INTERNATIONAL RESEARCH JOURNAL OF PHARMACY
www.irjponline.com
ISSN 2230 – 8407

Research Article

STUDY OF ANTI-BACTERIAL ANTIBIOTICS RESISTANCE AMONG GRAM-POSITIVE/NEGATIVE ORGANISMS IN INTENSIVE CARE UNIT OF TERTIARY CARE TEACHING HOSPITAL

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Article Received on: 10/04/20 Approved for publication: 13/05/20

DOI: 10.7897/2230-8407.110554

ABSTRACT

Antibiotics are chemical substances derived from microorganism that destroys or inhibits the growth of other microorganisms and is used in the treatment of external or internal infections. The main objective is to identify and to analyze the resistant microbes to various antibacterial antibiotics in intensive care unit of tertiary care teaching hospital. It is an observational prospective study was conducted in 259 patients for a period of 6 months in various ICUs in a tertiary care teaching hospital. Patients who are at high risk of infection and prescribed with antibiotics were included and Patients admitted in Pediatrics, Neonatal and Oncology ICU's were excluded. The collected data were analysed with IBM. SPSS statistics software 23.0 Version. To describe about the data descriptive statistics frequency analysis, percentage analysis were used. The study population comprised of 118 (45.55%) male patients and 141 (54.4%) female patients. *E. coli* was found to be predominant in the study. The most sensitive organism for various prescribed antibiotics in the study was *Staphylococcus* (71.43%) and most resistant was *Proteus* (45.83%). *E. coli* showed more resistant to Ampicillin (50.64%) and sensitivity to co-trimoxazole (48.05%). For *Staphylococcus* Amoxicillin showed more resistance (57.14%) and teicoplanin showed more sensitivity (85.71%). In case of higher end antibiotics Teicoplanin showed more sensitivity (85.71%) towards *Staphylococcus* whereas Imipenem showed resistance (39.13%) towards *Acinectobacter*. Majority of Gram negative shows more drug resistance. Therefore, treatment of common bacterial infections needed to be guided by culture based antibiotic susceptibility testing's; individualisation of therapy and proper antimicrobial guidelines should be adopted to overcome resistance.

Keywords: Antibiotics, Sensitivity, Resistance, Monotherapy, Microorganism.

INTRODUCTION

Antibiotics, also called antibacterial, are among the most commonly prescribed drugs of any kind worldwide, Antibiotics are chemical substances derived from microorganism that destroys or inhibits the growth of other microorganisms and is used in the treatment of external or internal infections. Most of the antibiotics are modified structurally to alter its pharmacokinetic or stability and microbial properties so as to produce a most effective antibiotic, almost most of them can be synthesized in laboratories. Appropriate use of bacteriologic cultures and new molecular techniques such as DNA probes and polymerase chain reaction will help in selecting the most appropriate antibiotic and limit antibiotic resistance resulting from the selective pressure of unbridled antibiotic use. The emergence of pathogenic bacteria resistant to most antimicrobial agents has become a problem in modern science. In June 2000, the WHO warned that the level of resistance to the drugs used to treat common infectious disease is reaching a crisis point[1]. Bacteria have evolved complex mechanisms to resist the action of antibiotics. They exhibit resistance based on the elaboration of an enzyme that renders antibiotic ineffective. For example, some of the common beta lactamases include a penicillinase of *S. aureus*, which is responsible for penicillin – resistant *staphylococci* and TEM-1- beta lactamase in *E. coli* which mediate ampicillin resistance[2]. There is a growing evidence to suggest that increasing use of antibiotics result in increased rate of antibiotic resistance. Within hospitals units or hospitals, it has been possible to show decreased resistance associated with decreases use of antibiotics. However, it has been more difficult to show clearly a reduction in the resistance in the community associated with such changes. Although treatment of infections is often initiated empirically, the determination of bacterial susceptibility to an antimicrobial agent is an essential test in a clinical microbiology because of widespread resistance to all classes of antimicrobial agents. Bacteria are mostly resistant to more than one antimicrobial agent. It has 3 main mechanisms: Reduced permeability, acid efflux, multiple resistance genes[3]. Resistance to any class of antimicrobial agent may be encoded on a transposon. Transposons may integrate either in plasmids or bacterial chromosomes and may be present in multiple copies, thereby enhancing their effectiveness in the expression of resistance. However, the only prudent use of antibiotics and infection prevention measures will limit or even prevent the spread of antibiotic resistance[4].

