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Research Article

MICRORESEARCH ON ANTIMICROBIAL RESISTANCE IN TERTIARY CARE HOSPITAL OF ANDHRA PRADESH

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ABSTRACT

Objective: In this study, we aim to investigate the prevalence of antimicrobial resistance (AMR) in an isolated bacteria from the infected population admitted in a tertiary care hospital. By this, we can the evaluate resistance load and be aware of the future danger of antibiotic resistance.

Methods: A descriptive study was conducted on a total of 127 patients admitted to tertiary care hospitals of Andhra Pradesh between September 2023 and April 2024, respectively. Bacteria isolated were tested for antibiotic resistance with 13 different antibiotics by disk diffusion methods. A comparative analysis was performed to identify the differences in resistance rate among the bacterial strains and observed the multiple antibiotic resistance load in the individual bacteria.

Results: Our descriptive analysis reveals varying degrees of antibiotic resistance in the organisms we studied. Twenty-seven of the 127 samples, we had in total had no evidence of bacterial resistance. In the specific sample area we used, the prevalence of antibiotic resistance was 78.7%, with amoxicillin having the highest rate of resistance at almost 55%, and the Chi-square test's p=0.001 showed a strong correlation between antibiotic resistance and bacteria isolated.

Conclusion: Our finding revels that there is increasing AMR load in South India district. Those resistance reports indicate the urgent need of antimicrobial stewardship coordination program and start the surveillance program to combat the antibiotic resistance on the general population. Furthermore, microsurveillance should be conducted in every district to detect antibiotic resistance load and develop new treatment strategies.

Keywords: Antibiotic resistance, Antibiotic stewardship program, Hospital of Andhra Pradesh, Micro survey.

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INTRODUCTION

Only antibiotics, which have been around for a century and can destroy disease-causing bacteria, can help treat infectious conditions caused by bacteria that otherwise could result in fatal complications or even death [1]. Without antibiotics, these bacteria could have the ability to harm or kill people. Following the discovery of antibiotics, a golden age of antibiotic use began, saving many lives from bacterial infections. However, as more and more instances of antibiotic resistance are being documented, it seems that the era of antibiotics' relative prosperity is coming to an end [2]. Due to the increasing antibiotic resistance, we have fewer options for deciding which drug is best for a certain bacterial infection condition [3].

The world's health is at risk from this, especially in India where antibiotic usage is widespread and surveillance systems are lacking to identify the problem [4]. Studies show that treating infections brought on by bacteria resistant to antibiotics is more challenging. The ability of physicians to cure major infections has been put at risk this century due to the widespread rise of antibiotic resistance [5]. The WHO as well as a number of other parties had been made aware of this problem which has developed a coordinated effort by creating an AMR control action plan [6].

According to surveys and studies on antibiotic resistance carried out by various organizations, India is the world's biggest consumer of antibiotics [7]. A large portion of these drugs are used in agriculture and animal husbandry, which are then consumed by the general public [8]. In addition, the widespread distribution of antibiotics without a prescription has played a role in the emergence of antibiotic resistance in India. Therefore, the use of resistance tests and culture interventions during inpatient stays aids in our understanding of the incidence of antibiotic resistance in the population, which is important information for developing and enhancing treatment plans.

In addition, the WHO 2023 report revealed that in 72 countries, 42% of bacteria were resistant to third-generation cephalosporin drugs. This finding alerted people to the widespread use of antibiotics without any effective strategies. It also revealed that, in addition to bacteria, there are drugs resistant to tuberculosis and malaria. According to such reports, if we do not start an action plan now, the world will enter an era of bacterial resistance in the future, making it impossible to treat bacterial infections. To alert to this crisis, the May 2015 World Health Assembly adopted a global action plan on antimicrobial resistance (AMR), which action plan has main focuses on preventing antibiotic resistance by developing awareness regarding antibiotic resistance through communication, training, and education [8].

According to Centers of Disease Control and Prevention, the antibiotic stewardship program should follow some core elements which include [9].

1. The hospital should be dedicated to providing necessary financial and technical support.
2. Coordinating of pharmacist and physician in program management and outcome.
3. A co-leader should be a previous drug expert pharmacist.
4. Continuous implementation and audit of such programs give a prospective view.
5. Continued tracking of the antibiotic prescribed helps for improvement of outcomes.

6. Regular reporting of antibiotic use and resistance to all the healthcare worker involve for patient care.
7. Educating the hospital staff about the ADR of antibiotics, antibiotic resistance, and prescribing.

