ISSN: 2581-5989
PubMed - National Library of Medicine - ID: 101738774

International Journal of Dental Science and Innovative Research (IJDSIR)
IJDSIR : Dental Publication Service
Available Online at: www.ijdsir.com
Volume – 4, Issue – 4, August - 2021, Page No. : 143 - 153

Emergence of Antimicrobial Resistance in bacterial isolates among COVID-19 individuals and General Population in a Tertiary Care Hospital of Rural Chengalpattu District, Tamil Nadu, India

[1]Sridhar G, Professor, Department of Microbiology, Associate Professor, Shri Sathya Sai Medical College, Sri Balaji Vidyapeeth, Chengalpattu, Tamil Nadu, India.

[2]Prasanna S, Department of Microbiology, Associate Professor, Shri Sathya Sai Medical College, Sri Balaji Vidyapeeth, Chengalpattu, Tamil Nadu, India.

[3]Karnaboopathy R, Department of Community Medicine , Associate Professor, Shri Sathya Sai Medical College, Sri Balaji Vidyapeeth, Chengalpattu, Tamil Nadu, India.

Corresponding Author: Prasanna S, Department of Microbiology, Associate Professor, Shri Sathya Sai Medical College, Sri Balaji Vidyapeeth, Chengalpattu, Tamil Nadu, India.

Citation of this Article: Sridhar G, Prasanna S, Karnaboopathy R, "Emergence of Antimicrobial Resistance in bacterial isolates among COVID-19 individuals and General Population in a Tertiary Care Hospital of Rural Chengalpattu District, Tamil Nadu, India", IJDSIR- August - 2021, Vol. – 4, Issue - 4, P. No. 143 – 153.

Type of Publication: Review Article

Conflicts of Interest: Nil

Abstract

Introduction: Globally antimicrobial drug resistance is an emerging threat to humanity. The spread of drug resistance has been attributed mainly to the widespread administration of various antibiotics. Compared to various units in general hospital the antimicrobial drug resistance is much higher in ICU, including critical care, neonatal and intensive cardiac care units.

Materials and methods: The study was carried out in the Microbiology, Central Laboratory of the Hospital. The study was conducted for a period of three months from June to August 2020 in a Tertiary care Hospital. A total of 549 samples were included in the prospective study in. An observational study was also conducted from March to May 2020, a total of 551 samples were analysed during this period. All data were tabulated and analysed using SPSS 23 software. Results were expressed in terms of percentages and significance was analysed using chi-square test.

Results: The study revealed a marginal onset of emergence of drug resistance in Nitrofurantoin, Norfloxacin, Ceftazidime, and Ciprofloxacin which is insignificant. Cefazolin resistance was very high during both the periods (70% and 68%) of study without any significant differences. However, it was also observed that a significantly higher sensitivity was noted in Nalidixic acid from 40% during retrospective period to 80% in prospective period. Insignificant increase in sensitivity was also observed in amoxicillin-clavulanic acid, ceftriaxone and ceftazidime.

Conclusion: The continuous administration of antibiotics over a period of time leads to a gradual or sudden emergence of resistance in the pathogenic bacteria highlighted in our present study.

Keywords: Antimicrobial resistance, COVID-19, ICU, Tertiary care centre

Introduction

Globally antimicrobial drug resistance is an emerging threat to humanity. The spread of drug resistance has been attributed mainly to the widespread administration of various antibiotics. Compared to various units in general hospital settings the antimicrobial drug resistance is much higher in Intensive care units, including critical care, neonatal and intensive cardiac care units. Antimicrobial resistance (AMR) is a clinical problem where the microorganism is able to survive exposure to antibiotic treatment and most of the serious infections acquired by ICU patients are of Nosocomial in origin.[1]

Both AMR Gram negative bacilli (GNB) and Gram-positive bacteria (GPB) are reported as important cause of hospital-acquired infections. Methicillin resistant Staphylococcus aureus (MRSA) identified in 1990 soon after the introduction of penicillinase resistant penicillins, started as a single clonal mutation and resulted in community acquired MRSA owing to diversification of clones.[1,2] This is evident from the first report of vancomycin resistant Staphylococcus aureus (VRSA) from the US in 2002, Brazil in 2005, Jordan and Indian 2006. In late 1980s similar resistance was reported with vancomycin resistant Enterococci. India being a developing country the incidence of infectious diseases is very high and still hold high morbidity and mortality. [1,2,3]

