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BACTERIOLOGICAL PROFILE OF HOSPITAL ACQUIRED PNEUMONIA IN A TERTIARY CARE TEACHING HOSPITAL, SOUTH INDIA

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Abstract— **Background: Hospital acquired infections continue to be an important cause of morbidity and mortality among hospitalized patients. Though Hospital Acquired Pneumonia (HAP) is widely analyzed by many researchers, not much is known about the incidence and bacteriological profile i.e., only few studies are being published by them. This study is conducted to evaluate bacteriological profile of HAP in Intensive Medical Care Unit (IMCU) patients. It may increase the awareness of clinicians about the need to reduce the morbidity and mortality by coming to know about the various pathogens causing HAP and its sensitivity and/or resistance to various antibiotics. The aim of this study was to analyze the incidence, epidemiology and antimicrobial susceptibility pattern of isolates from HAP patients in IMCU. Materials and Methods: This prospective study was conducted over a period of one year among 2454 patients admitted in IMCU of Coimbatore Medical College & Hospital, Tamil Nadu. The Specimens Sputum, Bronchoscopic Alveolar Lavage (BAL), Endotracheal aspirate (ETA) and Blood were collected and processed using standard laboratory techniques. Results: Out of 2454 cases, 253(10.3%) patients developed HAP. Totally 145 sputum samples, 70 BAL and 38 ETA were collected and processed.The commonest organism isolated was Klebsiella pneumoniae (48.2%) followed by Pseudomonas aeruginosa (15.3%), E.coli (8.4%), Acinetobactor species (7.7%), Proteus species (6.9%), MRSA (6.2%), MSSA (5.1%), Serratia species (0.7%), Enterobactor species (0.7%), Streptococcus pneumoniae(0.4%) and Candida albicans (0.4%). All Gram negative bacterial isolates had 100% sensitivity to Imipenem. 82% (n=108) of Klebsiella pneumoniae and 52% (n=12) of E.coli were found to be ESBL producers. Staphylococcus aureus had a maximum sensitivity to Vancomycin followed by third generation cephalosporins. 54.84% (n=17) of Staph.aureus were Methicillin Resistant strains. Conclusion: The antibiotic susceptibility pattern of the isolates will help the clinicians to choose the appropriate antimicrobial agents for prophylactic as well as treatment purposes.**

Index terms- **Hospital Acquired Pneumonia; Intensive Medical Care Unit; Antibiotic susceptibility.**

I. INTRODUCTION

Hospital acquired infections continue to be an important cause of morbidity and mortality among hospitalized patients [Hunter (2006)].The critically ill patient is at particular risk of developing Intensive Care Unit (ICU) acquired infection, with the lungs being especially vulnerable [Hoffken (2002)]. Hospital acquired pneumonia (HAP) is currently the second most common hospital infection accounting for 13 to 18 percent of all nosocomial infections, with estimates of associated mortality ranging from 20 to 50 percent. [Hoffken et al (2002)]. The majority of cases of HAP occur outside of ICUs. However the highest risk is in patients on mechanical ventilation. Estimates of incidence range from 4 to 7 episodes per 1000 hospitalizations [Thomas (2006)]. Intubated patients may have rates of pneumonia 7 to 21- fold higher than patients without a respiratory therapy device [Robert (2005)]. Infection rates are twice as high in large teaching hospitals as compared with smaller institutions [Robert (2005)].