Some other studies show that the extensive development of resistant bacteria and viruses among people is also likely due to population growth, crowding, migration, and urbanization, which promote the transmission of resistant microorganisms [10,11]. In the upcoming years, the spread of bacteria that are resistant to antibiotics may trigger a global epidemic if they are not stopped at an early stage of transmission or if they continue to gain resistance. The government and health organizations need to be fully involved in ground-level research and education about antibiotic resistance [12].

Our aim of the study is to investigate the prevalence of antibiotic resistance in the isolated bacterial strains from the patients admitted in ward of tertiary care hospitals. By analyzing those data, we tend to find out the most common resistant strains and their patterns of resistance to various antibiotics. This research will guide us for antibiotic stewardship programs, improving clinical outcomes and persisting the effectiveness of antibiotic for the coming generation. This information also helps for gathering knowledge and awareness of antibiotic resistance among the population.

METHODS

Our descriptive cross-sectional study included all patients diagnosed with bacterial infections and in need of antibiotic treatments. It was carried out in a tertiary care hospital in Andhra Pradesh between September 2023 and April 2024, respectively. Samples from the affected person were collected, including blood, sputum, urine, and wound samples. The bacterium was then isolated, and resistance and sensitivity tests were carried out using disk diffusion methods. Patients who met inclusive, such as being willing to give consent and not have been previously exposed to antibacterial agents, were included in the sample collection process. The exclusive criteria, such as those who had previously been exposed to antibiotics, had a medical condition that affected their immune system, or were taking immunosuppressive medication, were excluded from participating in the study. Samples were delivered individually to the laboratory for analysis, and the report results were used in our investigation.

The antibiotic substitutability test was conducted using the Kirby-Bauer disk diffusion techniques test and typical clinical practice antibiotics such as penicillin, cephalosporin, fluoroquinolones, and carbapenem. The clinical and laboratory guidelines of the institution were followed in interpreting the results. To investigate the incidence of antibiotic resistance in the prevalent bacterial strain found in the Andhra Pradesh district of East Godavari, our study focuses on major pathogens, including *Escherichia Coli*, *Staphylococcus*, *Klebsiella pneumonia*, and others. A descriptive cross-section study design was used to understand the pattern of antibiotic resistance in bacteria obtained from a patient admitted to a tertiary care hospital. Every detected bacterium's antibiotic susceptibility and resistance were noted and examined in detail. The formula used to calculate the prevalence was the total number of antibiotic resistance discovered divided by the total number of cases taken and multiplied by 100.

$$\text{Prevalence percentage} = \frac{\text{Total number of antibiotic resistance}}{\text{Total no. of cases taken}} \times 100$$

Antibiotic resistance values <15 are regarded as having a low prevalence, whereas values >15 are regarded as having a high prevalence. As part of the descriptive analysis of the data, the percentages of isolates resistant to each antibiotic were looked at to determine the prevalence of antibiotic resistance in this area. A comparison analysis was conducted using SPSS 20.0 to analyze the resistance rates of various antibiotics. A Chi-square test was conducted with a significant level set at 0.05, and the results were statistically presented in tables and graphs to provide a broad understanding of the patterns of antibiotic resistance in South India.

RESULTS AND DISCUSSION

The bacteria that we tested have different degrees of antibiotic resistance, according to our descriptive analysis. We had 127 total sample out of this 27 of them show no signs of bacterial resistance.. The bacteria that showed the highest resistance rates among those that were identified were ampicillin (70%), amoxillin+clavum (49%), azithromycin (33%), nitrofurantoin (23%), and ceftriaxone (27%) as shown in Table 3. The bacteria that showed the lowest resistance were cefepime, cefotaxime + clavulanic, and vancomycin, which were <10%. Tables 1 and 2 show the fraction of antibiotic resistance in the isolated bacteria, which included 55 g positive (43.3%) and 72 g negative (56.7%) samples. These results indicated a increasing prevalence of AMR in the south Indian population. Every bacterium can withstand 4.64 antibiotics on average, compared to the antibiotics listed below. The graphical illustration of microbial resistance to multiple antibiotics is a critical issue that needs to be resolved faster (Figure 1). This suggests that bacteria are becoming multidrug resistant, or resistant to several antibiotics.

Using a prevalence formula to examine the prevalence of antibiotic resistance in our particular sample area, we discovered a notably high prevalence rate of 78.7%. To examine the relationship between antibiotics and bacteria, we also ran a Chi-square test. The resultant $p=0.001$, which is statistically significant and suggests that there is a high likelihood that a particular bacteria will become resistant to that antibiotic. This could be the result of overprescribing or overusing the same antibiotic. This result suggests that all therapeutic areas require the implementation of new antibiotic stewardship practices. A nurse, doctor, or pharmacist who provides healthcare should also be involved in raising public knowledge of the risks associated with antibiotic resistance and its expanding issue. Our study emphasizes the necessity of intervention measures that will assist maintain the efficacy of antibiotics for future generations while also controlling resistance in South India.