The development of drug resistance within and across bacteria may be due various contributing factors like point mutation, transposons and plasmids which play a greater role in the transfer of single or multidrug resistance (MDR) between different bacterial strains. Moreover, it would be difficult to control the transferrable multidrug resistance mediated by the plasmids just by reducing the use of antibiotics in a community.[3]

Since nosocomial infections are the most commonest mode of spread of MDR bacteria among the hospitalised patients there is a greater need to consider social factors such as demographic changes, deficient hygienic practices and overcrowding which have been enumerated for the emergence of AMR and this is supported by the multidrug resistant (MDR) Escherichia coli that has been isolated in carriers and in water samples by a study carried out in rural Tamil Nadu.[1,4]

Infectious diseases caused by methicillin resistant staphylococci (MRSA), Vancomycin resistant Enterococcus (VRE), Clostridium difficile; extended spectrum β-lactamase producing Gram negative bacilli (GNB) eventually prolong the treatment process there by increasing the hospital stay and contribute to mortality.[5]

Since AMR is an emerging threat to the community there needs a central monitoring agency to closely follow up the sensitivity and resistance pattern of different bacterial isolates from clinical samples from various hospitals and tertiary care centres across the country. This would emphasize appropriate antibiotic stewardship that includes optimal dose selection, duration of treatment and control of AM use in order to prevent the emergence of newer strains such as New Delhi Metalloproteinase (NDM) which pose fresh challenges. Therefore, to reduce the development AM resistance regular monitoring of sensitivity pattern is essential. Hence the present study has been designed to closely monitor the emergence sensitivity and resistance pattern of bacterial isolates among COVID-19 individuals in a tertiary care Hospital of rural Chengalpattu district of Tamil Nadu which has never been subjected in the past for such an investigation.

Materials and method

The study was carried out in the microbiology division of the Central Laboratory of the Hospital. The study was conducted for a period of three months from June to August 2020 in a Tertiary care hospital, Tamil Nadu. Institution ethical committee clearance was obtained before the commencement of the study**.** Various clinical samples including blood, urine, sputum, wound, ear swab, throat swab, sputum, stool, pleural fluid, pus, high vaginal swabs etc., received from both outpatient and in patients units including COVID-19 ward, TBCD, OBG, Surgery, Medicine, Paediatrics, ICU, Ophthalmology, ENT and Dermatology were processed in the Microbiology division of the Central Laboratory. A total of 549 samples were included in the prospective study. The specimens for antimicrobial sensitivity testing were studied by Gram stains and the isolates were identified by their characteristic culture growth on nutrient, blood and MacConkey agar.

After confirmation of the organism, culture growths were tested for in vitro antimicrobial susceptibility testing by disc diffusion method (Kirby Bauer method) on Muller Hinton agar. Evaluation by Gram stain, biochemical tests, culture media and disc diffusion methods were carried out daily as per Clinical and Laboratory Standards Institute (CLSI) guidelines. An observational study was also conducted from March to May 2020. The data regarding culture and sensitivity of the organisms isolated from different clinical specimens were collected from the records of both out-patients (OP) and in-patients (IP) from the Microbiology Department. A total of 551 samples were analysed during this period.

Antibiotics tested for sensitivity against gram negative bacteria and gram-positive bacteria include ampicillin, amoxicillin clavulanic acid, gentamicin, amikacin, imipenem, ceftriaxone, cefuroxime, ceftazidime, cefazolin, norfloxacin, nalidixic acid, nitrofurantoin, ciprofloxacin, and vancomycin. Organisms resistant to more than one group of drugs were considered as MDR. After getting an informed consent from the subjects, they were requested to answer a simply formulated questionnaire. From the patient's case sheet other relevant data was obtained. All data were tabulated and analysed using SPSS 23 software. Results were expressed in terms of percentages and significance was analysed using chi-square test.

Results

The total number of samples received to our microbiology laboratory from out-patient and in-patients of the various departments for culture and sensitivity during the prospective study period (June, July, August) was 549 and during the retrospective study period (March, April, May) was 551. Table-1 shows the age wise distribution of clinical samples collected over a period of six months from March to August 2020 which includes both prospective and retrospective group. It was observed that patients who are between 20 to 40 years of age and age group above 40 contributed more clinical samples (42% and 48% respectively) compared to patients who are less than 20 years of age (13%).

