tested.

Keywords: Microbiology; Culture; Antibiotics; Resistance

Introduction

The development of 'intensive care' as a medical discipline dates back to the mid of the 20th century. What was started as a supportive therapy in the form of artificial respirators for hundreds of victims of Copenhagen polio epidemic in the 1950s has now become a highly specialized medical discipline in itself [1]. Sepsis remains the most important confounding factor in the morbidity and mortality of ICU patients. For combating sepsis appropriate antibiotic therapy can be initiated either in culture guided way or empirically. To protect from flaring up of inherent or nosocomial infection, cultures are sent and empirical therapy based on environmental and hospital factors is undertaken.

Presently, at our institute empirical antibiotic therapy is either based on the studies conducted in the western countries or is according to the treating physician's clinical experience which might not adequately reflect the resistance patterns prevalent in our institute. Therefore, the present study was undertaken to observe the antibiotic sensitivity patterns of various microbes isolated from patients in the General Intensive Care Unit (GICU).

Objectives

1. To study the microorganism(s) profile in the GICU during the study period, in endotracheal tube (ETT) cultures.

2. To study the antibiotics to which these microorganism(s) are susceptible.

Materials and Methods

The study was conducted in the General Intensive Care Unit (GICU) of the Indira Gandhi Medical College and Hospital (IGMC), Shimla and Himachal Pradesh (H.P.) as a cross-sectional study based on data collection in the form of empirical antibiotics, microorganism(s) profiles and their antibiotic sensitivity pattern without intervention of existing GICU protocols. Data collected from the patients admitted in the GICU during July 2014 to June 2017 was included in the present study.

Inclusion criteria

All patients admitted to the GICU with endotracheal tube (ETT) in situ for duration of less than 24 h at the time of admission to the GICU.

Sample collection

As per the protocol at our GICU, endotracheal tube (ETT) culture samples were collected at:

(a) 36 to 48 h of intubation, i.e., second day of intubation; and

(b) On seventh day of intubation.

Observation of reports

The culture reports were collected and following observations were made:

(a) The microorganism(s) profile present in the endotracheal tube (ETT) cultures; and

(b) The antibiotic susceptibility profile of the microorganism(s) isolated.

Statistical analysis

The data collected was evaluated using Microsoft office excel software for calculation of percentages and proportions.

Ethical clearance

Ethical clearance for the study was taken from institutional ethics committee.

Results

A total of 946 Endotracheal (ET) culture samples were collected from 525 patients admitted in the GICU over a period of three years. Total number of patients in our study on second day was 525 which decreased to 421 by seventh day as 55 patients were intubated and 49 patients collapsed before seventh day. So, samples from these 104 patients couldn't be taken on seventh day.

Demographic characteristics

In our study, 45.33% of patients were females while remaining 54.67% patients were males belonging to different age groups. Majority of the patients (41.33%) belonged to 31-50 year age group **(Table 1)**.

Table 1 Age and sex distribution of patients in our study.

Age Group	Number of Female Patients	Number of Male Patients
15-30 years	80	59
31-50 years	83	134
>50 years	75	94
Total	238	287

Microorganism Profile

Of the total 946 ET culture samples 533 were positive. The ET culture samples found positive on second day were 45.33% (238/525), while the ET culture samples found positive on seventh day were 70.07% (295/421). A total of 551 microorganisms were isolated from the 533 positive cultures (240 microorganisms on second day and 311 microorganisms on seventh day). As far as the bacteriological profile of ET culture isolates was concerned, Gram negative bacilli (GNB) accounted for 95.28% of ET culture isolates while only gram positive microorganism isolated was *Staphylococcus* spp. accounting for the remaining 4.72% ET culture isolates.

Most common microorganisms isolated from ET culture in our study were Non Fermenter Group of microorganisms (39.74%) followed by Klebsiella (21.23%) and Pseudomonas (11.61%).

