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A CROSS-SECTIONAL RESEARCH TO ASSESSMENT TIGECYCLINE, POLYMYXIN & FOSFOMYCIN EFFECTS TO DETERMINE CPE (CARBAPENEMS PRODUCING ENTEROBACTERIACEAE)

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Abstract:

Objective: *The objective of the research was to determine the susceptibility of CPE (Carbapenems Producing Enterobacteriaceae) against Tigecycline, Polymyxin-B and Fosfomycin.*

Material and Methods: *The design of our research was descriptive and cross-sectional. We have completed the research at Mayo Hospital, Lahore from July 2016 to February 2017. The samples were injected on MacConkey agar and blood; aerobic incubation was carried out for a time period of 18 to 24 hours at 35 to 37ºC. As per the Clinical Laboratory Standard Institute (CLSI) regulations and guidelines gram negative identification of rods through colony morphology, biochemical reactions and Gram's staining, these were Carbapenems screened resistance with meropenem and imipenem(10µg) discs along with regular 1st and 2nd line antibiotics through Kirby – Bauer disc diffusion method. After inoculation on the MHA (Mueller–Hinton Agar) all inaccessible CPE (Carbapenems Producing Enterobacteriaceae) were preserved. The antimicrobial vulnerability against Tigecycline, Polymyxin– B and Fosfomycin was carried out through Kirby – Bauer disc diffusion technique with the help of disc Polymyxin–B (300 units), Tigecycline and Fosfomycin respectively (15 µg) and (200 µg). Greater than twenty-four mm zone diameters were considered sensitive for the Tigecycline (15 µg), sixteen and twelve mm respectively for (Fosfomycin 200 µg) and (Polymyxin – B 300 units).*

Results: *Among 171 collected clinical specimens of those participants who comply with the criteria of the research. The age was calculated in Mean ± SD as (42.02 ± 22.367) with Confidence Interval value as (38.65 – 45.40). In the total sample of 17 patients, a total of 110 were male 64%; whereas, 61 were female 36%. According to research results, males dominated the females in number. The outcomes of vitro susceptibility observed all 171 cases (100%) CPE isolates susceptible to Polymyxin – B; whereas, the incidence of vulnerability against the Tigecycline was observed as 49 cases (29%) and Fosfomycin 132 cases (77%).*

Conclusion: *We observed CPE as (100%) Polymyxin – B susceptible; whereas, in the case of Fosfomycin it is 77% and Tigecycline susceptibility as 29%.*

Keywords: *Carbapenems Producing Enterobacteriaceae (CPE), Polymyxin – B, Fosfomycin and Tigecycline.*

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INTRODUCTION:

The improvement of bacteria resistance was observed against antibiotics after the discovery of antibiotics through the production of different enzymes. These enzymes whether cephalosporinases or penicillinases lead to resistance progression and development Carbapenems are taken as sole β – lactam agents which are active against this extended spectrum B – lactamase producing the strains, but an irrational Carbapenems also use results in resistance development to this antibiotics class as well [1]. These Carbapenems are mostly expressed through Klebsiella pneumonae, Salmonella enterica, Klebsiella oxytoca, Enterobacteraerogenes, Citrobacter freundi, Enterobacter cloacae, and Serratiamarcescens Proteus mirabilis and in the non-fermenting Gram-negative bacilli are expressed as Pseudomonas putida, Pseudomonas aeruginosa and Acinetobacter bauminisp. In 1987 the first introduction of the Carbapenems was made back. Beta-lactam antibiotics are actually taken out from Thienamyc which is the product of Streptomyces cattleya. The most utilized Carbapenems are Meropenem and Imipenem; whereas, others include Doripenem, Faropenem, Panipenem and Ertapenem. The most used antibacterial spectrum activity is repeated beta-lactams. Their effectivity against gram-positive, anaerobic bacteria and gram-negative is well-known [2]. Unluckily, antimicrobial resistance is followed by antimicrobial use & in 1996 first case Of Carbapenem resistance was observed. In United States of America Carbapenem-resistant prevalence GNR is observed near (5.6%), and an increase has been observed one decade (0.6%), it is observed 8% in India and 18.5% in Pakistan. The last option for the treatment of the infections are Carbapenems and also considered as antimicrobials because of the increased beta-lactamase spectrum or plasmid-mediated (AmpC, pAmpC) producing the organisms for the family of Enterobacteriaceae. These pathogens also resist other antibiotic classes such as quinolones, aminoglycosides and trimethoprim-sulfamethoxazole and other related classes [3]. A serious threat to the patients admitted in the hospital is CPE Infections. CPE often shows resistance to numerous related antibiotics classes which limits the therapeutic options. In the clinics and hospitals, the infections having CPE outcomes cause a burden to the healthcare system. This type of situation can be handled through Tigecycline, Fosfomycin and polymyxins (Polymyxin – B and colistin) taken as the possible candidate therapies for CPE caused infections. As per the research results against the CPE held at UK states about the pattern of sensitivity Polymyxin-B is 92%, Fosfomycin is 60.5% and Tigecycline is 46.9% [4]. The logic behind our research was the probe of a suitable antimicrobial agent against CPE for the guidance of health providers and clinicians for the overall formulation of the antimicrobial strategy of the treatment for drug-resistant organisms.