HAP results in a significant increase in the cost of care of hospitalized patients. Its development prolongs a patient's stay in the ICU and most of the extra cost is due to an increased length of hospital stay [Thomas (2006)]. The causes of HAP are varied and differ across different patient populations and different types of ICUs [Kimberly (2006)]. Hospital acquired bacterial pneumonia is frequently polymicrobial with gram negative bacilli predominating [Robert (2005)]. This varied presentation underscores the need for the intensivists treating the patients with HAP to have a clear knowledge of the ambient microbiological flora in their ICU [Kimberly (2006)]. Delayed administration of adequate antibiotic therapy is linked to an increased mortality rate. Hence, the focus of initial antibiotic therapy should provide rapid antibiotic coverage for all likely pathogens. The antibiotic spectrum may then be focused or narrowed based on the results of cultures. A guideline-based approach using the local hospital or ICU antibiogram may help in appropriate and adequate initial therapy and hence reduce the overall use of antibiotics and the associated selection pressure for multi drug resistant organisms [Porzecanski et al (2006)].

Though HAP is widely analyzed by many researchers, not much is known about the incidence and bacteriological profile i.e., only few studies are being published by them. This study was conducted prospectively to evaluate the bacteriological profile of HAP in ICU patients. It may increase the awareness of clinicians about the need to reduce the morbidity and mortality by coming to know about the various pathogens causing HAP and its sensitivity and/or resistance to various antibiotics. The clinicians need to establish a suitable antibiotic policy by working out local ICU antibiogram charts. The aim

of this study was to analyze the incidence, epidemiology and antimicrobial susceptibility pattern of isolates from HAP patients in IMCU.

II. Materials and Methods

This prospective study was conducted over a period of one year among patients admitted in Intensive Medical Care Unit (IMCU) of Coimbatore Medical College & Hospital, Tamil Nadu. The study population comprised all patients admitted to the IMCU from May 1, 2007 to April 30, 2008. Approval was obtained from the Institutional Ethical Committee prior to conducting the study and informed consent from all patients under study was also obtained.

HAP was diagnosed based on standard diagnostic criteria adapted by the Centers for Disease Control and Prevention for the diagnosis of pneumonia if signs of pneumonia occurred after 48 hours following IMCU admission [CDC Guidelines (1997)]. HAP was considered when new or progressive chest radiographical infiltrates occurred ≥48 hours after hospital admission in conjunction with the following clinical criteria: **At least <u>one</u> of the following:** 1. Fever (> 38° C/ 100.4° F) with no other recognized cause 2.Leukocytosis (≥ 12,000 WBC/mm^3) or leucopenia (< 4,000 WBC/ mm^3) 3. For adults ≥ 70 years old, altered mental status with no other recognized cause **And At least <u>two</u> of the following:**

1. New onset of purulent sputum / change in the character of the sputum / increased respiratory secretions / increased suctioning requirements.
2. New Onset or worsening cough / dyspnea / tachypnea (Respiratory Rate > 25 breaths / min)
3. Rales or bronchial breath sounds
4. Worsening gas exchange : O_2 desaturations [$P_a O_2$ / $F_i O_2$ ≤ 240] / increased O_2 requirements / increased ventilation demand

The following cases were excluded from the study:

1. Patients who died within 48 hours from the time of admission to the IMCU
2. Patients discharged or went home against medical advice within 48 hours of admission
3. Patients who were diagnosed to have pneumonia during the time of or within 48 hours of admission (Pneumonia in these cases were presumed to have developed from a previous hospital admission or community)

A. Data collection:

Data collection began from the time of admission to the IMCU and continued until the occurrence of HAP, death or discharge from IMCU whichever occurred first. On IMCU admission name, age, sex, address, date of admission, diagnosis on admission, underlying illness, presence of immuno compromised state, history of smoking and alcoholism were recorded. A thorough general & systemic examination of the patient was also done. When HAP occurred, the time of onset from hospital admission, temperature, chest radio graphical involvement and leukocyte count were recorded. Intervention – related variables including need

for supplemented O2 & device used, need for mechanical ventilation, suctioning devices used, naso gastric tube placement, stress ulcer prophylaxis, steroids, sedatives and antibiotics actually given for at least 48 hrs were also recorded. The data on the hospitalization outcome including length of hospital stay and discharged versus mortality was also determined. The specimens collected were sputum, Bronchoscopic aspirate (BAL), Endotracheal aspirate (ETA) and Blood

B. Processing of specimens:

1) Direct Microscopy:

The BAL, ETA and sputum samples were subjected to Gram staining and Potassium Hydroxide (KOH) mount using standard laboratory techniques [Forbes et al (2007)] to assess the quality of the samples for further processing.