Non fermenters (excluding Pseudomonas and Acinetobacter) contributed to 38.75% isolates on second day and 40.51% isolates on seventh day, averaging to a total of 39.74% isolates. Pseudomonas and Acinetobacter were excluded from the NFG (Non Fermenter Group of microorganisms) group, while compiling data in our study, due to their higher incidence, while tests for the isolation of remaining members of the NFG (Bordetella, Legionella, Moraxella, Stenotrophomonas, etc.) were not performed. So, results of *Pseudomonas* spp. and *Acinetobacter* spp. were compiled separately. The combined (second day and seventh day) sensitivity pattern of NFG in decreasing order was: ampicillin-sulbactam (41.97%), doxycycline (46.25%), gentamicin (36.52%) and meropenem (24.86%). They demonstrated high degree of resistance to cephalosporins [ceftazidime (96.25%), ceftriaxone (97.71%) and cefepime (100%)] and 98.66% resistance to ciprofloxacin **(Table 2)**.

Table 2 Antibiotic sensitivity of NFG.

Antibiotic	Day 2 sensitivity	Day 7 sensitivity
Gentamicin	56.98%	21.42%
Ceftriaxone	3.40%	1.14%
Meropenem	39.78%	16.67%
Pip-Taz	20.22%	9.09%
Doxycycline	51.11%	42.14%
Amp-Sulb	57.64%	30.83%

Klebsiella accounted for 30.83% and 13.82% of ET culture isolates on second day and seventh day, respectively. The sensitivity of Klebsiella to most of the antibiotics tested was more on second day as compared to seventh day **(Table 3)**.

Table 3 Antibiotic sensitivity of Klebsiella.

Antibiotic	Day 2 Sensitivity	Day 7 Sensitivity
Gentamicin	51.80%	44.06%
Ciprofloxacin	30%	28.81%
Ceftazidime	37.50%	32.20%
Tigecycline	60.62%	49.15%
Imipenem	47.50%	35.89%
Meropenem	50%	42.30%

Only 11.61% isolates were from *Pseudomonas* spp. (11.25% on second day and 11.89% on seventh day). Pseudomonas demonstrated 100% sensitivity to colistin and polymyxin B, the last resort antibiotics **(Table 4)**.

Table 4 Antibiotic sensitivity of Pseudomonas.

Antibiotic	KLB	Entbac	Pseudo	*Escherichia coli*	Citro	Acin	NFG
Amclav	0%	0%	Nt	0%	0%	0%	Nt
Ceftaz	35.45%	15.70%	11.11%	0%	0%	0%	3.75%
Cipro	29.09%	0%	11.11%	0%	0%	Nt	1.34%
Genta	48.60%	0%	25%	25%	33.33%	Nt	36.52%
Tige	55.45%	Nt	Nt	Nt	Nt	0%	16.67%
Imi	42.72%	Nt	32.80%	100%	100%	28.35%	27.17%
Mero	38.18%	18.42%	26.67%	Nt	Nt	25.14%	24.86%
Amika	33.33%	21.05%	12.50%	0%	Nt	Nt	16.67%
Pip-Taz	28.50%	21.05%	42.80%	0%	Nt	20.18%	20.22%
Netil	84.60%	26.32%	Nt	100%	0%	53.33%	10.50%
Aztreo	Nt	Nt	30.64%	Nt	Nt	28.57%	Nt
Pol.B	Nt	Nt	100%	Nt	Nt	Nt	Nt
Colistin	Nt	Nt	100%	Nt	Nt	Nt	Nt
Doxy	Nt	0%	Nt	33.33%	100%	16.67%	45.97%
Levo	Nt	Nt	Nt	Nt	50%	66.67%	27.27%
Amp-Sulb	Nt	Nt	Nt	Nt	Nt	Nt	41.95%

Table 5 Antibiotic sensitivity of endotracheal culture isolates [Amclav: Amoxycillin-Clavulanic Acid, Ceftaz: Ceftazidime, Cipro: Ciprofloxacin, Genta: Gentamicin, Tige: Tigecycline, Imi: Imipenem, Mero: Meropenem, Amika: Amikacin, Pip-Taz: Piperacillin-Tazobactam, Netil: Netilimicin, Aztreo: Aztreonam, Pol.B: Polymyxin B, Doxy: Doxycycline, Levo: Levofloxacin, Amp-Sulb: Ampicillin-Sulbactam, KLB: Klebsiella, Entbac: Enterobacter, Citro: Citrobacter, Acin: Acinetobacter, NFG: Non Fermenter Group of Microorganisms, Pseudo-Pseudomonas, Nt: Not Tested].