MATERIAL AND METHODS

A prospective observational study was conducted in 259 patients in various ICUs at Sri Ramachandra medical college and Research Institute (SRMC and RI), Porur, Chennai, Tamil Nadu, India for the period of 6 month. The study protocol was approved by the institutional Ethics Committee of Sri Ramachandra Institute of Higher education and Research, Deemed to be

university, Chennai, Tamil Nadu and India (CSP/19/Nov/81/394). The data collected only after getting written informed consent from the patients in the various ICUs in a tertiary care teaching hospital. The study was conducted in compliance with the declaration of Helsinki, International conference of Harmonization-Good clinical practices guidelines (ICH-GCP). Patients who are at high risk of infection and prescribed with antibiotics were included and Patients admitted in Pediatrics, Neonatal and Oncology ICU's were excluded. The collected data were analysed with IBM. SPSS statistics software 23.0 Version. To describe about the data descriptive statistics frequency analysis, percentage analysis were used. To find the significance in categorical data Chi-Square test was used. In the above statistical tool the probability value 0.05 is considered as significant level.

RESULTS

The study population comprised of 118 (45.55%) male patients and 141 (54.4%) female patients. Out of 259 patients, *Acinectobacter sp* was found in 12 female (8.5%) and 11 male (9.3%), *Pseudomonas sp* was found in 10 female (7.1%) and 8 male (6.8%), *E. coli* was found in 41 female (29%) and 36 male (30.5%), *Klebsiella sp* was found in 30 female (21.3%) and 26 male (22%), *Enterococcus sp* was found in 15 female (10.6%) and 13 male (11%), *Staphylococcus sp* was found in 8 female (5.7%) and 6 male (5%), *Proteus sp* was found in 2 female (50%). Among various organisms, the most sensitive organism to different antibiotics was found to be *Staphylococcus sp* (71.43%) followed by *Enterococcus sp* (61.73%), *Klebsiella sp* (53.57%), *Proteus sp* (50%), *Acinectobacter* (48.36%), *E. coli* (44.65%) and *Pseudomonas sp* (36.36%) and the most resistant organism for various antibiotics was found to be *Proteus sp* (45.83%) subsequently *Klebsiella sp* (44.03%), *E. coli* (42.95%), *Pseudomonas sp* (42.42%), *Staphylococcus sp* (42.13%), *Enterococcus sp* (41.66%) and *Acinectobacter* (38.64%). The common organisms observed from various culture reports were shown in Table 1. The Resistance patterns of micro-organisms for various antibiotics were shown in Table 2. Among all higher end antibiotics in our study Teicoplanin showed more sensitivity (85.71%) towards *Staphylococcus sp* whereas Imipenem showed resistance (39.13%) towards *Acinectobacter sp.* The Resistance patterns of micro-organisms for various antibiotics were shown in Table 3. The comparisons of resistance to various organisms with regards to monotherapy and combination therapy were shown in Table 4. The comparison shows that combination drug therapy of Penicillin derivatives shows less resistance when compared to monotherapy. In case of cephalosporin derivatives, the monotherapy shows less resistance than combination therapy.

Table 1: Common organisms observed in various culture reports

Organism	Blood	Tracheal aspirate	Wound and pus	Urine	CSF	Total	
						N	%
Acinetobacter sp	16	5	1	-	1	23	8.88
Pseudomonas sp	-	2	2	14	-	18	6.94
E. coli	23	2	3	40	9	77	28.62
Klebsiella sp	17	-	-	32	7	56	22.77
Enterococcus sp	8	-	1	19	-	28	10.8
Staphylococcus sp	12	-	1	-	1	14	5.4
Candida sp	-	-	-	11	-	11	4.24
Proteus sp	4	-	-	-	-	4	1.54
Others	12	-	3	13	-	28	10.81
Total						**259**	**100**

