Original Article

Multidrug-Resistant Clinical Infections; Results from a Point Prevalence Study in a Tertiary Resource-Limited Hospital, South-West Nigeria

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ABSTRACT

Multidrug-resistant (MDR) infections are on the rise globally, often exhibiting significant geographical variability and posing a great threat especially in the low- and middle-income countries. We aimed at investigating the prevalence and patterns of MDR clinical infections in our local Hospital. This was a point prevalence study involving admitted patients in our hospital, following routine sample processing, data was extracted from the microbiology processing forms and clinical files of the patients using a well-structured proforma. Ethical approval was sought and obtained for the study. Analysis was done with the IBM Statistical Package for Social Sciences (SPSS) version 22. There were 101 patients with complete documentation. The age range was from 2 – 65 years, with 58 (57.4%) female and 43 (42.6%) male. There were 17 isolated organisms, of these, 13 (76.5%) were multidrug-resistant. No significant association was found between sex, age, and sub-specialties of the patient and MDR infections. The overall prevalence of MDR infections found among the patients was 12.9%. and more common among the males (61.5%). More MDR infections were recorded among patients in Nephrology subspecialties. The common isolates were S. aureus (n=6, 35.3%), then E. coli (n=3, 17.6%), P. aeruginosa (n=5, 29.4%), Klebsiella spp. (n=6, 17.6%), 76.5% of these organisms were MDRO. The study documents prevalent high multidrug-resistant bacterial infections, calling for urgent and improved effort in the implementation of infection control measures and antibiotic stewardship in our hospitals so as to limit the spread of multidrug-resistant bacteria.

Keywords: Antimicrobial resistance, Multidrug-resistant organisms, Multidrug-resistant infections

INTRODUCTION

Multidrug-resistant (MDR) infections are significant in the global health challenge, these infections are caused by bacteria resistant to multiple classes of antimicrobial agents which often makes treatment of infectious diseases difficult. Multidrug resistance is defined as non-susceptibility to at least one agent in three or more antimicrobial categories.[1] The increasing level of MDR clinical infections is directly linked to an increased burden of antimicrobial resistance (AMR) in many microorganisms pathogenic for humans.[2]

The emergence and patterns of MDR infections are driven by various biological, social, and environmental factors, complicating both the treatment and control efforts globally.[3] One of the primary causes of MDR infections is the overuse and misuse of antibiotics in human medicine and agriculture. The extensive use of antibiotics in livestock farming also contribute significantly to the

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development of resistant bacterial strains. These resistant bacteria can be transmitted to humans through the food chain, direct contact, or environmental spread; this highlights the interconnected nature of resistance patterns.[4,5]

The patterns of MDR infections also exhibit significant geographical variability. The low- and middle-income countries (LMICs) often experience higher rates of MDR infections due to inadequate healthcare infrastructure, limited access to effective antibiotics, and weaker antimicrobial stewardship programs with grave consequences.[6–8] This geographic disparity underscores the need for region-specific strategies in addition to the global effort to combat MDR infections effectively.

Clinically, MDR infections lead to higher morbidity and mortality rates, prolonged hospital stays, and increased healthcare costs. It also poses a significant threat to medical gains in surgery, maternal and child care and in the care of patients with malignancies. The treatment of MDR infections often requires complex and expensive therapies, which may be less effective compared to standard treatments for non-resistant infections.[8,9] This situation places a considerable strain on healthcare systems and emphasizes the importance of developing new antimicrobial agents and treatment protocols.

Some particular nosocomial pathogens have been identified to be of high priority; being part of a group of the most significant pathogens involved in extensive AMR. These include the members of *Enterobacterales, Moraxellales,* and *Pseudomonadales* families. These pathogens are closely associated with high-level AMR and are the commonest multidrug-resistant organisms (MDRO) responsible for the wide-spread MDR infections.[2,10]

Globally, there has been several reports on a high level of MDR infections across developed and developing nations, an estimated 2.8 million antibiotic resistant infections occurs per year in the United States with about 35,000 deaths annually. In Nigeria, studies from across different parts found a prevalence of between 35% to 70% MDR infections among patients admitted in hospitals across the country with varying outcomes.[11,12] We aimed at investigating the prevalence and patterns of MDR clinical infections in our Teaching Hospital.

