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iajpb.editor@gmail.com
editor@iajpb.com

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XDR Monitoring at a University Medical Center: An Intermittent Observational Study

M.Chandana, P.Sindhu, S.Divya & V.Sireesha

ABSTRACT

Background: In order to analyze the rising trend of XDR colonized/infected individuals from both the community and hospital settings, the research zeroed in on patients with XDR organisms and risk factors. The research used a tertiary care hospital's periodic observational study as its methodology. Previous hospital-identified changes in antibiotic resistance patterns informed the periodic duration selection. December 2018–January 2019 and May 2019–June 2019 and November 2019–December 2020 were the selected time periods. Even though it was a prospective research, in order to get the data, there was no sampling or experimentation. The patient's medical record and the microbiology lab provided all the necessary facts. The results show that, out of the entire culture material, 5-6% were XDR isolates. Among the organisms we examined, Klebsiella accounted for 70%. As time went on, the number of infected patients increased, although colonization was initially greatest. Prolonged exposure to antibiotics (>50%), prior hospitalization (>40%), catheter (70%), and advanced age (mean age-58.2 years) were the most significant risk variables acknowledged. The average length of stay in the hospital was three times longer than that of a typical hospital stay. Despite several prospective studies looking at the link between antibiotic exposure details and resistance development, it has proven difficult to isolate specific parameters relating to previous antibiotic exposure and resistance.

Key words: antibiotic resistance, XDR, infection, colonization.

INTRODUCTION/ BACKGROUND

There has been a concerted attempt to reduce the prevalence of antibiotic resistance, which is a major public health concern on a global scale. The CDC first advocated for antibiotic stewardship programs in 2014, which aim to optimize antibiotic usage via coordinated evidence-based initiatives.1Hospitals have been required by the Joint Commission to establish antibiotic stewardship programs since 2017, and global leaders committed to fight the development of resistance at the 71st UN General Assembly in 2016. But thus far, stewardship initiatives have mostly targeted medical professionals and drugstores.Antibiotic resistance mechanisms are being acquired by multidrug-resistant organisms and their increasing circulation inside the hospital, according to the research results of Giancarlo et al. (2018).2Clinicians and epidemiologists still face challenges in managing and regulating measures based on the amount of drug resistance to antibiotics, which is determined experimentally and regularly via the analysis of isolate antibiograms.3 A major public health problem, especially in healthcare facilities, is the exponential growth of bacteria and other microorganisms that are resistant to antibiotics, which has been linked to the ever-increasing usage of these drugs. It seems that antibiotic-resistant organisms are

Department of Pharmaceutics,
Ratnam Institute of Pharmacy, Pidathapolur (V),
Muthukur (M), SPSR Nellore Dt.- 524346 A.P., India.

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genetically and physiologically well-suited to generate devastating illnesses that are difficult to manage due to the limited therapeutic choices available.4, 5Numerous improper medications were initiated due to a small rise in the number of asymptomatic patients with XDR isolates in culture sensitivity reports. There was a high risk of contamination, which might have led to an inaccurate result and the improper antibiotic treatment. Therefore, a prospective study of XDR patients was conducted to address the issue. As the use of more expensive antibiotics increased, so did the number of XDR isolates.The development of new anti-infective agents is sluggish, and the incidence of drug-resistant strains is on the rise. There will likely be an increase in the number of illnesses that are not curable in the near future.5

individuals with XDR organisms, along with other characteristics such as treatment type, were the subject of this research, which aimed to analyze the rising trend of XDR colonized individuals in both community and hospital settings.