2) Culture Procedures:

The samples were mechanically liquefied and homogenized by vortexing for 1 min and then serially diluted in 0.9% sterile saline solution with final dilutions of 10-2, 10-3 and 10-4. The diluted samples were inoculated onto Blood Agar plate (BAP) with 10% sheep blood, Chocolate Agar plate with 10% sheep blood (CAP) and Mac Conkey Agar plate and Sabourauds Dextrose Agar plate (SDA) by using 4mm Nichrome wire loop (Himedia, Mumbai) which holds 0.01ml of solution for quantitative culture. All plates were incubated overnight at 37° C and CAP at 37° C with 5% CO2 and one SDA plate was kept at room temperature. All plates were checked for growth overnight and then after 24 & 48 hrs of incubation. SDA plates were checked for any growth daily for the first week and twice a week up to four week. Growth of any bacterial isolate below the threshold (Table 1) was assumed to be due to colonization or contamination. All the bacterial pathogens with colony count above the diagnostic threshold were identified by colony morphology, microscopy and detailed biochemical testings using standard laboratory techniques [Forbes et al (2007)]

Table1. Criteria for the assessment of a good quality respiratory sample in HAP [Leroy et al (2002), Baselski et al (1994)].

	ETA	**BAL**	**SPUTUM**
Neutrophils	>25/ LPF	77- 82%	>25/ LPF
SEC	<10/LPF	<1%	<10/ LPF
ICO	No data	≥5%	No data
Quantitative culture threshold (cfu / ml)	$\geq 10^5$-10^6	$\geq 10^4$	$\geq 10^5$-10^6

Antimicrobial susceptibility test:

Antimicrobial susceptibility test of the bacterial isolates was performed on Mueller Hinton Agar (Hi-media, Mumbai) plates by Kirby Bauer's disc diffusion method and antibiotic sensitivity pattern studied according to Clinical Laboratory Standards Institute (CLSI). Gram negative bacilli were tested for the following antimicrobials (Hi-media, Mumbai): Gentamicin(10µg), Amikacin(30 µg),Amoxycillin/Clavulanic acid (20/10 µg),Cotrimoxazole (25µg), Cephalexin(30µg), Cefotaxime (30 µg),Ceftazidime (30 µg), Ceftriaxone (30 µg), Cefpodoxime(10 µg), Aztreonam(30 µg), Cefepime(30 µg), Ciprofloxacin(5 µg), Ofloxacin(5 µg),Gatifloxacin(5 µg) and Imipenem(10 µg). Gram positive cocci were tested for the following antimicrobials (Hi-media, Mumbai): Ampicillin(10 µg),Amoxycillin/Clavulanic acid(20/10 µg), Oxacillin(1 µg), Gentamicin(10 µg), Amikacin (30 µg), Cotrimoxazole(25 µg), Cephalexin(30 µg), Cefuroxime (30 µg), Cefotaxime (30 µg), Ceftazidime(30 µg), Ciprofloxacin(5 µg), Ofloxacin(5 µg), Erythromycin(15 µg) and Vancomycin(30 µg).

Isolates showing inhibition zones ≤22 mm for cetazidime, ≤27 mm for cephotaxime, ≤25 mm for ceftriaxone, ≤22mm for Cefpodoxime and ≤27 mm for Aztreonam were identified as potential ESBL producers [Jacoby (1996)] and they were confirmed by Double disk potentiation test [Parasakthi (2001)].