Table 2: Resistance patterns of micro-organisms for various antibiotics

Antibiotics	*Acinectobacter sp* (N = 23)		*Pseudomonas sp* (N = 18)		*E. coli* (N = 77)		*Klebsiella sp* (N = 56)		*Staphylococcus Sp* (N = 14)		*Proteus sp* (N = 4)	
	n	%	n	%	n	%	n	%	n	%	n	%
Ampicillin	-	-	11	61.11	39	50.64	27	48.21	6	42.85	-	-
Cefotaxime	11	47.82	9	50	34	44.15	26	46.42	4	28.57	1	25
Ceftazidime	12	52.17	6	33.33	31	40.25	27	48.21	-	-	2	50
Cefepime	10	43.47	8	44.44	32	41.55	-	-	-	-	2	50
Piperacillin + tazobactam	07	30.43	6	33.33	29	37.66	22	39.28	5	35.71	-	-
Imipenem	09	39.13	7	38.88	30	38.96	-	-	-	-	-	-
Amikacin	10	43.47	9	50	33	42.85	-	-	-	-	-	-
Ciprofloxacin	13	56.52	10	55.55	31	40.25	21	37.5	5	35.71	-	-
Cefoperazone + ssulbactam	6	26.08	7	38.88	28	36.36	20	35.71	-	-	-	-
Linezolid	-	-	-	-	-	-	-	-	5	35.71	-	-
Vancomycin	-	-	-	-	-	-	-	-	-	-	-	-
Polymyxin B	-	-	-	-	-	-	-	-	-	-	1	25
Clindamycin	-	-	-	-	-	-	-	-	4	28.57	-	-
Erythromycin	-	-	-	-	-	-	-	-	3	21.42	-	-
Trimethoprim + sulfamethoxazole	-	-	-	-	30	38.96	-	-	8	57.14	1	25
Amoxicillin + Clavulanic acid	-	-	-	-	34	44.15	-	-	8	57.14	-	-
Gentamicin	-	-	4	22.22	37	48.05	-	-	7	50	3	75
Cefazolin	-	-	-	-	32	41.55	-	-	-	-	-	-
Teicoplanin	-	-	-	-	-	-	-	-	-	-	-	-
Nitrofurantoin	7	30.43	6	33.33	-	-	-	-	-	-	-	-

Table 3: Sensitivity patterns of micro-organisms for various antibiotics

Antibiotics	*Acinectobacter sp* (N = 23)		*Pseudomonas sp* (N = 18)		*E. coli* (N = 77)		*Klebsiella sp* (N = 56)		*Staphylococcus sp* (N = 14)		*Proteus sp* (N = 4)	
	n	%	n	%	n	%	n	%	n	%	n	%
Ampicillin	-	-	-	-	-	-	-	-	-	-	-	-
Cefotaxime	-	-	9	50	36	46.75	-	-	-	-	1	25
Ceftazidime	09	39.13	8	44.44	35	45.45	-	-	-	-	2	50
Cefepime	09	39.13	7	38.88	33	42.85	27	48.21	-	-	2	50
Piperacillin + tazobactam	10	43.47	8	44.44	37	48.05	31	55.35	-	-	3	75
Imipenem	12	52.17		-	-	-	-	-	-	-	-	-
Amikacin	08	34.78	6	33.33	36	46.75	31	55.35	-	-	1	25
Ciprofloxacin	9	39.13	4	22.22	36	46.75	28	50	-	-	2	50
Cefoperazone + sulbactam	12	52.17	9	50	38	49.35	32	57.14	-	-	3	75
Linezolid	-	-	-	-	-	-	-	-	11	78.57	-	-
Vancomycin	11	47.82	9	50	39	50.64	35	62.5	08	57.14	-	-
Polymyxin B	13	56.52	4	22.22	-	-	-	-	-	-	-	-
Clindamycin	-	-	-	-	-	-	-	-	10	71.42	-	-
Erythromycin	-	-	-	-	-	-	-	-	11	78.57	-	-
Trimethoprim + sulfamethoxazole	-	-	6	33.33	37	48.05	-	-	6	42.85	0	0
Amoxicillin + Clavulanic acid	-	-	-	-	36	46.75	-	-	-	-	1	25
Gentamicin	12	52.17	9	50	34	44.15	-	-	-	-	1	25
Cefazolin	-	-	-	-	33	42.85	-	-	-	-	1	25
Teicoplanin	-	-	-	-	-	-	-	-	12	85.71	-	-
Nitrofurantoin	-	-	-	-	34	44.15	-	-	-	-	-	-

Table 4: Comparison of resistance between monotherapy and combination therapy

S. No.	Species	Type	Penicillin	Cephalosporin
1	*Acinetobacter sp*	M	0	33
2	*Pseudomonas sp*	M	11	23
3	*E. coli*	M	39	129
4	*Klebsiella sp*	M	27	53
5	*Enterococcus sp*	M	8	15
6	*Staphylococcus sp*	M	6	4
7	*Acinetobacter sp*	C	7	6
8	*Pseudomonas sp*	C	6	7
9	*E. coli*	C	63	28
10	*Klebsiella sp*	C	22	20
11	*Enterococcus sp*	C	14	0
12	*Staphylococcus sp*	C	13	0