MATERIALS AND METHODS

Study Area

This study was carried out at UniOsun Teaching Hospital, (UTH) Osogbo, Osun State. UTH is a tertiary hospital with a compliment of about 400 beds and offers a wide range of clinical services across various medical specialties such as Internal Medicine, Surgery, Obstetrics and Gynecology, Paediatrics, Orthopaedics, Radiology, Dermatology and Ophthalmology. The hospital complex includes various departments, wards, clinics, laboratories and operational theatre all adequately equipped.

Osun State is located in southwestern Nigeria between latitude $7^0$28'N and longitude $4^0$34'E and about 218km northeast of Lagos. UTH is the teaching hospital affiliated with Osun State University, established by the State government to provide quality health care delivery to its people.

Study Design

The study was a point prevalence study involving all eligible in-patients across the wards in the hospital. The study was conducted in May, 2024.

Study Population

Patients on admission on the wards at UniOsun Teaching Hospital.

Sample Size Determination

This was a total population study involving all eligible patients on admission in the hospital at the time the study was conducted.

Inclusion Criterion

All patients who were on admission in the Medical, Surgical and Surgical sub-units, Pediatrics, Gynecology wards and the Intensive Care Units of the hospital were eligible.

Exclusion Criterion

All patients with inadequate and incomplete data were excluded from the study.

Laboratory Procedure For Isolation of Bacteria

All clinical samples for microbial analysis were sent to the Medical Microbiology Laboratory in the

hospital. For blood culture, blood collected in BACTEC (Becton Dickinson, Belgium) culture bottles were incubated over 24 hrs to 5days in a semi-automated BACTEC 9050 blood culture machine (Becton Dickinson, Belgium). The blood culture bottles which signalled to be positive were then sub-cultured on 5% sheep blood agar, chocolate agar and MacConkey agar plates. MacConkey agar plates were incubated aerobically while; sheep blood agar and chocolate agar were incubated in 5% CO_2 conditions at 37°C for 18-24 hours.

Semi quantitative urine culture was done with a calibrated loop with a loopful (0.001 mL) of well mixed un-centrifuged urine inoculated onto the surface of cysteine lactose electrolyte deficient medium (CLED). The culture plates were incubated aerobically at 37°C for 18-24 hours. Culture of a single bacterial species from the urine sample at a concentration of 10^5cfu/ml associated with microscopy findings of >10 white blood cells (WBCs) per high power field was taken as significant bacteriuria.

Cerebrospinal fluid (CSF) samples were examined macroscopically and microscopically, a direct Gram staining was done on the specimen and then plated immediately on blood agar, MacConkey and chocolate agar. MacConkey agar plates were incubated aerobically while; blood agar and chocolate agar were incubated in 5% CO_2 condition at 37°C for 18-24 hours.

A direct Gram was done on specimens on swabs, including ear, eye, wound swabs and also wound biopsy and aspirates. They were cultured immediately on blood and MacConkey agar. Incubation was under aerobic condition at 37°C for 18-24 hours. All tests were done according to the recommendations of Clinical and Laboratory Standards Institute (CLSI).[13]

Identification of Bacterial Isolates

Identification of the isolates was by colonial morphology on agar plate, Gram staining, then, biochemical tests such as citrate utilization, urease test, reaction on triple sugar iron agar, indole production, oxidase and motility tests were carried out on the Gram-negative bacilli, catalase and coagulase tests were carried out on Gram-positive bacilli. All tests were done according to the recommendations of Clinical and Laboratory Standards Institute (CLSI).[13]