METHODOLOGY

A tertiary care hospital served as the setting for the study's periodic observational component. Previous hospital-identified changes in antibiotic resistance patterns informed the periodic duration selection. November 2018–December 2019; May 2019–June 2019; November 2019–December 2020; and November 2020–December 2020 were the chosen research periods. Researchers opted for a periodic research schedule so they could see any major changes in the resistance pattern. Even though it was a prospective research, in order to get the data, there was no sampling or experimentation. The patient's medical record and the microbiology lab provided all the necessary facts. Researchers were the only ones who could access the data, which prevented any other parties from seeing the raw material. The research comprised in-patients whose XDR isolates were verified by culture. Due to challenges in obtaining the necessary data, we did not include outpatients. A short-term pilot study validated the data collecting form utilized for data procurement. This survey takes into consideration a wide range of factors, including demographics, facts about the isolate, therapy, history of antibiotic exposure, length of hospital stay, details about the specimen, and more.
We used Excel for all of our calculations and analyses. Statistical analysis was performed on the data collected throughout the research using central frequencies and percentages.

RESULTS

Table 1 displays the fundamental characteristics, which include demographics, total sample, and past hospitalization. Over the course of this investigation, 27,840 patients were admitted to various healthcare facilities. In all, 11444 specimens yielded about 209 XDR isolates. Over all time periods, the most common XDR were found in male patients who were 60 years old or older. Many of these individuals had recent hospitalizations (within the last 90 days).

In Figure 1, we can see that, with the exception of the months of May and June 2020, the number of patients who were exposed to antibiotics in the last 90 days was larger than the number of patients who were not exposed throughout all study periods. More over half of the other periods were exposed. In May and June of 2020, consumption was down because of the COVID epidemic.

Prior admission antibiotic use revealed a preponderance of cefoperazone/sulbactam, meropenem, levofloxacin, and nitrofurantoin. In addition to other antibiotics, those with certain restrictions were also administered. Antibiotic consumption was lower in May and June 2019 compared to previous seasons (Figure 2).

The study's first, second, and fourth phases all pointed to urinary tract infections as the leading cause of infection. There was a significant incidence of skin and soft tissue infections during the third and fifth weeks. The number of XDR isolates found in infections other than urinary tract infections and skin/soft tissue infections was lower. After 27.41% in the first phase, 16.12% in the second, 31.11% in the

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third, 18.75% in the fourth, and 33.33% in the fifth were prior XDR isolates with the same organism. Within each phase, the percentage of previous XDR isolates containing distinct organisms increased: 4.8% in the first, 3.22% in the second, 2.22% in the third, 9.37% in the fourth, and 7.69% in the fifth. The percentage of patients having a history of multi-drug-resistant or extensively drug-resistant strains of the same organism was 35.9% in the most recent phase, rising to 19.35% in the previous phase, 16.12% in the second, and 6.67 percent in the third. In all phases except the first, when 67.2% of patients received urinary catheters, the percentage was above 75% (Table 2).

Antibiotics used during current admission of infection showed that meropenem was the most used antibiotic.

Table 1: Basic Parameters and demographics.

		Nov-Dec 2018	May-Jun 2019	Nov-Dec 2019	May-Jun 2020	Nov-Dec 2020
Total no of patients admitted		5898	6200	6185	4615	4942
Total of XDR patients		58(0.98%)	22(0.35%)	32(0.52%)	25(0.54%)	29(0.59%)
Total samples tested		2496	2625	2409	1887	2027
Total isolates obtained		905(36.2%)	956(36.4%)	726(30.1%)	589(31.2%)	628(31%)
Total XDR isolates		62(6.8%)	31(3.24%)	45(6.2%)	32(5.4%)	39(6.2%)
Age	≤18 years	1(1.72%)	-	-	-	2(6.9%)
	19-60 years	18(31.03%)	8(36.4%)	13(40.6%)	11(44%)	13(44.8%)
	>60 years	39(67.2%)	14(63.6%)	19(59.4%)	14(56%)	14(48.27%)
Gender	Male	34(58.6%)	15(68.2%)	20(62.5%)	16(64%)	21(72.4%)
	Female	24(41.37%)	7(31.8%)	12(37.5%)	9(28.12%)	9(31.03%)
No. of previous hospitalisations past 90 days	Zero	8(13.8%)	4(18.18%)	13(40.62%)	10(40%)	8(27.6%)
	One	29(50%)	12(54.54%)	12(37.5%)	11(44%)	9(31.03%)
	Two	16(27.59%)	3(13.63%)	7(27.87%)	2(8%)	9(31.03%)
	Three	4(6.9%)	4(18.18%)	-	2(8%)	3(10.3%)
	four	1(1.72%)	-	-	-	-