Table 1: Shows the age wise distribution of clinical samples collected over a period of six months from March to August 2020

Age	Retrospective (March, April & May) n (%)	Prospective (June, July & August) n (%)
Below 20	72 (13.1)	51 (9.3)
20-40	231 (41.9)	232 (42.3)
Above 40	248 (45)	266 (48.4)
Total	551 (100)	549(100)

Table 2 shows the Sex wise distribution of clinical samples collected over a period of six months from March to August 2020 which includes both prospective and retrospective group. It was noted that a greater number of clinical samples were collected from female patients (65%) while compared to Male patients (37%) during the entire study period.

Table 2: Shows the Sex wise distribution of clinical samples collected over a period of six months from March to August 2020

Sex	Retrospective (March, April & May) n (%)	Prospective (June, July & August) n (%)
Male	192 (34.8)	206 (37.5)
Female	359 (65.2)	343 (62.5)
Total	551 (100)	549 (100)
Organism	Retrospective (March, April & May) N (%)	Prospective (June, July & ugust) N (%)
Acinetobacter baumannii	53 (9.62)	45 (8.20)
Citrobacter koseri	3 (0.54)	1 (0.18)
Citrobacter freundii	15 (2.72)	17 (3.10)
Escherichia coli	156 (28.31)	109 (19.85)
Enterobacter aerogenes	1 (0.18)	7 (1.28)
Enterococcus faecalis	25 (4.54)	35 (6.8)
Klebsiella oxytoca	34 (6.17)	41 (7.47)
Klebsiella pneumoniae	75 (13.61)	90 (16.39)
MRCONS	1 (0.18)	3 (0.55)
Proteus mirabilis	2 (0.36)	22 (4.01)
Proteus vulgaris	5 (0.91)	5 (0.91)
Pseudomonas aeruginosa	36 (6.53)	56 (10.20)
Staphylococcus aureus	65 (11.80)	68 (12.39)
Staphylococcus epidermidis	60 (10.89)	13 (2.37)
Streptococcus faecalis	1 (0.18)	000

Streptococcus pneumoniae	5(0.91)	4 (0.73)
Streptococcus pyogenes	14 (2.54)	29 (5.28)
Alkaligenes faecalis	000	1 (0.18)
Chromobacterium violaceum	000	1 (0.18)
Total	551 (100)	549 (100)

Table 3 shows the distribution of various clinical Samples over a period of six months from March to August 2020. Out of a total of 549 samples collected during the prospective study period it was observed that urine samples (28.23%) were followed by pus (24.77%), sputum (22.4%) and high vaginal swab (21.86%) followed by others (2.74%). While during the retrospective period out of 551 samples collected, urine samples were still higher (48.5%) followed by high vaginal swab (17.6%), sputum (15.2%) and pus (14.3%) followed by others (4.4%).

Table 3: Shows the distribution of various clinical Samples over a period of six months from March to August 2020

Sample	Retrospective (March, April & May) N (%)	Prospective (June, July & August) N (%)
Blood	16 (2.9)	4 (0.73)
Bronchial aspirate	3 (0.5)	2 (0.36)
Eye swab	1 (0.2)	3 (0.55)
High vaginal swab	97 (17.6)	120 (21.86)
Pleural fluid	1 (0.2)	3 (0.55)
Pus	79 (14.3)	136 (24.77)
Sputum	84 (15.2)	123 (22.40)
Throat swab	3 (0.5)	3 (0.55)
Urine	267 (48.5)	155 (28.23)
Total	551 (100)	549 (100)

Table 4 shows the isolation of various pathogenic bacteria from clinical samples over a period of six months from March to August 2020. Out of a total of 549 samples collected during the prospective study period it were observed that among the organisms isolated Escherichia coli was the predominant organism (19.85%) followed by Klebsiella pneumoniae (16.39), Staphylococcus aureus (12.39%), Pseudomonas aeruginosa (10.2%), Acinetobacter baumannii (8.2%) and others (32.97%). While during the retrospective period out of 551 samples collected, Escherichia coli was isolated in 28.31% of the cases followed by Klebsiella pneumoniae (13.61%), Staphylococcus aureus (11.8%), Staphylococcus epidermidis (10.89%), Pseudomonas aeruginosa (6.53%), Acinetobacter baumannii (9.62%) and others (19.24%).