Antimicrobial Susceptibility Testing

Antimicrobial susceptibility testing was done by the modified Kirby-Bauer disc diffusion method. Mueller-Hinton agar plates were incubated for 18-24 hours after inoculation with test organisms and placement of antibiotic discs. All isolated bacteria were tested against regular antibiotics used in the management of patients including; ciprofloxacin (5µg), ofloxacin (5µg), ampicillin (10µg), ceftriaxone(30µg), ceftazidime (30µg), cefotaxime (30µg), cefuroxime (30µg), co-amoxiclav (20/10µg), gentamicin (10µg), imipenem (10µg), and nitrofurantoin (300µg) which was used for urinary isolates only. The results were interpreted according to CLSI guidelines.[13]

A well-structured proforma was used in extraction of relevant data from the patients' microbiology forms and clinical record files. Multidrug resistance in an isolate is defined as non-susceptibility to at least one agent in three or more antimicrobial categories tested.[1]

Ethical Consideration

The ethical approval for the study was obtained from the Research and Ethics Committee of UTH, Osogbo. The protocol number is UTH/EC/2024/06/953.

Data Collection

With the aid of a structured proforma and Excel spread sheet, relevant data was obtained from the medical record files of the patients and the microbiology laboratory forms. The data retrieved included relevant biodata, date of admission, clinical diagnosis, nature of specimen collected for analysis, isolated organism, antimicrobial susceptibility pattern, current antibiotic treatment and presence of co-morbidities.

Data Analysis and Statistical Techniques

All data was electronically secured from public access and analyzed using the IBM Statistical Package for Social Sciences (SPSS) version 22

(IBM, Armonk, NY, USA). Categorical variables were summarized and presented on frequency tables with simple proportions and charts as appropriate. An inferential bivariate analysis was performed using Chi-square and P <0.05 was considered significant.

RESULTS

A total of 101 patients who had complete documentation in their microbiology processing forms and clinical files were involved in this study. The age range was from 2 years – 65 years, there were 58 (57.4%) female and 43 (42.6%) male recruited across different clinical units and wards of the hospital, including Surgery, Medicine and Pediatrics. The patients were also sampled for use of catheters and presence of co-morbidities such as hypertension and diabetes (Table 1).

Only 16 (15.8%) of these patients had a current antimicrobial culture and susceptibility testing report with 17 isolated organisms, of these, 13 (76.5%) were multidrug-resistant organisms (Figure 1).

Table 2 shows associations between some variables and multidrug-resistant infections. There were no significant associations between the sex, age, and management sub-specialties of the patients, being hypertensive or diabetic and MDR infections. However, there was a significant association between non-use of catheter and MDR infections.

The overall prevalence of MDR infections found among the patients was 12.9% (n=13). Although, there were more females (n=58, 57.4%), MDR infections were more common among the males (n=8, 61.5%), but there was no significant association between sex and MDR infections (Table 3).

The commonest isolate was *Staphylococcus aureus* (n=6, 35.3%). The other organisms isolated were *E. coli* (n=3, 17.6%), *P. aeruginosa* (n=5, 29.4%), *Klebsiella* spp. (n=3, 17.6%). More than half (n=13, 76.5%) of these organisms were MDRO, with 5 of the 6 isolates of *S. aureus* (83.3%) being multidrug-resistant and all (n=5,100%) of *P. aeruginosa* being multi-drug resistant (Table 4).

More MDR infections were recorded among patients in Nephrology subspecialties (n=5, 38.45%), followed by General Surgery subspecialty (n=3, 23.1%), Urology and Orthopaedic units both with 15.4% (n=2) of MDR infections, there was no significant association between these subspecialties and MDR infections (Table 5).