III. Results

During the one-year study period, among 2658 patients admitted to the IMCU, only 2454 cases were followed and included in this study. The remaining 204 cases were excluded. (118 died within 48hrs of admission, 86 were discharged or went home against medical advice). Out of 2454 cases, 253(10.3%) patients developed HAP. Totally 145 sputum samples, 70 BAL and 38 ETA were collected and processed. Isolates in pure growth or mixture of two organisms at quantitative threshold were considered as significant isolates. All 253 specimens in this study showed significant growth of organisms. About 274 organisms were isolated from 253 samples.

Table 2. Pathogens isolated from HAP patients.

Name of the Pathogen isolated	**No of isolates (%)**
Klebsiella pneumoniae	132 (48.2)
Pseudomonas aeruginosa	42 (15.2)
Escherichia coli	23 (8.4)
Proteus species	19 (6.9)
Acinetobactor species	21 (7.7)
Serratia	2 (0.7)
Enterobactor species	2 (0.7)
Methicillin Sensitive Staphylococcus aureus (MSSA)	14 (5.1)
Methicillin Resistance Staphylococcus aureus (MRSA)	17 (6.2)
Streptococcus pneumoniae	1 (0.4)
Candida albicans	1 (0.4)

The commonest organism isolated was Klebsiella pneumoniae (48.2%) followed by Pseudomonas aeruginosa (15.3%), E.coli (8.4%), Acinetobactor species(7.7%), Proteus species (6.9%), MRSA (6.2%), MSSA (5.1%), Serratia (0.7%), Enterobactor species (0.7%), Streptococcus pneumoniae(0.4%) and Candida albicans (0.4%) [Table.2]. Twenty one samples had showed mixed growth of two organisms likewise Klebsiella pneumoniae and Pseudomonas aeruginosa in 15 cultures (7 Sputum, 6 BAL & 2 ETA), Klebsiella pneumoniae and E.coli in 3 cultures (2 Sputum &1 BAL), Klebsiella pneumoniae and MRSA in 2 cultures (1 Sputum & 1 BAL), Klebsiella pneumoniae and MSSA in 1 sputum culture.

Klebsiella pneumoniae, E.coli and P. aeruginosa had a maximum sensitivity pattern to Imipenem followed by Cefepime, Gatifloxacin and Amikacin. All Gram negative bacterial isolates had 100% sensitivity to Imipenem. Among 132 K.pneumoniae isolates 82% (n=108) were found to be ESBL producers. Among 23 E.coli isolates 52% (n=12) were ESBL producers. Staphylococcus aureus had a maximum sensitivity to Vancomycin followed by third generation cephalosporins. No Vancomycin resistant Staph.aureus was detected. 54.84% (n=17) of Staph.aureus were Methicillin Resistant strains [Table.3].

Table 3. Antimicrobial susceptibility pattern of Bacterial isolates.

ANTIMICROBIAL AGENT Disc content(µg)	K.pneumoniae (132)	P.aeroginosa (42)	E.coli (23)	Acinetobactor(21)	Proteus sp (19)	Serratia (2)	Enterobactor sp (2)	Staph.aureus (31)	Str. Pneumoniae (1)
Gentamicin (10)	75	21	13	13	15	2	1	14	1
Amikacin (30)	121	27	22	17	19	2	2	19	1
Ampicillin (10)	-	-	-	-	-	-	-	16	1
Oxacillin (1)	-	-	-	-	-	-	-	14	1
AmoxyClav(20/10)	29	0	7	-	-	-	-	24	1
Cotrimoxazole(25)	44	4	11	4	11	1	2	7	0
Cephalexin(30)	8	16	8	12	10	1	0	26	1
Cefuroxime(30)	8	16	8	12	10	2	1	26	1
Cefotaxime(30)	21	39	13	21	18	2	2	29	1
Ceftazidime(30)	21	39	14	21	19	2	2	27	1
Cefepime(30)	127	42	23	21	19	2	2	-	-
Ciprofloxacin(5)	102	30	12	12	17	2	1	23	1
Ofloxacin(5)	123	31	12	17	17	2	2	25	1
Gatifloxacin(5)	127	40	20	18	19	2	2	-	-
Imipenem(10)	132	42	23	21	19	2	2	-	-
Erythromycin(15)	-	-	-	-	-	-	-	26	1
Vancomycin(30)	-	-	-	-	-	-	-	31	1