Abbreviations: Nov-November, Dec- December, Jun- June, IP- inpatients, OP-outpatients

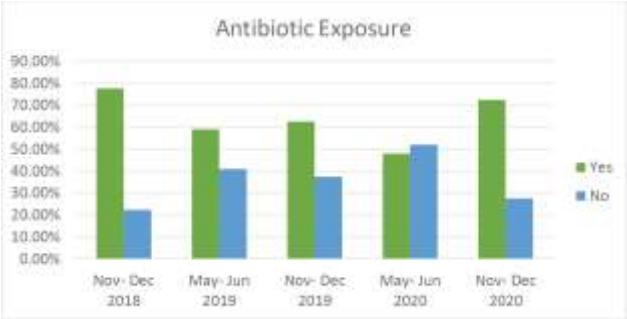

Figure 1: Antibiotic exposure in past 90 days.

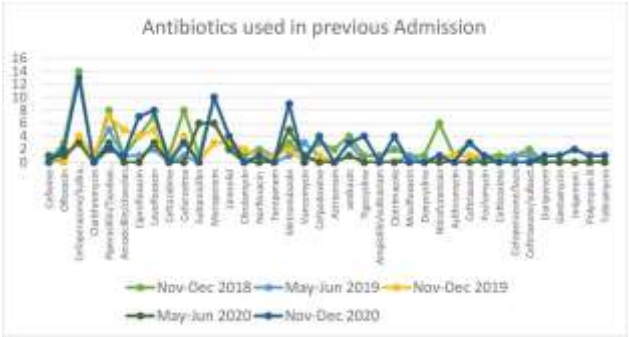

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Figure 2: Antibiotics used in previous admission.

In addition to cefoperazone/sulbactam, there are additional antibiotics such as ofloxacin, metronidazole, polymyxin B, and Levofloxacin. The most antibiotic prescriptions were recorded in the months of November and December 2018. In Figure 3, The XDR organisms that were found were klebsiella, pseudomonas, Acinetobacter, E. coli, Enterobacter, and Citrobacter. The percentage of Klebsiella bacteria in these mainly isolated organisms varied among phases: 62.9%, 87.1%, 62.22%, 62.50%, and 76.62%. In May–June 2019, Citrobacter had the lowest identification rate at 3.22%. Colonization or contamination is characterized by the absence of symptoms in the patient, in contrast to infected people. Most of the isolates that were shown to be infectious were originally contaminated or colonized, and as the experiment progressed, they exhibited signs of increasing infection. As a risk factor for XDR, 66 individuals were determined to have a community-acquired illness, while 103 patients had extended exposure to antibiotics. The most common way that infections may spread was via healthcare settings, including hospitals. Throughout all stages, the therapy was determined to be suitable for all instances with the exception of eleven. The typical length of stay for a patient is about 4 days, whereas those with XDR isolates spent 11–15 days in the hospital. (Section 3)

Antibiotics such as meropenem, tigecycline, polymyxin B, colistin, fosfomycin, and cefoperazone/sulbactam were often prescribed to patients with XDR isolation. In Figure 4,

DISCUSSION

Patients who are infected with XDR often have an increased risk of prolonged illness and mortality. The cost of care for their patients can be more than double when compared to those without.[6] In our study, a total of less than 1% of patients had XDR in all periods and it was less than 0.6% in all other periods except

Table 2: Type, sample, source and history of infection.