Table 1: Socio-demographic characteristics of participants

Variables	Frequency (n=101)	P ercentage
Age (Mean±SD) years	44.61±11.6	
Range	2.0 - 90.0	
Sex		
Male	43	42.6
Female	58	57.4
Managing Unit		
Surgery	70	69.3
Medicine	29	29.7
Pediatrics	2	2.0
Present catheter use	12	11.9
Diabetic	6	5.9
Hypertensive	18	17.8
Num ber with bacterial growth	*16	15.8

*16 participants with growth and 17 isolates with a patient having 2 isolates

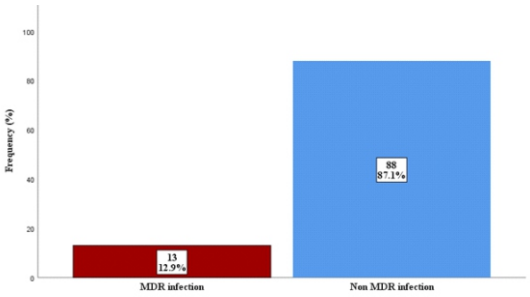

Figure 1: Prevalence of Multi-Drug Resistant Clinical Infections

Table 2: Association between Multi-Drug ResistantClinical Infections and Selected characteristics

	MDR infection (n=13)	Non - MDR infections (n=88)	χ^2	p - value
Age (Mean±SD) years	51.77±12.8	43.64±12.5	0.402	0.164
Sex				
Male	8(18.6)	35(81.4)	2.195	0.138
Female	5(8.6)	53(91.4)		
Managing unit				
Surgery	7(10.0)	63(90.0)	2.391	0.303
Medicine	6(20.7)	23(79.3)		
Pediatrics	0(0.0)	2(100.0)		
Present catheter use				
Yes	5(41.7)	7(58.3)	10.069	0.002*
No	8(9.0)	81(91.0)		
Diabetic				
Yes	0(0.0)	6(100.0)	0.942	0.332
No	13(13.7)	82(86.3)		
Hypertensive				
Yes	4(22.2)	14(77.8)	1.708	0.191
No	9(10.8)	74(89.2)		

Table 3: Prevalence of Multidrug Resistant Infection in both Genders

Variable (Gender)	Prevalence		X^2	P - Value
	Yes	No		
Female	5(8.6%)	53(91.4%)	2.195	0.138
Male	8(18.6%)	35(81.4%)		

Table 4: Proportion of Multi-Drug Resistance in Different Isolates

	Number of organisms isolated	Number of MDRO	Percentage MDRO
Staphylococcus aureus	6	5	83.3%
Klebsiella spp.	3	1	33.3%
Pseudomonas aeruginosa	5	5	100.0%
Escherichia coli	3	2	66.7%

Table 5: Prevalence of multidrug resistant infection across different sub-specialties

Managing unit	Prevalence	
	MDR	NON-MDR
Orthopaedic unit	2(15.4%)	11(84.6%)
Urology unit	2(20%)	8(80%)
General surgery	3(23.1%)	10(76.9%)
Endocrinology	0(0%)	5(100%)
Nephrology	5(33.3%)	10(66.7%)
Plastic surgery	0(0%)	3(100%)
Neurosurgery	0(0%)	5(100%)
Ophthalmology	0(0%)	3(100%)
Haematology	0(0%)	2(100%)
Cardiology	0(0%)	1(100%)
Paediatric	0(0%)	2(100%)
Post Natal	0(0%)	10(100%)
Anaesthesia	0(0%)	1(100%)
Gynaecology	0(0%)	8(100%)
None	1(16.7%)	5(83.3%)
ENT	0(0%)	4(100%)

DISCUSSION

One of the major approaches in the management of widespread antimicrobial resistance and by extension multidrug-resistance infection is regional as well as global active antibiogram surveillance. We investigated the prevalence of multidrug-resistance infections in our teaching hospital by a point prevalence study. A total of 101 patients were recruited into the study, the prevalence of multidrug-resistant infections found among these patients was 12.9%.