IV. DISCUSSION

The present study showed that the incidence of HAP was 10.3% (n=253) out of 2454 cases admitted in IMCU, Coimbatore Medical College Hospital over a period of one year. This incidence was lower than the study by Mukhopadhyay et al (2003) from Lucknow (53.9%), Rakshit et al (2005) from Mumbai (47%), Vincent et al (1995) from Europe (46.9%), Dey et al (2007) from Manipal (45.4%), Sopena et al (2005) from Spain (36.4%), Berba et al (1999) from Philadelphia (28.2%) and Merchant et al (1998) from Mumbai (16.7%). This was higher than the incidence reported by Chevret et al (1993) from France (8.9%), Alp et al (2004) from Netherlands(6.8%), Trivedi et al (2000) from Mumbai (9.38%) and Pawar et al (2003) from New Delhi (2.6%). It is possible that our incidence rate may be an over estimate of the HAP in the hospital because of the nature of the clinical criteria used. Studies based solely on clinical criteria alone are criticized because of the non-specificity of parameters like fever, leukocytosis and infiltrates on the chest radiographs. However, the stringent steps followed to make a diagnosis of HAP in this study and the close monitoring before and after the diagnosis of HAP occurred should make our estimate very close to the true HAP incidence. It is unlikely that a true HAP case would have been missed because we did quantitative culture of all specimens (BAL, Sputum and ETA) to discriminate between the true pathogen and the contaminant using the diagnostic threshold for each specimen.

Klebsiella pneumoniae (48.2%) was the commonest organism isolated in this study. Most of the previous studies reported Pseudomonas aeruginosa as the commonest isolate from HAP patients in IMCU [Rakshit et al (2005), Mukhopadhyay et al (2003) ,Pawar et al (2003), Leroy O (2002)]. But Pseudomonas aeruginosa was the second common organism in the present study. Acinetobacter species (7.7%) was the fourth common isolate in this study. Dey et al (2007), Rajasekhar et al (2006) and Alp et al (2004) reported that Acinetobacter species as the commonest organism in their study. E. coli was the commonest organism in the study by Tullu et al (2000). It was third commonest organism in the present study. These findings indicate that the causative pathogens always vary in different setups. The present study suggests that the colonization rate for Klebsiella pneumoniae may be higher in IMCU.

The rate of polymicrobial infection was found to be only 8.3% in this study which was lower than the study by Mukhopadhyay et al (2003) (16.3%) and Singhal et al (2005) (12.3%). The lower rate of colonization of IMCU environment by more than one type of organisms may be the reason for the lower incidence of polymicrobial infection.

Antimicrobial resistance among Gram negative bacilli is increasing worldwide and is of particular concern in the Intensive Care Unit setting. A direct correlation has been shown between resistance of Gram negative bacilli and patient mortality, cost of patient care and length of stay in the hospital [Aly (2008)]. In a study by Kaul et al (2007) about the Gram- negative bacterial antibiotic susceptibility patterns in IMCU, Christian Medical College, Vellore showed that Klebsiella resistance to cefotaxime and ceftazidime ranged from 25-50% and 14-91%, while E.coli resistance to these antibiotics ranged from 50-70% and 50-80% respectively. In this study Klebsiella resistance to cefotaxime and ceftazidime was 84% and E.coli resistance to these antibiotics were 43% and 39% respectively. The resistance of K.pneumoniae and E.coli to third generation cephalosporins was higher in this study.