Antibiotic	KLB	Entbac	Pseudo	*Escherichia coli*	Citro	Acin	NFG
Amclav	0%	0%	Nt	0%	0%	0%	Nt
Ceftaz	35.45%	15.70%	11.11%	0%	0%	0%	3.75%
Cipro	29.09%	0%	11.11%	0%	0%	Nt	1.34%
Genta	48.60%	0%	25%	25%	33.33%	Nt	36.52%
Tige	55.45%	Nt	Nt	Nt	Nt	0%	16.67%
Imi	42.72%	Nt	32.80%	100%	100%	28.35%	27.17%
Mero	38.18%	18.42%	26.67%	Nt	Nt	25.14%	24.86%
Amika	33.33%	21.05%	12.50%	0%	Nt	Nt	16.67%
Pip-Taz	28.50%	21.05%	42.80%	0%	Nt	20.18%	20.22%
Netil	84.60%	26.32%	Nt	100%	0%	53.33%	10.50%
Aztreo	Nt	Nt	30.64%	Nt	Nt	28.57%	Nt
Pol.B	Nt	Nt	100%	Nt	Nt	Nt	Nt
Colistin	Nt	Nt	100%	Nt	Nt	Nt	Nt
Doxy	Nt	0%	Nt	33.33%	100%	16.67%	45.97%
Levo	Nt	Nt	Nt	Nt	50%	66.67%	27.27%
Amp-Sulb	Nt	Nt	Nt	Nt	Nt	Nt	41.95%

Acinetobacter (8.16%), Enterobacter (6.89%), Staphylococcus (4.72%) and *Escherichia coli* (4.17%) and Citrobacter (3.44%) accounted for less than thirty percent of the ET culture isolates in our study.

The *Acinetobacter* spp. (8.16%) in our study was 100% resistant to ceftazidime, cefopodoxime and ceftriaxone. The sensitivity patterns were as follows: tobramycin (100%), tetracycline (75.55%) and netilmicin (53.33%). **Table 5** shows combined antibiotic sensitivity patterns of endotracheal culture isolates.

Enterobacter spp. was isolated in seventh day ET samples but not found in second day samples. Their sensitivity pattern was as follows: ceftazidime (15.7%), meropenem (18.42%), amikacin (21.05%), netilimicin (26.32%), piperacillin-tazobactam (21.05%).

Among the Citrobacter isolates, which accounted for nearly 3.44% isolates, none was resistant to all the antibiotics tested. It demonstrated 100% resistant to amoxicillin-clavulanic acid, ceftazidime, and ciprofloxacin while 100% sensitivity to doxycycline on both second day and seventh day. The sensitivity to imipenem was 100% on seventh day while it was not tested on second day.

Escherichia coli contributed to nearly 4.17% ET culture isolates. None of them were resistant to all the antibiotics tested on second day while in 66.67% patients; they were resistant to all the antibiotics tested on seventh day.

The only gram positive isolate in our study was *Staphylococcus aureus* spp. (4.72%) which demonstrated 96.16% resistance to penicillin , 92.29% resistance to erythromycin and 25% resistance to levofloxacin while no resistance to linezolid **(Table 6)**.

Table 6 Antibiotic sensitivity (combined day 2 and day 7) of *Staphylococcus aureus* in endotracheal culture isolates.

Antibiotic	Percentage sensitivity
Clindamycin	50%
Erythromycin	7.71%
Levofloxacin	75%
Linezolid	100%
Penicillin	3.84%
Cotrimoxazole	0%
Meropenem	Not tested
Imipenem	Not tested
Ampicillin	Not tested

Discussion

Ventilator associated nosocomial infections in the critically ill patients continue to be a frequent complication often culminating fatally.