DISCUSSION

An observational study was observed in 259 patients for the period of six monthin various ICUs of tertiary care teaching hospital. A similar observational study was conducted from Saravanan and Raveendaran for a period of 1 year with 999 patients in a tertiary care hospital[6]. In this study there were more female patients 54% than male patients 46%. This in not in concordance with the observation study conducted by Javiya VA *et al* reported that out of 276 patients 62.5% were male and 37.5% were female patients[8]. In our study more organisms have been isolated from urine culture (49.8%), followed by blood (35.5%), tracheal aspirate (3.4%). But in a study conducted by Lockhart *et al* reported that more organisms were isolated from respiratory tract (52.1%) followed by urine (17.3%), blood (14.2%)[5]. Among various organism isolated from the study *Staphylococcus sp* (N = 14) showed sensitivity to Clindamycin (71.42%). This is in contrast to the study conducted by Rathod V S *et al* recorded that *staphylococcus sp* showed resistance to Clindamycin by (64.55%)[12]. Similarly, in case of Sensitivity for *K. pneumoniae* (N = 56) drug Amikacin (55.3%) accounted most which is in accordance with the study by Abdulrahman Abdulla Kader *et al* showed sensitivity by (62%)[8]. In this study *staphylococcus sp* showed highest resistance towards Piperacillin tazobactam (35.71%) which is not in accordance with the study conducted by Lockhart *et al* were *K. pneumoniae* showed higher resistance towards Piperacillin (35.32%)[5]. In this study *P. aeruginosa* showed highest resistance towards ciprofloxacin (55.55%). A similar study conducted by Haken Hanberger *et al* reported that *P. aeruginosa* showed more resistance to ciprofloxacin (44.4%)[11]. A study conducted by Lockhart *et al* reported that (77.2%) of *Acinetobacter sp* were susceptible to ceftazidine but our study showed only (39.13%) susceptibility towards ceftazidine[5]. Another study conducted by Karlowsky *et al* reported that *Pseudomonas sp* showed more sensitivity towards Amikacin (80%) a contrary report obtained from our study were *pseudomonas sp* showed more sensitivity to Piperacillin tazobactam (50%), Cefotaxime (50%)[13]. In this study *K. pneumoniae* (N = 56) showed more susceptibility towards a higher end antibiotics Vancomycin (62.5%). A conflicting study was seen in Akram M *et al* were *K. pneumoniae* showed more susceptibility towards Imipenem (85%)[9]. A study conducted by Atul Kothari and Vishal Sagar reported that high end antibiotic Piperacillin tazobactam showed a (90.3%) susceptibility towards *E. coli* whereas in our study only (48.05%) of susceptibility was observed[10]. Lockhart *et al* conducted a study in which *Acinetobacter sp* showed high susceptibility to a high-end antibiotic like Imipenem (88%) whereas in our study (52.17%) have been seen susceptible to Imipenem[5]. A study by Javiya VA *et al* detailed that monotherapy of Penicillin, Cephalosporin,

Fluoroquinolones, tetracyclines and macrolides confirmed marked resistance than combination therapy. Similar observations have been found towards penicillin but in case of Cephalosporins, the combination therapy shows more resistance than monotherapy which is contrary to the study[7].

CONCLUSION

The study revealed that *E. coli, Klebsiella sp, Acinectobacter sp, Pseudomonas sp, Enterococcus sp, Staphylococcus sp* and *proteus* were the most common isolates in clinical samples. Isolates showed high levels of resistance to Ampicillin, Imipenem, Co-trimoxazole and Gentamicin and showed sensitivity to Teicoplanin, Linezolid, Erythromycin and Clindamycin. Majority of Gram-negative organism showed more drug resistance than Gram positive isolates. Therefore, treatment of common bacterial infections needed to be guided by culture based antibiotic susceptibility testing; Individualisation of therapy and proper antimicrobial guidelines should be adopted to overcome resistance.

ACKNOWLEDGEMENT

The authors express sincere thanks to all the clinical staffs in ICUs for their constant encouragement to carry out this work.

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Cite this article as:

K. Venkata Sai Kavya *et al*. Study of anti-bacterial antibiotics resistance among gram-positive/negative organisms in Intensive care unit of Tertiary Care Teaching Hospital. Int. Res. J. Pharm. 2020;11(5):53-56 http://dx.doi.org/10.7897/2230-8407.110554

Source of support: Nil, Conflict of interest: None Declared