Table 4: Shows the isolation of various pathogenic bacteria from clinical Samples over a period of six months from March to August 2020

Organism	Retrospective (March, April & May) N (%)	Prospective (June, July & August) N (%)
Acinetobacter baumannii	53 (9.62)	45 (8.20)
Citrobacter koseri	3 (0.54)	1 (0.18)
Citrobacter freundii	15 (2.72)	17 (3.10)
Escherichia coli	156 (28.31)	109 (19.85)
Enterobacter aerogenes	1 (0.18)	7 (1.28)
Enterococcus faecalis	25 (4.54)	35 (6.8)
Klebsiella oxytoca	34 (6.17)	41 (7.47)
Klebsiella pneumoniae	75 (13.61)	90 (16.39)
MRCONS	1 (0.18)	3 (0.55)
Proteus mirabilis	2 (0.36)	22 (4.01)
Proteus vulgaris	5 (0.91)	5 (0.91)
Pseudomonas aeruginosa	36 (6.53)	56 (10.20)
Staphylococcus aureus	65 (11.80)	68 (12.39)
Staphylococcus epidermidis	60 (10.89)	13 (2.37)
Streptococcus faecalis	1 (0.18)	000
Streptococcus pneumoniae	5(0.91)	4 (0.73)
Streptococcus pyogenes	14 (2.54)	29 (5.28)
Alkaligenes faecalis	000	1 (0.18)
Chromobacterium violaceum	000	1 (0.18)
Total	551 (100)	549 (100)

Table-5 shows the sensitivity and resistance pattern of various antibiotics to the organisms isolated. About 10 antibiotics shared significant variation in their sensitivity and resistance pattern between the retrospective and prospective study period (Fig-1 & Fig-2). Comparison of the behaviour of same set of antibiotics used between the prospective and retrospective study period reveals significantly high rate of emergence of drug resistance in gentamicin (82%), high level gentamicin (70%), followed by cefuroxime (37%), Imipenem (32%), oxacillin (28%), ampicillin(28%), vancomycin (17%) and amikacin(15%).

Table 5: Shows the sensitivity and resistance pattern of various antibiotics to the organisms isolated.

Antibiotic		Retrospective Data (%) Mar, Apr, May	Prospective Data (%) Jun, July, Aug	χ^2- Value	p-value
AMIKACIN -AK	Sensitivity	95	85	5.55	0.018
	Resistance	05	15		

AMPICILLIN-AMP	Sensitivity	86	72	5.91	0.015
	Resistance	14	28		
IMIPENEM (IMP)	Sensitivity	83	68	6.08	0.014
	Resistance	17	32		
GENTAMICIN (GEN)	Sensitivity	92	18	110.6	0.000
	Resistance	08	82		
CEFAZOLIN (CZ)	Sensitivity	30	32	0.094	0.760
	Resistance	70	68		
Amoxicillin clavulanic acid-AMC	Sensitivity	44	58	3.922	0.048
	Resistance	56	42		
Ceftazidime- CAZ	Sensitivity	65	63	0.087	0.768
	Resistance	35	37		
Cefuroxime-CXM	Sensitivity	80	63	7.091	0.008
	Resistance	20	37		
Ceftriaxone-CTR	Sensitivity	75	84	2.485	0.115
	Resistance	25	16		
Vancomycin-VA	Sensitivity	92	83	3.703	0.054
	Resistance	08	17		
Oxacillin-OX	Sensitivity	94	72	17.15	0.000
	Resistance	06	28		
High level gentamicin-HLG	Sensitivity	80	30	50.51	0.000
	Resistance	20	70		
Nalidixic acid-NA	Sensitivity	40	80	33.33	0.000
	Resistance	60	20		
Norfloxacin- NX	Sensitivity	85	80	0.866	0.352
	Resistance	15	20		
Nitrofurantoin-NIT	Sensitivity	90	85	1.143	0.285
	Resistance	10	15		
Cefepime-CPM	Sensitivity	85	76	2.580	0.108