		Nov-Dec 2018	May-Jun 2019	Nov-Dec 2019	May-Jun 2020	Nov-Dec 2020
type of infection	Urinary tract infection	33(53.2%)	14(45.16%)	14(31.11%)	11(34.37%)	9(23.07%)
	Skin and soft tissue infection	10(16.13%)	2(6.45%)	22(48.89%)	6(18.75%)	22(56.41%)
	Respiratory tract infection	9(14.52%)	9(29.03%)	2(4.44%)	10(31.25%)	3(7.69%)
	Urosepsis	4(6.45%)	1(3.22%)	1(2.22%)	-	-
	Blood stream infection	3(4.8%)	5(16.12%)	6(13.33%)	1(3.12%)	5(12.82%)
	Others*	3(4.8%)	-	-	4(12.5%)	-
Culture sample	Urine	34(54.83%)	14(45.16%)	14(31.11%)	11(34.37%)	9(23.07%)
	Pus	12(19.35%)	2(6.45%)	22(48.89%)	9(28.12%)	19(48.71%)
	Blood	4(6.45%)	6(19.35%)	7(15.55%)	1(3.12%)	5(12.82%)
	Sputum	9(14.52%)	9(29.03%)	2(4.444%)	3(9.37%)	3(7.69%)
	Others**	3(4.8%)	-	-	8(25%)	3(7.69%)
XDR history	Previous XDR isolate with same organism	17(27.41%)	5(16.12%)	14(31.11%)	6(18.75%)	13(33.33%)
	Previous XDR isolate with different organism	3(4.8%)	1(3.22%)	1(2.22%)	3(9.37%)	3(7.69%)
MDR	Previous MDR isolate with same organism	12(19.35%)	5(16.12%)	3(6.67%)	3(9.37%)	14(35.9%)

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	Previous MDR isolate with different organism	6(9.68%)	-	3(6.67%)	-	3(7.69%)
Urinary Catheter	Yes	39(67.2%)	21(95.45%)	26(81.25%)	19(76%)	24(82.76%)
	No	19(32.76%)	1(4.55%)	6(18.75%)	6(24%)	5(17.24%)

Other- CNS infection, otitis media, intraabdominal infection*
*Others**- Broncho-alveolar lavage, body fluid, ear swab, CSF*
Abbreviations: XDR- extensive drug resistance, MDR- multi drug resistance.

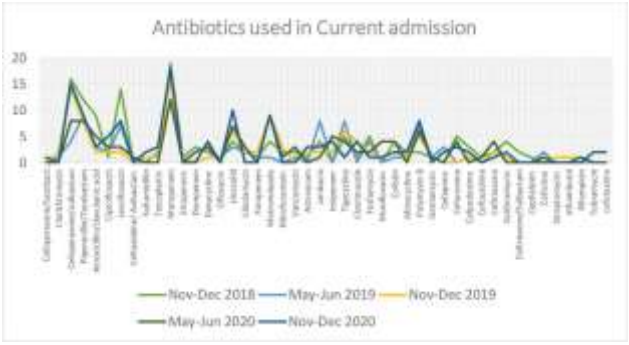

Figure 3: Antibiotics used in Current admission.

This past November and December, due to pollution and colonization. According to Silpi et al. (2016), around 1.6% of patients in central India have XDR. In addition, our overall isolate count was 12.1%, which is half of what Silpi et al. (2016) found. The decrease may be attributed mostly to the following factors: strict adherence to infection control protocols, appropriate use of antibiotics, meticulous personal cleanliness, a robust health care infrastructure, etc.7

Patients older than 60 years old were more likely to identify with XDR isolates across all time periods. Our patients had a mean age of 58.2 years, while Bahman et al. 2020 had a mean age of 49.8 years. Older people are more likely to have co-occurring medical conditions, which means they end up in the hospital more often.8

Males have more XDR than females, according to our research and Bahman et al. 2020. As a result of societal habits such as smoking and drunkenness, which lower immunity and generate other comorbidities that lead to hospitalization and resistance, many men engage in these behaviors.8 Cellulitis infections are common in men, whereas UTIs are common in women. Patients with a history of hospitalization have an increased risk of developing drug-resistant illnesses, according to research from the Center for Disease Dynamics, Economics, and Policy (CDDEP).9 Hospitalization occurred just once for almost 60% of the participants in our research. How long a patient spends in the intensive care unit also affects the rate of resistance.

