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Incidence of Hospital Acquired Multidrug Resistant Organisms in a Tertiary Care Facility

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Abstract

Background: Irrational use of antimicrobials and gaps in infection control practices have resulted in alarmingly high prevalence of multidrug resistant organisms (MDRO) globally. The objective of our study was to highlight the incidence of hospital acquired MDROs in our facility.

Method: A retrospective analysis of surveillance data collected from January - December 2013 in a tertiary care hospital of Saudi Arabia. The Centre for Disease Prevention and Control (CDC) surveillance definitions were used, while the MDRO definition was modified. Descriptive analysis was performed and incidence density was calculated. SPSS version 20 (IBM, Chicago, USA) was used for analysis.

Result: In total 1737 MDRO isolates were identified. Of these n = 1,326 (76%) were hospital acquired and the mean incidence rate was 4.8 cases/1,000 patient-days. The most common risk factors were prolonged stay (≥ 5 days) n = 1134 (85.5%), indwelling medical devices 955 (72%) and antimicrobial therapy in past 90 days 949 (71.5%). *Klebsiella pneumoniae* n = 307(23%), *Acinetobacter baumannii* n = 270 (20%), Methicillin Resistant *Staphylococcus aureus* n = 183 (14%), *Pseudomonas aeruginosa* n = 160 (12%) and *Escherichia coli* n = 159 (12%) were the most prominent nosocomial pathogens. Resistance among gram negatives for cephalosporins ranged from 94% to 98%. *A. baumannii* (98%) and *P. aeruginosa* (89%) were resistant to carbapanems. More than 90% of *A. baumannii* were extensive drug resistant.

Conclusion: The study indicated an alarmingly high incidence of hospital acquired MDRO in a single center. The increasing resistance warrants the need for a robust and continuous surveillance system for monitoring regional trends in MDRO susceptibility patterns and comprehensive infection control and antimicrobial stewardship programs.

Background

The World Health Organization (WH)) defines "rational use of drug" as "patients receive medications appropriate to their clinical needs, in doses that meet their own individual requirements, for an adequate period of time, and at the lowest cost to them and their community" [1]. The increasing irrational use of antimicrobials in humans and veterinary medicine has consequently increased the emergence of antibiotic resistant organisms or multidrug resistant organisms (MDRO) [2]. Primary reasons for concern about MDRO are the diminishing treatment options increasing cost of care, length of stay, mortality and morbidity [3-6]. Antimicrobial resistance has been a global problem. The published literature from the Gulf Cooperation Council (GCC) region had highlighted an alarming prevalence of antimicrobial resistance and the dawn of post antibiotic era [7-11]. In Saudi Arabia too, the increasing misuse and overuse of antibiotics resulted in the emergence of antimicrobial resistance among organisms of epidemiological importance [7,9,12].

However, very little efforts had been implemented at national and regional level to control the emergence of antimicrobial resistance. It has been documented that the resistance patterns depend on the antibiotic consumption [13,14]. Unfortunately, we do not have a centralized and standardized surveillance system that could better explain the resistance patterns in our region. There is a tremendous need to formulate a robust and continuous surveillance system for monitoring regional trends in antimicrobial consumption and MDRO susceptibility patterns.

The purpose of this study was to highlight the incidence of hospital acquired MDRO in our facility, justifying the need of developing and implementing a comprehensive local and national infection control and antimicrobial stewardship programs. It will also provide a benchmark for similar facilities using the same surveillance definitions and methodology.

Methods

Facility

Prince Sultan Military Medical City (PSMMC) is one of the largest tertiary care military hospitals for armed forces personnel and their dependents, in Riyadh, Saudi Arabia. The PSMMC provides a broad range of services to a wide variety of patient populations. It is a 1,100 bed facility with most of the clinical areas being multi-bedded.