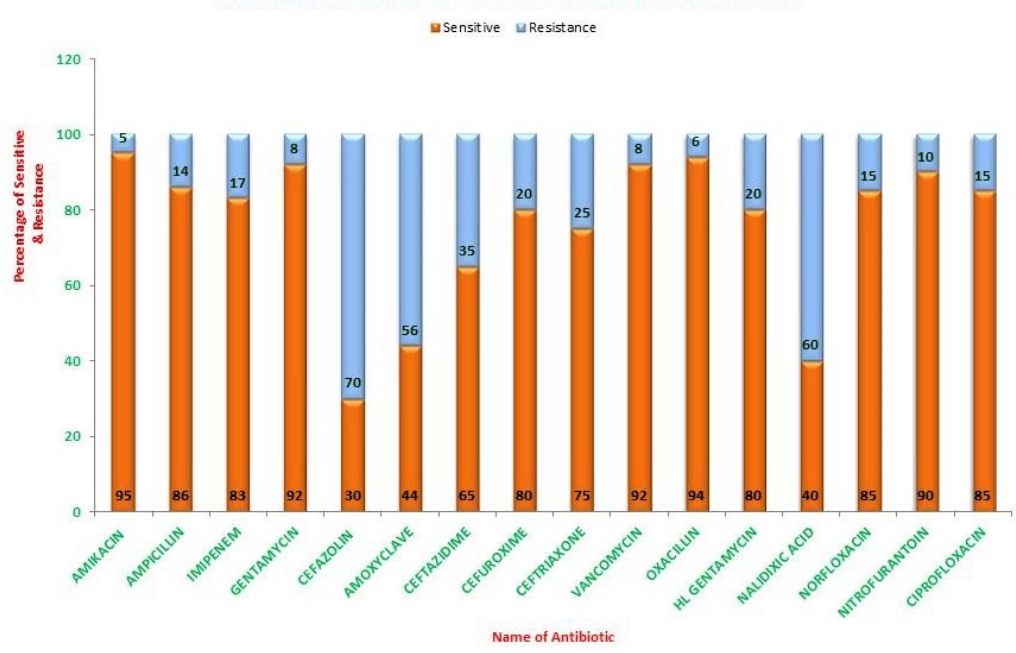

Fig.1: Sensitivity and resistance pattern of retrospective study period (March, April and May 2020)

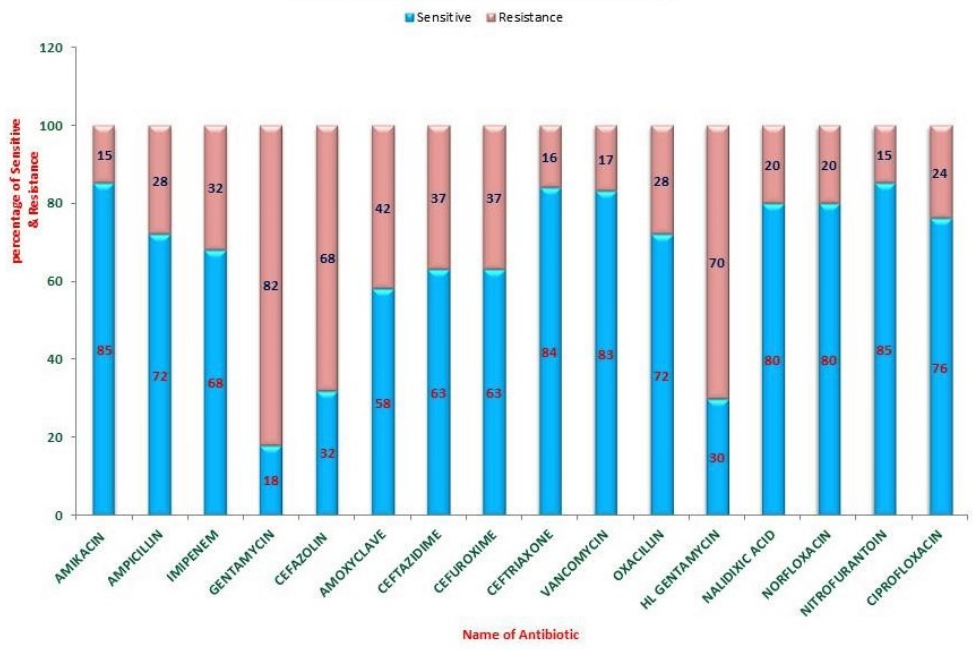

Fig. 2: Sensitivity and resistance pattern of prospective study period (March, April and May 2020)

The study also revealed a marginal onset of emergence of drug resistance in nitrofurantoin, norfloxacin, ceftazidime, and ciprofloxacin which is insignificant. Cefazolin resistance was very high during both the periods (70% and 68%) of study without any significant differences. However, it was also observed that a significantly higher sensitivity was noted in nalidixic acid from 40% during retrospective period to 80% in prospective period. Insignificant increase in sensitivity was also observed in amoxicillin-clavulanic acid, ceftriaxone and ceftazidime.