All isolates of Acinetobacter, Serratia and Enterobactor were sensitive to third generation cephalosporins. 92% of Pseudomonas aeruginosa and 94% of Proteus were sensitive to cefotaxime and ceftazidime. These findings were similar to the study by Kaul et al (2007) from Christian Medical College, Vellore, who reported that in Pseudomonas aeruginosa and the other non-fermenting gram-negative bacteria (NFGNB) Ceftazidime resistance decreased. Among Aminoglycosides, most of the GNB were sensitive to Amikacin than Gentamicin. Highest sensitivity rates were detected for Gatifloxacin than Ciprofloxacin and Ofloxacin among Quinolones. These findings were similar to previous studies on antimicrobial resistance among gram-negative bacteria by many authors [Joseph (2001), Muhammad (2007), Rajasekhar et al (2006)].

All Gram negative bacilli isolated in this study had a maximum sensitivity pattern to Imipenem and Cefepime. This was similar to the study by Lockhart et al (2007) about antimicrobial resistance among Gram-Negative Bacilli causing infections in Intensive Care Unit patients in the United States between 1993 and 2004 and Rakshit et al (2005) from Mumbai.

Gram-negative bacilli producing ESBL appear to be on the rise in Asian countries and pose a serious problem in pulmonary infections [Lagamayo (2008)]. In the present study the occurrence of ESBL production among K.pneumoniae and E.coli were 82% and 52% respectively. For Klebsiella pneumoniae this finding was higher than the study by Feizabadi et al (2008) (72.8%), Gonlugur et al (2004) (12.2%), Hosoglu et al (2007) (68.3%), and lower than the study by Verhamme et al (2007) (100%), Vitkauskiene et al (2007) (88.9%) and Dey et al (2007) (100%). For E.coli this finding was higher than the study by Gonlugur et al (2004) (20.8%),

Asian HAP Working group [Lagamayo (2008)](2.3% to 40%) and lower than the study by Hosoglu et al (2007) (74.6%), Dey et al (2007)(100%). In this study ESBLs were predominantly present among K. pneumoniae compared to E. coli. Our findings are similar to that of most of the studies in Europe and USA [Jacoby (1991)]and the Indian studies by Jain et al (2007) and Shanmuganathan et al (2004). But studies by Gonlugur et al (2004), Hosoglu et al (2007) and Kumar et al (2006) showed higher incidence of ESBLs among E.coli than K.pneumoniae. The indiscriminate use of third-generation cephalosporins has been proposed as a reason for the rise of ESBL producing strains in India [Lagamayo (2008)].

Among the Staphylococcus aureus isolates in this study, the occurrence of Methicillin resistance was observed in 54.84%. This was higher than the study by Leroy et al (2002) (33%) and lower than the study by Mukhopadhyay et al (2003)(59.45%) and Rakshit et al(2005) (100%). No Vancomycin resistant Staphylococcus aureus was detected in the present study.

V. CONCLUSION

To conclude, the result of this study will enlighten the knowledge of the health care providers about the incidence of HAP and the pathogens causing HAP. The antibiotic susceptibility pattern of the isolates from HAP will help the health care providers to choose the appropriate antimicrobial agents for prophylactic as well as treatment of Hospital Acquired Infections.

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Conflicts of interest

There are no conflicts of interest

REFERENCES

[1] Alp E, Guven M, Yildiz O, et al. Incidence, risk factors and mortality of nosocomial pneumonia in Intensive Care Units: A Prospective study. Ann Clin Microbiol Antimicrobials 2004, 3:17.

[2] Aly NY, Al-Mousa HH, Al Asar el SM. Nosocomial infections in a medical-surgical intensive care unit. Med Princ Pract 2008;17(5):373-7.

[3] Baselski VS, Wunderink RG. Bronchoscopic diagnosis of Pneumonia. Clin Microbiol Rev. 1994; 7.4: 533-558.

[4] Berba R, Alejandria M,Rosacos J, et al. Incidence, Risk factors and Outcome of Hospital Acquired Pneumonia in Critically Ill Patients at the Philippine General Hospital. Phil J Microbiol Infect Dis1999; 28(2):29-38.