Microbiological testing method

All specimens received at the microbiology laboratory were

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processed according to the standard operating procedures of the laboratory. Organisms were identified biochemically by catalase, coagulase, oxidase and using API 20 E and API20NE (Biomerieux, France) for gram negatives. The antimicrobial sensitivity testing was performed with an automated system (MicroScan Walkaway 96 plus System, Siemens Healthcare Diagnostics, USA) using gram negative & gram positive minimum inhibitory concentration panels. Antibiotic agents tested were:penicillins (methicillin, amoxicillin, amoxicillin-clavulanate, piperacillin-tazobactam), cephalosporins (cefuroxime, cetriaxone, ceftazidime), flouroquinolones (ciprofloxacin, norfloxacin, levofloxacin), carbapanems (imipenem, meropenem), aminoglycosides (gentamicin, amikacin),trimethoprim-sulphamethoxazole, clindamycin, teicoplanim, vancomycin, linezolid, colistin and rifampicin. Clinical Laboratory Standards (CLSI, M100-S23) criteria were used for the interpretation of susceptibility results.

Definition of MDRO

The United States Center for Disease Control and Prevention (CDC) and European Centre for Disease Prevention and Control (ECDC) came up with a consensual surveillance definition for MDRO, which states, "acquired non-susceptibility to at least *one* agent in three or more antimicrobial categories" [15]. The same definition is being used by the GCC – Centre for Infection Control. However, the observed practice within our facility indicated irrational use of antimicrobials. The published literature also suggests increasing use and misuse of antimicrobials in different areas of Saudi Arabia [16-19]. Therefore, the Infection Control Department at PSMMC in collaboration with Division of Infectious Diseases and Department of Microbiology devised an MDRO definition for our facility. This definition was a modified version of CDC and GCC MDRO definitions and stated that "a gram-negative organism is considered MDRO if it's resistant to *all* agents tested in at least three classes of antimicrobials". The antimicrobials classes are: - β-lactams (penicilins and cephalosporins), aminoglycosides, fluoroquinolones and carbapenems.

According to the CDC, a laboratory identified (LabID) MDRO is one which is isolated from a specimen that was collected for therapeutic reasons and will not include the samples taken for active screening. The MDRO which were isolated after 3rd day of admission i.e. on day 4 or after will be considered hospital acquired MDRO otherwise will be labeled as community acquired. Any duplicate isolate from the same patient was not included in the analysis. The MDRO identified by the laboratory were immediately informed to Infection Control Practitioners (ICPs) who then thoroughly reviewed patients clinical and laboratory records to check if it was a new episode of infection or continuation of previous infection. The data was then reviewed by senior ICP and an Infection Control Coordinator before admission in the surveillance system. This process ensured that contaminants, duplicates and screening isolates were not entered in the database. The database was created for our facility using Microsoft Access (Microsoft Inc., Redmond, USA) and was accessible only by the infection prevention and control staff.

Statistical analysis

A retrospective surveillance study based on data collected during 2013. The incidence of hospital acquired MDRO was calculated as incidence density (events per 1,000 patient days) and descriptive analysis with frequency and percentage was performed for risk factors, isolates and susceptibility. SPSS version 20 (IBM, Chicago, USA) was used for analysis.

Ethical approval

The study proposal was approved by research ethics committee of Prince Sultan Military Medical City

Results

During 2013, a total of 1737MDRO isolates were identified among 278,528 patient days. Of these isolates, 1326 (76%) were hospital acquired whereas 365 (21%) were community acquired and 46 (3%) were transferred from other hospitals (if MDRO was isolated within 3 days of transfer from another facility).

The overall incidence density was 4.8 cases per 1,000 patient days. The rate remained stable throughout the study period and did not show any statistically significant change in trend (R-square = 0.12 and p value = 0.093). No seasonal variation was detected in the rates, as indicated in figure 1. Though the rate decreased in March, June and December, but this was statistically insignificant. Hypothetically, the decrease in March could be attributed to admission of patients with Middle Eastern Respiratory Syndrome (MERS) corona virus, the decrease in June could be due to preceding hand hygiene campaign in May and infection control link nurse program while the lower rate in December could be due to the preparation for mock survey for accreditation. During all these three points, the infection control activities and compliance to practices was increased, hence could have resulted in decreased rates.