Table 3: Isolate details and Therapy.

		Nov-Dec 2018	May-Jun 2019	Nov-Dec 2019	May-Jun 2020	Nov-Dec 2020
Organism Isolated	*Klebsiella*	39(62.9%)	27(87.1%)	28(62.22%)	20(62.5%)	30(76.62%)
	Pseudomonas	18(29.3%)	1(3.22%)	5(11.11%)	1(3.12%)	5(12.82%)
	Acinetobacter	4(6.45%)	-	10(22.22%)	4(12.5%)	2(5.13%)
	E. Coli	1(1.61%)	-	2(4.44%)	5(15.62%)	-
	Enterobacter	-	2(6.45%)	-	2(6.25%)	2(5.13%)
	Citrobacter	-	1(3.22%)	-	-	-

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Type of growth	Contamination/ Colonisation	47(75.8%)	15(48.38%)	20(44.44%)	16(50%)	14(35.9%)
	Infection	15(24.19%)	16(51.61%)	25(55.56%)	16(50%)	25(64.1%)
Route of infection	Community acquired	18(29%)	7(22.58%)	17(37.78%)	14(43.75%)	10(25.64%)
	Hospital acquired/ health care associated	34(54.84%)	18(58.06%)	23(51.11%)	14(43.75%)	19(48.71%)
	Prolonged exposure to antibiotics	10(16.13%)	6(19.35%)	5(11.11%)	4(12.5%)	10(25.64%)
Therapy	Inappropriate	4(6.9%)	1(4.54)	3(9.37%)	3(12%)	-
	Appropriate	54(93.1%)	19(95.44%)	29(90.62%)	22(88%)	29(100%)
Duration of hospital stay	0-5 days	9(15.51%)	2(9.1%)	6(18.75%)	5(20%)	6(20.69%)
	6-10 days	12(20.69%)	4(18.18%)	6(18.75%)	5(20%)	3(10.34%)
	11-15 days	18(31.03%)	3(13.64%)	4(12.5%)	6(24%)	7(24.13%)
	16-20 days	6(10.34%)	5(22.72%)	4(12.5%)	3(12%)	4(13.8%)
	>20 days	8(13.79%)	4(18.18%)	6(18.75%)	1(4%)	2(6.9%)
	>1 month	5(8.62%)	4(18.18%)	6(18.75%)	5(20%)	7(24.13%)

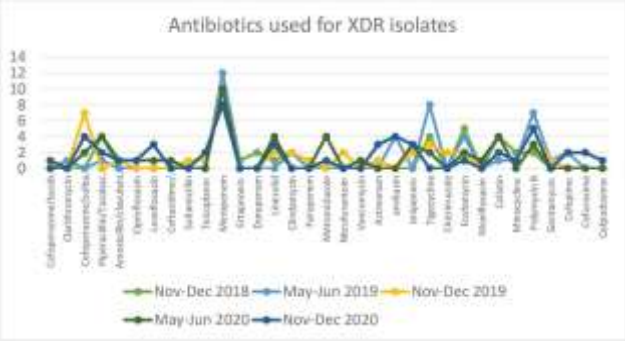

Figure 4: Antibiotics used for XDR isolates.

Although there have been some prospective studies looking at the link between antibiotic exposure details and resistance development, it has been difficult to isolate specific parameters relating to previous antibiotic exposure and resistance.10,11

Depending on the research, antibiotic resistance might be influenced by the prevalence of prior antibiotic exposure, which ranges from 40% to 90%.