[5] Centers for Disease Control and Prevention: Guidelines for Prevention of Nosocomial Pneumonia. MMWR Recomm Repsxfv 1997,46(RR-1):1-79.

[6] Chevret S, Hemmer M, Carlet J, Langer M. Incidence and risk factors of pneumonia acquired in Intensive Care Units. Results from a multicentre prospective study on 996 patients. European Cooperative Group on Nosocomial Pneumonia. Intensive Care Med 1993; 19 (5):256-64.

[7] Dey A, Bairy I. Incidence of multi drug-resistant organisms causing Ventilator-Associated pneumonia in a tertiary care hospital: A nine month's prospective study. Ann Thorac Med 2007; 2:52-57.

[8] Feizabadi M, Yeganeh MS, Nili F, Mirsalehian AA, Mirafshar SM. PFGE analysis of MDR isolates of Klebsiella pneumoniae cultured from patients at Tehran hospitals. Euro society of Clin Microbiol Infect Dis. 2008 April; p1683.

[9] Forbes BA, Sahm DF, Weissfeld AS. Bailey & Scott's Diagnostic Microbiology. 12th edi. 2007.

[10] Gonlugur U, Bakici MZ, Akkurt I, Efeoglu T. Antibiotic susceptibility patterns among respiratory isolates of Gram Negative Becilli in a Turkish University hospital. BMC Microbiol. 2004; 4:32.

[11] Hoffken G, Niederman MS. Nosocomial pneumonia; the importance of a de-escalating strategy for antibiotic treatment of pneumonia in the ICU. Chest 2002; 122:2183-2196.

[12] Hosoglu S, Gundes S, Kolayli F, et al. Extended spectrum beta- lactamases in ceftazidime- resistant E.coli and Klebsiella pneumoniae isolates in Turkish hospitals. Indian J Med Microbiol 2007; 25:346-50.

[13] Hunter JD. Ventilator Associated Pneumonia. J Postgrad Med 2006; 82: 172-178.

[14] Jacoby GA, Mediros AA. More extended-spectrum beta-lactamases. Antimicrob Agents Chemother 1991; 35:1697-704.

[15] Jacoby GA, Han P. Detection of Extended Spectrum β-Lactamases in clinical isolates of Klebsiella pneumoniae and Escherichia coli. J Clin Microbiol.1996; 34.4: 908-911.

[16] Jain A, Mondal R. Prevalence and antimicrobial resistance pattern of extended spectrum β- lactamase producing Klebsiella spp isolated from cases of neonatal septicaemia. Indian J Med Res 2007; 125:89-94.

[17] Joseph P. Lynch III. Hospital-Acquired Pneumonia: Risk Factors, Microbiology, and Treatment. Chest 2001; 119: 373-384.

[18] Kaul S, Brahmadathan KN, Jagannati M, Sundarsanam TD, Pitchamuthu K, Abraham OC, John G. One year trends in the gram-negative bacterial antibiotic susceptibility patterns in a medical intensive care unit in south India. Indian J med Microbiol 2007; 25:230-5.

[19] Kimberly A. Davis. Ventilator-Associated pneumonia: A Review. J Intensive Care Med. 2006; 21:211-226.

[20] Kumar MS, Lakshmi V, Rajagopalan R. Occurrence of extened spectrum beta- lactamases among Enterobacteriaceae spp. Isolated at a tertiary care institute. Indian J Med Microbiol 2006; 24:208-11.

[21] Lagamayo EN. Antimicrobial resistance in major pathogens of hospital- acquired pneumonia in Asian countries. Am J Infect Control 2008; 36:S101-8.

[22] Leroy O, Giradie P, Yazdanpanah Y, et al. Hospital Acquired Pneumonia: microbiological data and potential adequacy of anti microbial regimens. Eur Respir J 2002; 20: 432-439.