The most common risk factors were prolonged stay (≥ 5 days) n = 1134 (85.5%), indwelling medical devices 955 (72%), antimicrobial therapy in past 90 days 949 (71.5%) and previous colonization/ infection of MDRO 689 (52%). The pareto analysis, in figure 2, indicated that controlling these factors might help in reducing the MDRO incidence rate by approximately 80%.

The most common organisms were gram negative (1090, 82.2%). Among all the hospital acquired MDROs *K. pneumoniae* (307, 23%), *A. baumannii* (270, 20%), *MRSA* (183, 14%), *P. aeruginosa* (160, 12%) and *E. coli* (159, 12%) were the most prominent pathogens (Figure 3).

The antibiotic susceptibility analysis for these organisms,

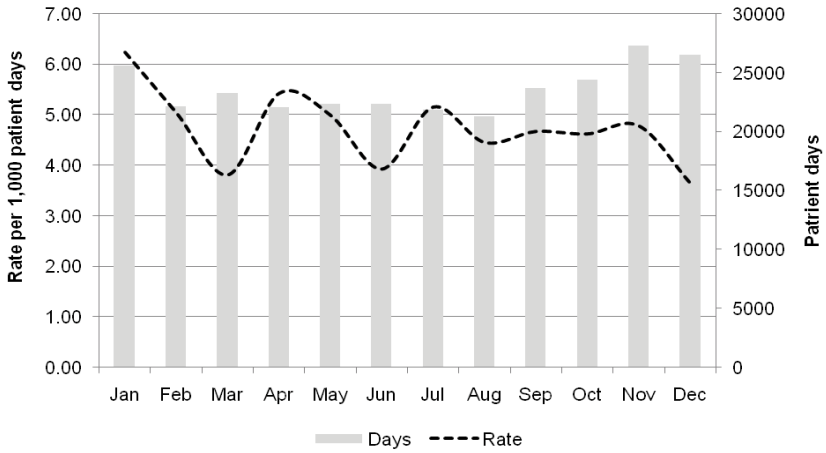

Figure 1: Trend in MDRO Incidence Rate in PSMMC during 2013.