Discussion

Antimicrobial agents are among the most commonly used drugs in treating patients attending the hospitals both as out-patients as well as in-patients. The emergence of drug

resistance in a hospital set up may be due to several factors of which Nosocomial spread of the infectious microbes plays a crucial role.

Resistance may be also due to prolonged stay in the hospital facilitating the spread among the patients, attendants, doctors and paramedical workers who handle the patients on daily basis. Without proper knowledge of the use of antimicrobials it would be difficult to understand the emergence of drug resistance in a hospital. [1,7]

Hence the use or miss use of antimicrobials are at most important in the effective monitoring of emergence of antimicrobial drug resistance in a community. Hospital infection control and using of antibiotics with proper precautions and preventive measures will be helpful. Preparation of local antibiotic policy will be helpful for the control of spread of drug resistance. Irrational use and misuse of antibiotic must be avoided based on the antibiotic policy[1]. In the present study majority of the patients admitted to various units in the hospitals were from different age groups ranging from 20 year to 40 and above and clinical samples were more from female patients (65%) than male Patients (37%) with urine samples being the highest (28%), and lowest eye swab (0.2%)

In our study Escherichia coli was the most predominant organism frequently isolated from clinical samples (28%) followed by Klebsiella pneumoniae (13.6%), Staphylococcus aureus (11.8%), Staphylococcus epidermidis (10.8%), Pseudomonas aeruginosa (10.2%) and Acinetobacter baumannii (9.6%), which almost coincides with similar observations.[8]

The changes over in the resistance pattern among the coliforms are considered to be due to horizontal and vertically acquired resistance. Escherichia coli and Klebsiella species are the leading causes for multi-drug resistance strains among the Enterobacteriaceae in most of the tertiary care centres and hospitals.[9,10,11,12,13,14,15,16]

Other infections caused by gram negative organisms like multi drug resistant Pseudomonas, Stenotrophomonas and Acinetobacter shown horizontal drug resistance transfer out from environment. They also showed this multi-drug resistance in skin carriage strains worldwide. [17,18,19]

The findings of our present study are indicative of emergence of high resistance to gentamicin (82%). Though least resistance was observed to gentamicin and amikacin in separate studies done by Revathy Saravanan and in community based surveillance study done by WHO, in contrast a higher sensitivity of 68% to amikacin and 9% to gentamycin in a prospective study performed in a tertiary care hospital in Chennai and Pondicherry during 2011 which is similar to our own observation. [78,9] We have also noted significant emergence of drug resistance to cefuroxime (37%), imipenem (32%), oxacillin (28%) ampicillin (28%) and vancomycin (17%) in our study. This suggests the possibility of changing sensitivity pattern with time difference.[1]

In India generally there is little control on the use of antibiotics especially with the easy availability of drugs across the counter without proper prescription adds up to the miss use of drugs to a very great extend leading to gradual emergence of drug resistance in a community or a hospital set up. This scenario is also coupled with primitive infection control in hospitals, poor sanitation, lack of awareness of disinfection and biomedical waste disposal serves as most suited condition for the transmission of antibiotic resistance. In the absence of a National Monitoring committee the exact scenario of emergence of antimicrobial resistance is not known. Hence by closely monitoring the sensitivity and resistance pattern of common pathogenic bacteria in a particular

region will be of greater help for successful antibiotic stewardship.

Conclusion

The present study is an attempt to investigate the possibility of emergence of antimicrobial drug resistance among COVID-19 individuals and general population in a tertiary care hospital during a short period comprising of prospective and retrospective clinical samples using same set antibiotics. It was observed that continuous administration of same antibiotics over a period of time leads to a gradual or sudden emergence of antimicrobial resistance in the pathogenic bacteria as evidenced by our present study. Long hospital stays and extended period of treatment with antibiotics or misuse of antimicrobials, steroids may lead to antimicrobial resistance, antibiotic associated diarrhoea and other opportunistic fungal infections.