The risk of developing infection is directly related to the time spent on the ventilator increasing from 5% at 10 days to 28% at 30 days while the mortality rates associated with these infections range from 40 to 80 percent [2].

Among the ET culture isolates, 45.33% were positive on second day while 70.07% were positive on seventh day. Similarly, in a study conducted by Patil et al. [3] it was found that number of tracheal isolates increased from 47% on first day to 98.73% on seventh day. Niederman et al. [4] in their study also found an increasing trend in tracheal colonization with the increasing duration of mechanical ventilation, i.e., 22% of their tracheal cultures were positive at the start of mechanical ventilation compared to 78% by the end of first week.

The US National Nosocomial Infections Surveillance (NNIS) reported 60% of nosocomial pneumonias to be caused by aerobic Gram Negative Bacilli (GNB) [5] in coherence to this finding in our study also; we found gram negative bacteria as the most common isolate from ET culture samples, accounting for 95.28% isolates. Only 4.72% organisms isolated were gram positive. This difference in the percentage of gram negative isolates in our study, with respect to that reported by NNIS can be attributed to different epidemiology of microbes in western and Indian patient and hospital scenarios.

Most common microorganisms isolated from ET culture in our study were Non Fermenter Group of organisms (39.74%) followed by Klebsiella (21.23%) and Pseudomonas (11.61%). In a retrospective study conducted in a tertiary health care centre in Bangalore by Kumari et al. [6] on 370 patients being ventilated, 274 (74%) were found to be culture positive whereas in our study we found 56.3% (533/946) of ET culture isolates to be positive. The most common GNB isolates in order of decreasing frequency were NFG (31.9%), *Pseudomonas aeruginosa* (21.5%), *Klebsiella* spp. (19%) which closely matched with the results of our study, as in our study also NFG was the most common isolate.

The resistance patterns of NFG isolates from tracheal specimens to various antibiotics in our study were: amikacin (83.33%), ciprofloxacin (98.66%), gentamicin (63.48%), ceftazidime (96.25%) and netilmicin (89.5%) while in the study conducted by Kumari et al. [6] in Bangalore, resistance patterns were as follows: amikacin (71.4%), ciprofloxacin (73.6%), gentamicin (76.5%), ceftazidime (78.7%) and netilmicin (38.3%).

In another study conducted in Saudi Arabia by Memish et al. [7], resistant pattern among *Stenotrophomonas maltophilia* (a non-fermenter) isolated from various specimens (blood, urine, sputum, wound swabs, etc.) was as follows: amikacin (67.1%), gentamicin (73.8%), tetracycline (90.7%) and imipenem (82.7%). Hence, it can be concluded that antibiotic resistance among non-fermenters is on the rise and is not confined to a single geographical area.

Klebsiella demonstrated 87.5% sensitivity to netilimicin on second day and 80% on seventh day averaging to 84.6% sensitivity. Contrary to our study, Klebsiella demonstrated highest sensitivity to amikacin (49.3%) in the tracheal specimens while demonstrating 85% resistance to netilmicin in the study conducted by Kumari et al. [6]

What was more threatening was the finding that Klebsiella demonstrated 100% resistance to amoxicillin-clavulanic acid. In the study conducted in Bangalore [6] sensitivity for amoxicillin-clavulanic acid was not done, however, among the penicillin group ampicillin was found to have a sensitivity of 1.5% for Klebsiella which correlates with our study and greatly reflects the increasing resistance to penicillins among the GNB.

Klebsiella isolates in the study conducted by Tandia et al. [8] at Bhopal, showed 50% sensitivity to meropenem and 16.6% sensitivity to ceftriaxone whereas it was 38.18% to meropenem in our study while ceftriaxone testing was not done for Klebsiella.

The sensitivity pattern of Pseudomonas in descending order to other antibiotics was: imipenem (50%), piperacillin-tazobactam (42.8%), aztreonam (30.64%) and meropenem (26.67%). This was quite contrasting to the study conducted by Zhanel et al. [9] in Canadian ICUs where Pseudomonas from respiratory isolates demonstrated 92.7% sensitivity to piperacillin-tazobactam and 87.5% sensitivity to meropenem. Imipenem and aztreonam were not tested for in this study. Overzealous and irrational use of higher antibiotics such as piperacillin-tazobactam and even meropenem may be responsible for such higher degree of resistance among *Pseudomonas* spp.