[23] Lockhart SR, Abramson MA, Beekmann SE, Gallagher G, Riedel S, Diekema DJ, et al. Antimicrobial resistance among Gram-Negative Bacilli causing infections in Intensive Care Unit patients in the United States between 1993 and 2004. J Clin Microbiol 2007; 45(10):3352-3359.

[24] Merchant M, Karnad DR, Kanbur AA. Incidence of nosocomial pneumonia in a Medical Intensive Care Unit and general medical ward patients in a public hospital in Bombay, India. J Hosp Infect. 1998 Jun; 39(2):143-8.

[25] Muhammad F.R, Yasmin H, Menon AR, et al. Pattern of Nosocomial Infection in two Intensive Care Unit of a tertiary care hospital in Karachi. JC PSP 2007; Vol. 17(3): 136-139.

[26] Mukhopadhyay C, Anudida B, Ayyagari A. Role of mechanical ventilation & development of multi drug resistant organisms in hospital acquired pneumonia. Indian J Med Res.2003 Dec; 118:229-235.

[27] Parasakthi N. Consensus guidelines for the management of infections by ESBL- producing bacteria. 2001.

[28] Pawar M, Mehta Y, Trehan N, Kulkarni V. Ventilator-Associated Pneumonia: Incidence, risk factors, outcome, and microbiology. J Cardio thorac Vasc. 2003; 17:22-28.

[29] Porzecanski I, Bowton DL. Diagnosis and treatment of ventilator associated pneumonia. Chest 2006; 130: 597-604.

[30] Rajasekhar T, Anuradha K, Suhasini T, Lakshmi V. The role of quantitative cultures of non-bronchoscopic samples in Ventilator-Associated Pneumonia. Indian J Med Microbiol 2006; 24:107-113.

[31] Rakshit P, Nagar VS, DeshPande AK. Incidence, Clinical outcome and risk stratification of ventilator-Associated Pneumonia- a Prospective cohort study. Indian J Crit Care Med 2005; 9: 211-216.

[32] Robert C Read. Bacterial infections of the lower respiratory tract. Topley & Wilson's. 10th edition, volume-1.2005:640.

[33] Shanmuganathan C et al. Learning from an outbreak: ESBL- the essential points. Indian J Med Microbiol 2004; 22(4):255-257.

[34] Singhal R, Mohanty S, Sood S, Das B, Kapil A. Profile of bacterial isolates from patients with ventilator associated pneumonias in a tertiary care hospital in India. Indian J Med Res 2005; 121:63-64.

[35] Thomas M File, Jr, MD. Hospital-acquired (nosocomial) pneumonia in adults. Up To Date. Verson 15.1: September 29, 2006.

[36] Trivedi TH, Shejale SB, Yeolekar ME. Nosocomial Pneumonia in medical Intensive Care Unit. J Assoc Physicians India.2000 Nov; 48(11): 1070-3.

[37] Tullu MS, Deshmukh CT, Baveja SM. Bacterial Nosocomial Pneumonia in Paediatric Intensive Care Unit. J Postgrad Med 2000; 46:18-22.

[38] Verhamme KMC, DeCooster W, Roo LD, Beenhouwer HD, Nollet G, Verbeke J, et al. Pathogens in Early-onset and Late-onset Intensive Care Unit- Acquired Pneumonia. J Infect Control Hosp Epidemiol 2007; 28(4):389-397

[39] Vincent JL, Bihari DJ, Suter PM, et al. The Prevalence of nosocomial infection in Intensive Care Units in Europe: Results of the European Prevalence of Infection in Intensive Care (EPIC) study. EPIC International Advisory Committee. JAMA 1995; 274: 639-644.

[40] Vitkauskiene A et al. Relationship between isolation of extened spectrum beta- lactamase producing Klebsiella pneumoniae and course of hospital- acquired pneumonia. Medicina 2007; 43(10):778-83.