Due to the high prevalence of multidrug-resistant and extensively drug-resistant patients, the most of the antibiotics prescribed in the past were broad-spectrum. This highlighted the critical requirement of broad-spectrum antibiotics for empirical treatment.

We discovered that most organisms in our research originated from UTIs and SSTIs since these infections were more often detected in pus and urine specimens. Another research that came to the same conclusion was Ravichandran et al. (2015). They observed that XDR isolates were more common in urine and pus. One major factor that increases the prevalence of XDR organisms in urine is the presence of a catheter.12 The research conducted by Joyce Wang et al. in 2017 lends credence to this outcome.13 Bacterial colonization and subsequent infection may result from the presence of a catheter, according to their research.

The usage of antibiotics is a known risk factor for

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multi- and X-drug-resistant (MDR and XDR) colonization and subsequent cross-resistance, according to research by A. P. Margiorakos et al. (2012) and Joyce wang et al. (2017).13, 14 Consistent with earlier research, our study found that individuals who have had MDR or XDR colonization with the same or distinct organisms are more likely to acquire colonization or infection with XDR organisms.

Many of the present admission board members had a history of using broad spectrum antibiotics, so that's what was recommended to them.

Across all five stages of the research, the most common organisms found were Klebsiella XDR (>60%), pseudomonas (>14%), and Acinetobacter (>12%). Silpi et al. (2016) found that klebsiella and pseudomonas were the most often discovered organisms. The number of klebsiella was greater in our research compared to Silpi et al. 2016.7

While earlier research indicated that infection was more common than contamination/colonization, we found that a large proportion of patients in the early stages of our study really had contamination/colonization.7-11 A shift to an infection-type growth pattern occurred over time. An mistake in sample collection was the primary cause of the elevated contamination/colonization levels, which were promptly addressed by the infection control staff.

The decrease in the proportion of infections acquired in the community towards the end may have been caused by the COVID epidemic. The decrease of community-acquired infections was aided by less exposure to hospital or antibiotics, better personal cleanliness, increased use of masks and sanitizer, and interpersonal interaction. A hospital stay of 11–16 days was the norm for the majority of patients. They include both patients who have been released from the hospital and those who have passed away. The diagnosis of the organism dictated the course of treatment.

The absence of appropriate guidelines and publications pertaining to XDR epidemiology data was one of our constraints. It wasn't a continual research; it was more of a periodic one.

CONCLUSION

Extremely drug-resistant (XDR) infections are on the rise, bringing with them a high treatment cost and a high fatality rate. This percentage ranged from 5% to 7% in our research. K. pneumoniae is becoming more resistant at an alarming pace. It was colonization at first, and then infection was shown to be the main factor. The presence of a urinary catheter, a history of MDR or XDR colonization or infection, prior exposure to antibiotics, and prior hospitalization are major risk factors for XDR colonization or infection. The majority of infections were associated with urinary tract infections (UTIs) and sexually transmitted infections (STIs). Patients without any health care-associated risk factors are now seeing an increase in community-acquired XDR infections/colonization.

ACKNOWLEDGEMENT

Nil

CONFLICT OF INTEREST

The authors declare no Conflict of interest.

ABBREVIATIONS

CDC: Centers for Disease Control and Prevention; **CDDEP:** The Center for Disease Dynamics, Economics and Policy; **ICU:** Intensive Care Unit; **MDR:** Multi-drug Resistance; **SSTI:** Skin and Soft tissue infection; **UTI:** Urinary tract infection; **XDR:** extensive drug resistance.

SUMMARY

A periodic observational study conducted in a tertiary care hospital antimicrobial resistance pattern. 5-6% was the XDR organism identified from the total culture isolation. Among this Klebsiella found to be the highest

in percentage with 70%. Major risk factors identified were prolonged antibiotic exposure, previous hospitalisation, catheter. The usage of antibiotics and its effect also discussed in this study. The study revealed that average hospitalisation will increase thrice when XDR infection hit the patient. XDR infections are increasing day by day which lead to increased economic burden and mortality.

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