Sheth et al. [10] in their study found Pseudomonas to be the second most common isolate showing 100% resistance to piperacillin-tazobactam and ceftazidime while 100% sensitivity to imipenem, meropenem and gentamicin which was quite contrasting to the results of our study which showed the following resistance patterns: piperacillin-tazobactam (57.2%), ceftazidime (88.89%), imipenem (50%) and gentamicin (75%).

In the retrospective study conducted in Mangalore by Peter and Sequiera [11], the sensitivity patterns of Acinetobacter were as follows: amikacin (44.66%), meropenem (25%) and imipenem (33.33%) while in our study the sensitivity profile of Acinetobacter to above antibiotics was: meropenem (25.14%) and imipenem (28.35%). Amikacin was not tested for *Acinetobacter* spp. in our study.

The only gram positive isolate in our study was *Staphylococcus aureus* spp. (4.72%) which demonstrated 96.16% resistance to penicillin, 92.29% resistance to erythromycin and 25% resistance to levofloxacin while no resistance to linezolid.

In the study conducted in Canadian ICUs by Zhanel et al. [9], resistance to levofloxacin was 6.9% while linezolid was not tested for in that study. The geographical variation might be responsible for these differences.

Pursuing with the probable differences in the microbiological spectrum present in intensive care units in different regions in the world, we find various studies demonstrating the same. In a Moroccon study it was again found that gram negative organisms were the most common isolates, Acinetobacter being the commonest. Also to be observed that antibiotic resistance was very high, being 100% of carbapenemase in *Acinetobacter baumanii* [12].

In a ten year long observational study by Kolpa and his associates in Poland it was observed that the most common isolated microorganism was *Acinetobacter baumannii* (25%) followed by coagulase-negative Staphylococci (15%), *Escherichia coli* (9%), *Pseudomonas aeroginosa* (8%), *Klebsiella pneumonia* (7%) and *Candida albicans* (6%). It was also noted that Acinetobacter was multi drug resistant in 87% of cases [13].

From the above studies, it is clear that antibiotic resistance is on the rise among the hospital acquired infections which not only add to the number of DALYs (Disability Adjusted Life Year) lost but also to the financial burden. It is estimated that in 1995, nosocomial infections cost $4.5 billion and accounted for nearly 88,000 deaths [14].

Considering the factors associated with high morbidity and mortality among ICU patients along with the financial burden they cause, a comprehensive approach is needed. And most important part of this approach is to determine the bacteriological profile among ICU as well as non-ICU patients, which invariably requires regular monitoring of the antibiotic sensitivity patterns of the isolates obtained from various patient samples. These culture reports need to be analysed with due care to formulate the guidelines for empirical therapy.

Summary

Out of the total 946 ET culture samples studied 533 (56.3%) showed growth of microorganisms. The number of ET culture isolates increased as the days of intubation increased, i.e., from 45.33% on second day to 70.07% on seventh day. NFG, *Klebsiella* spp. and *Pseudomonas* spp. contributed to more than 70% of the ET culture isolates.

The ET culture isolates demonstrated high degree of resistance to most of the antibiotics tested. None of the microbe tested was sensitive to amoxycillin-clavulanic acid, i.e., they were 100% resistant.

Conclusion

From the above points, it appears that: (a) Antibiotic resistance is on the rise in our GICU setup which is situated in hilly area. Also the micro-organism profile and resistance patterns are not very different from those found in plain areas; and (b) strict antibiotic prescription guidelines should be formulated.

It is further recommended that: (a) culture and antibiotic susceptibility studies should be performed in different departments at regular intervals; (b) cycling or rotation of a class of antibiotic (or a specific member of a class) with a different class (or a specific member of that class) that exhibits a comparable spectrum of activity should be done every four to six months; and (c) the empirical antibiotics should also be tested for the given microbe isolated.

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