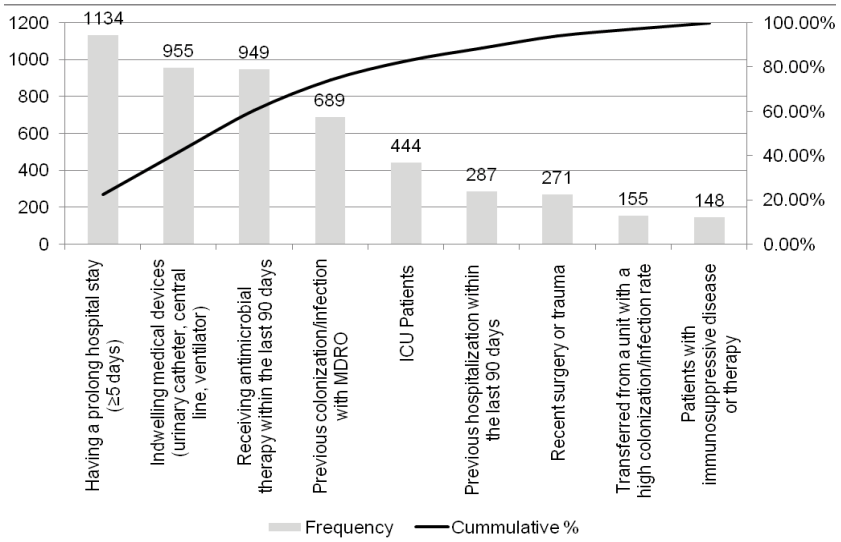

Figure 2: Pareto Analysis of Risk Factors for Hospital Acquired MDROs

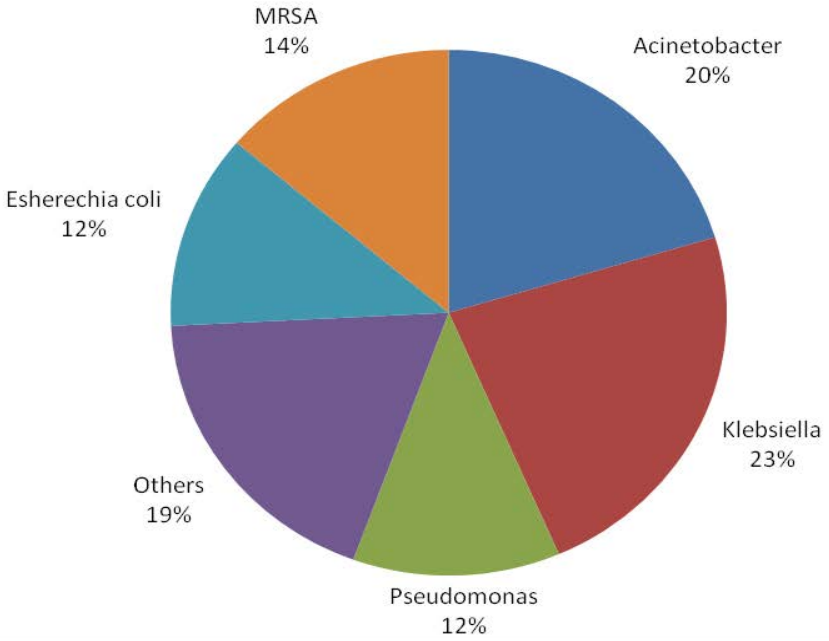

Figure 3: Most Common Hospital Acquired MDROs (%).

presented in table 1, indicate that almost all of the *A. baumannii* isolates were resistant to penicillins, carbapanems, fluroquinolones and cephalosporins and three-fourth of the isolates were resistant to aminoglycosides. Approximately all the *K. pneumoniae* isolates were resistant to cephalosporins and penicillins and a majority was resistant to fluroquinolones (76%) also. However, approximately 16% were resistant to carbapanems. Similarly *P. aeruginosa* were resistant to cephalosporins and carbapanems and approximately three fourth were resistant to fluroquinolones and aminoglycosides each. Nearly all the *E. coli* isolates were resistant to cephalosporins and a big number to fluroquinolones also, but majority were susceptible to carbapanems and aminoglycosides.

Discussion

The multi drug resistance among healthcare acquired organisms is an emerging global threat. The irrational use of antimicrobials has played an eminent role in developing such organisms [13,20]. The prevalence of such organisms have induced direct and indirect financial burden on both the patients and the providers and have limited the treatment options [3,6]. Like other parts of the world, the emergence of MDRO has created an alarming situation in the gulf region [10,21,22]. Though very little has been published from the region and it does not address any substantial initiative by the local authorities.

In our study, we presented the findings from a single center surveillance data. Most of our MDROs were acquired within the hospital setting. This indicated an alarming gap in infection control practices. As our facility is multi-bedded so lapse in proper implementation of isolation precautions cannot be ignored. However, isolation is just one intervention which would be more effective when combined with other prevention strategies [23]. As reported by other researchers, most of the healthcare acquired MDRO from our facility were gram negatives [10, 24-26]. Among gram negatives, the greatest concern which has been repeatedly highlighted was the presence of MDR *A. baumannii* [27,28]. The *A. baumannii* isolates detected during the study period were almost resistant to all the drugs being tested. If the definition given by Manchada et al., was followed, all the *A. baumannii* isolates would have been classified as extensive drug resistant (XDR) i.e. resistant to three classes (all penicillins, cephalosporins, fluroquinolones, and aminoglycosides) and carbapanems [29]. The treatment for carbapenem resistant and XDR *A. baumannii* has been widely studied and indicates limited therapeutic options for the organism [30-32].