References

1. Raghunath D. Emerging antibiotic resistance in bacteria with special reference to India. J Biosci. 2008; 33:593-603. https://doi.org/10.1007/s12038-008-0077-9
2. Kollef MH, Fraser VJ. Antibiotic resistance inintensive care unit setting. Ann Intern Med. 2001; 134: 298-314.
3. Gupta SK, Gupta P, Sharma P, Shrivastava AK, Soni SK. Emerging andre-emerging infectious diseases future challenges and Strategy. J Clin Diagn Res. 2012; 6:1095-100.
4. Seidman JC, Anitha KP, Kanungo R, Bourgeois AL, Coles CL. Riskfactors for antibiotic-resistant E. coli in children in a rural area. Epidemiol Infect. 2009; 137: 879-88
5. Safdar N, Maki DG. The commonality of risk factorsfor nosocomial colonization and infection with antimicrobial resistant Staphylococcus aureus, Enterococcus, Gram negative bacilli, Clostridium difficile and Candida. Ann Intern Med. 2002; 136: 834-844.
6. The impact of antimicrobial use on the emergence of antimicrobial-resistant bacteria in hospitals. Infect Dis Clin North Am. 1997;11:757-765.
7. Revathy Saravanan, Vinod Raveendaran. Antimicrobial resistance pattern in a tertiary care hospital: An observational study in Journal of Basic and Clinical Pharmacy. 56 : Vol. 4 | Issue 3 | June-August 2013.
8. World Health Organization. Community-based surveillance of antimicrobial use and resistance in resource-constrained settings. Report on five pilot projects. WHO/EMP/MAR/2009.
9. Narayanaswamy A, Mallika M. Prevalence and susceptibility of extended spectrum beta-lactamases in urinary isolates of Escherichia coli in a tertiary care hospital, Chennai-South India. Internet J Med Update. 2011; 6:39-43.
10. Umadevi S, Kandhakumari G, Joseph NM, Kumar S, Easow JM, Stephen S, et al. Prevalence and antimicrobial susceptibility pattern of ESBL producing gram negative bacilli. J Clin Diagn Res. 2011; 5:236-9.
11. Baby Padmini S and Appalaraju B. Extended spectrum βlactamases in urinary isolates of Escherichia coli and Klebsiella pneumoniae prevalence and susceptibility pattern in a tertiary care hospital; Indian J. Med. Microbiol. 2004; 22: 172–174.
12. Kumar M S, Lakshmi V and Rajagopalan R. Occurrence of extended spectrum, βlactamases among Enterobacteriaceae spp isolated at a tertiary care institute; Indian J. Med. Microbiol. 2006; 24: 208–211.

13. Gupta E, Mohanty S, Sood S, Dhawan B, Das B K and Kapil A. Emerging resistance to carbapenemns in a tertiaty care hospital in north India; Indian J. Med. Microbiol. 2006; 124: 95–98.
14. Sunanda Shrikhande, Sarfaraz Ahmed, Sandeep Bhoyar. Prevalence of antimicrobial resistance pattern of extended spectrum β-lactamase producing Klebsiella spp isolated from cases of neonatal speticaemia; Indian J. Med.Res. 2007; 125: 89–94.
15. Arora S, Saha S and Bal M. Imipenen-resistance among multidrug resistant clinical strains in urinary infections from Kolkata; Indian J. Med. Res. 2007; 125**:** 689–691.
16. Prashant K and Badrinath S. In vitro susceptibility pattern of Actinctobacter species to commonly use cephalosoporins, quinolones and aminoglycosides; Indian J. Med. Microbiol. 2004; 22: 97–103.
17. Sinha M and Srinivasa H. Mechanisms of Resistance to Carbapenems in Meropenem resistant Acinetobacter isolates from clinical samples; Indian J. Med. Microbiol. 2007; 25: 121–125.
18. Yavankar S P, Pardesi K R and Chopade B A. Species distribution and Physiological characterization of Acinetobacter Genospecies from Healthy Human Skin of Tribal population in India; Indian J. Med. Microbiol. 2007; 25: 336–345.
19. Munoz-Price L S and Weinstein R A. Acinetobacter Infection in current concepts; N. Engl. J. Med. 2008; 358: 1271–1281.