AMR caused 1.27 million deaths in the US in 2019 [12]. By 2050, AMR bacteria may be directly to blame for 10 million deaths worldwide, posing a threat to public health worldwide [13]. The World Health Organization states that the overuse and abuse of antimicrobial agents in people, animals, and plants is the main source of AMR. Moreover, there are not enough government agencies, monitoring programs, or studies in place to limit or curtail the use of antibiotics. This seems to be going to cause a worldwide health crisis in the near future along with a significant financial loss.

Since antibiotic resistance is so common, effective antibiotic stewardship programs are desperately needed in South India, as demonstrated by our observations. The average isolated bacteria that we looked at have multidrug resistance, according to our findings. Antibiotic usage, misuse, and over-availability without a prescription are all possible drug-related variables that further exacerbate this illness. Environmental factors include low socioeconomic status, which makes patients prefer non-medical practitioners over specialists, inadequate infection control protocols, ignorance of environmental hygiene, excessive use of pesticides in food products, and ignorance of the risks associated with antibiotic resistance.

In the sample of hospitals in South India that we collected, we found that 78.7% of the patients were resistant to antibiotic. Salman *et al.*'s report reported 100% resistance to cefotaxime; [14]. However, our study found that 14% of the sample had cefotaxime resistance, indicating that cefotaxime resistance is still in its early stages. In contrast, Hamzah *et al.*'s report revealed that 14.5% of urine samples had amoxicillin

Table 1: Antibiotic susceptibility test against different species of Gram-positive bacteria

Classes of antibiotic	Antibiotic	Gram-positive bacteria (%)									
		Streptoccalaureus		*Streptococcal pyogenes*		Candida species		*Streptococcus pneumonia*		*Staphylococcus* Saprophytes	
		R	S	R	S	R	S	R	S	R	S
Penicillin	Amoxicillin	20 (80)	5 (20)	3 (60)	2 (40)	3 (37.5)	5 (62.5)	4 (57)	3 (43)	5 (50)	5 (50)
	Amoxicillin+ clavulanic acid	23 (92)	2 (8)	3 (60)	2 (40)	2 (25)	6 (75)	2 (28.5)	5 (71.5)	2 (20)	8 (80)
	Piperacillin	7 (28)	18 (72)	1 (20)	4 (80)	1 (12.5)	7 (87.5)	0	7 (100)	2 (20)	8 (80)
Aminoglycoside	Amikacin	23 (92)	2 (8)	2 (40	3 (60)	1 (12.5)	7 (87.5)	0	7 (100)	-	-
	Gentamicin	17 (68)	8 (32)	1 (20)	4 (80)	3 (37.5)	5 (62.5)	-	-	-	-
Cephalosporin	Cefoperazone+ Sulbactum	0	25 (100)	0	5 (100)	1 (12.5)	7 (87.5)	0	7 (100)	2 (20)	8 (80)
	Cefoxitin	1 (4)	24 (96)	1 (20)	4 (80)	1 (12.5)	7 (97.5)	1 (14.2)	6 (85.8)	-	-
	Cefepime	2 (8)	23 (92)	2 (40)	3 (60)	2 (25)	6 (75)	3 (42.8)	4 (57.2)	-	-
	Cefotaxime	0	25 (100)	3 (60)	2 (40)	4 (50)	4 (50)	-	-	4 (40)	6 (60)
	Ceftriaxone	8 (32)	17 (68)	3 (60)	2 (40)	5 (62.5)	3 (37.5)	6 (85.7)	1 (14.3)	8 (80)	2 (20)
Fluoroquinolones	Ciprofloxacin	20 (80)	5 (20)	3 (60)	2 (40)	7 (87.5)	1 (12.5)	3 (42.8)	4 (57.2)	7 (70)	3 (30)
	Levofloxacin	-	-	0	5 (100)	-	-	-	-	-	-
Macrolides	Azithromycin	0	25 (100)	1 (20)	4 (80)	2 (25)	6 (75)	4 (57.1)	3 (42.9)	5 (50)	5 (50)
	Erythromycin	-	-	1 (20)	4 (80)	-	-	-	-	4 (40)	6 (60)
Nitrofuran	Nitrofurantoin	0	25 (100)	-	-	3 (37.5)	5 (62.5)	-	-	-	-
Others	Clindamycin	15 (60)	10 (40)	-	-	4 (50)	4 (50)	6 (85.7)	1 (14.3)	-	-
	Vancomycon	2 (8)	23 (92)	-	-	-	-	-	-	-	-