Table 1: Antibiotic Resistance for Most Common Pathogens
Data are expressed as total number of pathogen tested (Percentage resistant)

Antimicrobials	Organisms									
	Acinetobacter		*Klebsiella*		*Pseudomonas*		*Others*		*Esherechia coli*	
Amikacin	254	(73.6%)	274	(25.5%)	135	(63.7%)	186	(49.5%)	130	(10.8%)
Gentamicin/Tobramycin	252	(75.0%)	282	(64.2%)	145	(72.4%)	338	(69.5%)	142	(41.5%)
Cefepime	241	(96.3%)	282	(98.2%)	134	(97.8%)	183	(82.0%)	136	(94.9%)
Ceftezidime	247	(93.1%)	276	(98.9%)	152	(94.7%)	187	(87.7%)	137	(94.9%)
Cefotaxime	57	(94.7%)	69	(98.6%)	27	(100.0%)	63	(92.1%)	45	(95.6%)
Cefuroxime	242	(100.0%)	285	(99.6%)	13	(100.0%)	207	(95.6%)	146	(97.2%)
Ceftriaxone	79	(100.0%)	76	(98.7%)	13	(100.0%)	64	92.2%)	37	(95.6%)
Ceftazidime	252	(92.3%)	277	(99.3%)	150	(94.7%)	197	(87.3%)	141	(95.7%)
Imipenem	211	(99.1%)	258	(14.7%)	151	(88.7%)	186	(23.7%)	127	(6.3%)
Meropenem	243	(97.9%)	252	(16.3%)	149	(87.9%)	172	(18.6%)	122	(6.6%)
Tazocin	66	(98.5%)	135	(66.7%)	85	(60.0%)	90	(24.4%)	65	(30.8%)
Methicillin	0	0	3	(66.7%)	0	0	28	(92.9%)	31	(90.3%)
Ampicillin	240	(99.58%)	283	(100.0%)	9	(100.0%)	239	(98.7%)	141	(100.0%)
Levofloxacin	100	(96.0%)	116	(56.9%)	70	(68.6%)	131	(56.5%)	62	(69.4%)
Ciprofloxacin	244	(97.1%)	281	(76.5%)	150	(76.0%)	347	(78.7%)	148	(76.4%)
Vancomycin	1	0	0	0	0	0	179	(28.5%)	0	0
Rifampicin	3	(66.7%)	1	(100.0%)	0	0	158	(30.4%)	0	0

Similarly a large number of our *P. aeruginosa* isolates were resistant to carbapenems. Almost all the isolates were resistant to cephalosporins, therefore excessive use of carbapanems might have resulted in increased resistance. The same phenomenon has been reported by Rahal et al., [33]. The emergence of carbapanems resistant organisms has been in discussion for decades but unfortunately no substantial initiative has been taken to overcome the issue. More than 90% of the 4 gram negative isolates were resistant to cephalosporins, indicating the limited therapeutic use of the drug without manipulation of pharmacokinetics and pharmacodynamics. Similar results were reported from Taiwan, Romania and Kenya [14,34-36].

Our risk factors analysis indicated that prolong hospital stay, indwelling medical devices, antimicrobial therapy and previous colonization or infection were the most common and frequently occurring risk factors. These predictors have been reported several times by other researchers [37-39]. They can be controlled through a comprehensive infection prevention and control program. In addition to continuous surveillance, the program should incorporate strategies to minimize hospital stay, introduce and enhance bundles implementation for reducing device associated infections and implement an aggressive antimicrobial stewardship program [40].

Based on our analysis, we observed that our findings are not different from rest of the world. An integrated and robust surveillance system is deemed necessary to understand the resistance patterns and prevent the new emergence. The local and national authorities should pay heed to the emerging global threat of antimicrobial resistance and should devise a national antimicrobial stewardship program for promoting judicious use of antimicrobial. This might not help us to revert the existing resistance pattern but will prevent further emergence.

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