Among the isolates from the patients, the prevalence of MDRO was 73.5% (n=13). This prevalence is higher to that found among clinical isolates from patients in Ghana (41.6%), in a four-year retrospective study involving over 1000 isolates.[14] Another study from northern Nigeria pooled 735 isolates from two tertiary centers and found an MDRO prevalence of 88.9%. [11] There are varying differences in the prevalence of antimicrobial resistance as well as multidrug-resistant infections across different regions depending on peculiar factors. However, there has been a global increase in the incidence of antimicrobial resistance as well as multidrug-resistant infections; an established threat to global health. [2]

A higher prevalence of MDR infection (61.5%) was found among males in our study; this is despite a higher number (57.4%) of female participants. While there is paucity of data to compare prevalence of MDR in males and females, the male gender has been found to have a higher risk of developing an MDR infection in other studies.[15] Rodríguez-Villodres *et al*. also documented a higher male preponderance from their study on MDRO, [15] and men have a higher risk of obstructive uropathy from either benign prostatic hypertrophy (BPH) or prostate cancer (CaP), these conditions are associated with a high surgical and instrumentation rate and recurrent urinary tract infections, hence these could also predispose to a higher rate of MDR infection. [15]

The patients in Nephrology unit were found to have a higher prevalence of MDR infections compared to other sub-specialties. These were patients with a form or another of renal disease, requiring repeated instrumentation, increased length of hospitalization and prolonged use of antibiotics which could have predisposed them to a higher rate of MDR infections than other patients. These factors are known to increase patients' risks of acquiring multidrug - resistant pathogens. [16]

Overall, there were more Gram-negative infections, however, the commonest organism (35.3%) responsible for infections among the patients involved in this study is the Gram-positive

Staphylococcus aureus which was isolated in 6 of the patients, with 5 (83.3%) of these isolates being multi-drug resistant. This finding is similar to that from a systematic review of MDRO across the world which found multidrug-resistant *S. aureus* to be the most common MDRO isolated across long-term health care facilities from different categories of patients across the world.[15] *Staphylococcus aureus* is a common human pathogen involved in diverse clinical presentations across all age groups and in both genders, over the past two decades, there have been several reports of increase in the prevalence of methicillin-resistant and vancomycin-resistant species. [17] This current resistant trend seen across the globe is a big threat to the management of infectious diseases caused by *S. aureus*, especially in a resource-poor setting as ours.

The Gram-negative bacilli isolated from our patients with MDR infections were mainly *Pseudomonas aeruginosa* (n=5, 29.4%), *Klebsiella* spp. (n=3, 17.6%), *Escherichia coli* (n=3, 17.6%). All (100%) the strains of *P. aeruginosa* isolated were MDRO, while 33.3% of *Klebsiella* spp. strains and 66.7% of the *Escherichia coli* strains were found to be MDRO. This finding was also similar to that of Olowookere from northern Nigeria with a higher prevalence of these MDRO among the clinical isolates obtained from two centers. [11] Several other studies have also shown that these Gram-negative bacilli are the most significant pathogens involved in extensive AMR and are the commonest clinical isolates responsible for the wide-spread MDR infections across the globe. [2] There are current ongoing efforts to encourage the development and production of new antibiotics with broad coverage for these organisms. [2]

CONCLUSION

The study has demonstrated high multidrug resistant bacterial infections, predominantly caused by *S. aureus*, *E. coli, Klebsiella* spp. and *P. aeruginosa* in our facility. These infections appear to be commoner in men and in patients with kidney disorders.

Recommendations

Based on the findings of this study, we recommend an improved effort in the implementation of infection control measures and antibiotic stewardship in our hospital so as to limit the spread of multidrug resistant bacteria in our healthcare facility, and by extension globally.

Limitations

This study is limited, being a point-prevalence study involving only our center with some of our patients either awaiting their microbiology assay results or already recovered from the ailment necessitating the hospital admission. Some of our patients also did not have complete records which necessitated their exclusion from this study.

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Conflict of Interests

We declare that we have no financial or personal relationships which may have inappropriately influenced us in writing this paper.

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