Table 2: Antibiotic susceptibility test against different species of Gram-negative bacteria

Classes of Antibiotic	Antibiotic	Gram-negative bacteria (%)							
		Escherichia coli		*Klebssiella pneumonia*		*Klebssiella oxytoca*		*Acinetobacter baumannii*	
		R	S	R	S	R	S	R	S
Penicillin	Amoxicillin	17 (100)	0	20 (71.4)	8 (28.6)	10 (66.6)	5 (33.4)	6 (50)	6 (50)
	Amoxicillin+ clavulanic acid	15 (88.2)	2 (11.8)	15 (53.5)	13 (46.5)	13 (86.6)	2 (13.3)	6 (50)	6 (50)
	Piperacillin	15 (88.2)	2 (11.8)	10 (35.7)	18 (64.3)	8 (53.3)	7 (46.7)	-	-
Aminoglycoside	Amikacin	10 (58.8)	7 (41.2)	5 (17.8)	22 (82.2)	5 (33.3)	10 (66.6)	-	-
	Gentamicin	-	-	8 (28.5)	20 (71.5)	5 (33.3)	10 (66.6)	-	-
Cephalosporin	Cefoperazone+ Sulbactum	8 (47)	9 (53)	2 (7.14)	25 (92.86)	2 (13.3)	13 (86.6)	2 (16.6)	10 (83.4)
	Cefoxitin	10 (58.8)	7 (41.2)	8 (28.5)	20 (71.5)	3 (45)	12 (55)	3 (25)	9 (75)
	Cefepime	11 (64.7)	6 (35.3)	5 (17.8)	22 (82.2)	2 (13.3)	13 (86.6)	-	-
	Cefotaxime	10 (58.8)	7 (41.2)	8 (28.5)	20 (71.5)	1 (6.6)	14 (93.3)	-	-
	Ceftriaxone	15 (88.2)	2 (11.8)	4 (14.2)	24 (85.8)	8 (53.3)	7 (46.7)	6 (50)	6 (50)
Fluoroquinolones	Ciprofloxacin	16 (96.11)	1 (3.89)	20 (71.4)	8 (28.5)	12 (80)	3 (20)	7 (58.3)	5 (41.7)
	Levofloxacin	10 (58.2)	7 (41.8)	15 (53.5)	13 (46.5)	-	-	3 (25)	9 (75)
Macrolides	Azithromycin	-	-	-	-	-	-	2 (16.6)	10 (83.4)
	Erythromycin	-	-	-	-	-	-	-	-
Nitrofuran	Nitrofurantoin	14 (82.3)	3 (17.7)	21 (75)	7 (25)	5 (33.3)	10 (66.7)	-	-
Others	Clindamycin	16 (98.11)	1 (1.89)	15 (53.5)	13 (46.5)	-	-	7 (58.3)	5 (41.7)
	Vancomycon	-	-	-	-	-	-	-	-

resistance [15]. The findings indicate that the southern districts of India are experiencing the early stages of antibiotic resistance. If the government and health agencies take proactive measures to address this issue, antibiotic resistance can be controlled in its early stages. The results also show that less common antibiotics, like vancomycin, have some level of resistance in the district. Vancomycin, for example, has 1.5% of resistance, while a research report from Nepal found no resistance to the drug [16].

India has been referred to by numerous researchers as the world's AMR capital. In India, AMR is becoming more prevalent due to factors such as malnourishment, overcrowding, poverty, and illiteracy. Researchers advise that tight regulations be put in place to restrict the distribution of antibiotics over the counter without a prescription and that the government should enhance the doctor-to-patient ratio to better connect professionals with the patient population [17].

A 2010 survey found that 12.9×10 units of antibiotics, or 10.7 units per person, were consumed in India [18]. The report also found that the amount of antibiotics sold at retail increased by 23% between 2000 and 2010 and that this number may have doubled by the present [19]. Antimicrobial agents are not only used extensively for human consumption; they are also used extensively in animals to prevent disease without the proper dosage calculation [20]. People who consume animal products also contribute to the rise in antibiotic resistance cases, which is predicted to double by 2030. In addition, the standard regulation of food safety does not suggest the use of antibacterial agents in chicken; nevertheless, poultry farms do not

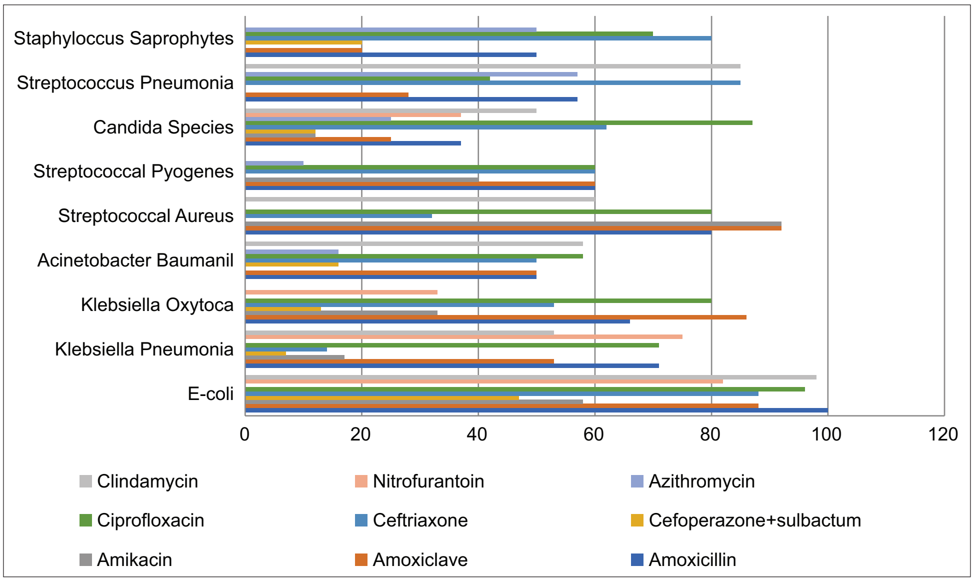

Fig. 1: Frequency of bacterial agent showing resistance to the specific antimicrobial agent. Where 100% frequency shows the highest prevalence of resistance and 0% represents there is no antibiotic resistance with that specific antibiotic

Table 3: Resistance of antimicrobial in number (percentage) of both Gram-negative and positive

Antibiotics	Resistance No. (%)
Amoxicillin	70 (55.11)
Amocicillin+clavulanic acid	49 (38.5)
Piperacillin	15 (11.8)
Amikacin	18 (14.17)
Gentamicin	23 (18.11)
Cefoperazone+Sulbactum	9 (7)
Cefoxitin	10 (7.8)
Cefepime	11 (8.6)
Cefotaxime	18 (14.17)
Ceftriaxone	27 (21.25)
Ciprofloxacin	22 (17.32)
Levofloxacin	16 (12.5)
Azithromycin	33 (25.9)
Erythromycin	5 (3.9)
Nitrofurantoin	23 (18.11)
Clindamycin	26 (20.4)
Vancomycin	2 (1.5)

follow this recommendation, which leads to an increase in antibiotic resistance in animals, as reported by researcher Christian on his article [21].

Our study, which involved 127 individual-specific samples – a small sample size compared to the entire Andhra Pradesh district population – showed a significant number of antibiotic resistance as well as multiple antibiotic resistance by different bacteria, as indicated in Tables 1 and 2. Both Gram-positive and negative bacteria displayed multiple drug resistance, which is concerning because there are few new antibiotics available on the market and few research facilities are producing new antibiotics. The FDA reports that a new antibiotic called Zevtera (Ceftobiprolemedocaril sodium for injection, effective against *Staphylococcus aureus*) will be approved by April 2024 [22]. Based on this report, we can conclude that the number of antibiotics approved and available for use indicates an adverse relationship with drug resistance, indicating an overabundance of antibiotics that may pose a therapeutic challenge in the future.

CONCLUSION

Our primary goal in conducting this study is to raise public and healthcare provider's awareness of antibiotic resistance. Despite the small sample size in our study, the high frequency of both single and multidrug resistance raises concerns because there has not been much progress in the discovery of new antibiotics. The public has to be informed that improper usage of antibiotics can result in a new epidemic in the coming years. To prevent AMR for future generations, we also need to continue research, implement effective antibiotic stewardship programs, and raise public awareness of the issue of antibiotic resistance.

Limitation

- Our study was conducted in a limited sample size in a short period of time which do not represent the whole population of the state
- This research was conducted in a single tertiary care hospital, which limits the generalization of the patient population
- Our research focuses on antibiotic resistance and does not explore the factors contributing it.
- Our data includes only the infected individual patient sample that was admitted to the hospital was obtained, there may be a high rate of resistance.

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