MATERIAL AND METHODS:

The design of our research was descriptive and cross-sectional. We have completed the research at Mayo Hospital, Lahore from July 2016 to February 2017. For sample collection WHO calculator was used and calculation, Tigecycline patterns sensitivity against CRE was 46.9%, error margin was 7.5% and confidence interval was 95%. 171 patients were included in the research selected through non-probability sampling method. The detection of CPE was carried out through MHT (Modified Hodge Test), the study was completed in the laboratory setting. Non-CPE cases including repeated samples are not included in the research. Before the commencement of this research Institutional permission and informed consent of the patients was also taken. Allotment of the identification number, gender and age were also documented by the hospital. The injection of specimens on Mac Conkey agar and blood; aerobic incubation was carried out at 35 to 37 ℃ for a time of 18 to 24 hours. As per the Clinical Laboratory Standard Institute (CLSI) regulations and guidelines gram negative identification of rods through colony morphology, biochemical reactions and Gram's staining, these were Carbapenems screened resistance with meropenem and imipenem (10 µg) discs along with regular 1st and 2nd line antibiotics through Kirby – Bauer disc diffusion method. After inoculation on the MHA (Mueller–Hinton Agar) all inaccessible CPE (Carbapenems Producing Enterobacteriaceae) were preserved. The antimicrobial vulnerability against Tigecycline, Polymyxin–B and Fosfomycin was carried out through Kirby–Bauer disc diffusion technique with the help of disc Polymyxin–B (300 units), Tigecycline and Fosfomycin respectively (15 µg) and (200 µg). Above 24 mm zone diameters were considered sensitive for the Tigecycline (15 µg), 16mm for (Fosfomycin 200 µg) and 12 mm for (Polymyxin – B 300 units). Collection of data was made on a specified Performa, we observed no association and involvement of the collected specimen in this research. Collected data were entered and statistically analyzed in SPSS. The values of Mean and SD for the age of the participants, Percentage and frequency was calculated for the variable outcomes and genders like Polymyxin – B sensitivity pattern, Tigecycline and Fosfomycin. The gender and age stratification effect modifier was controlled in terms of sensitive/resistant

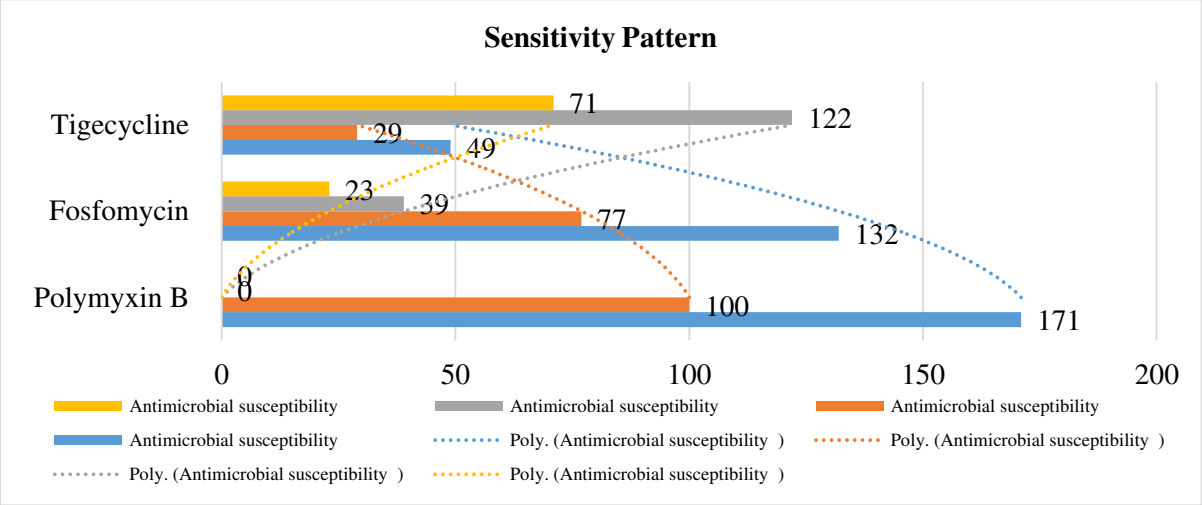
to observed results of the variables. Post-stratification was carried out through the application of the Chi-Square test while the p-value was taken as (≤0.05).

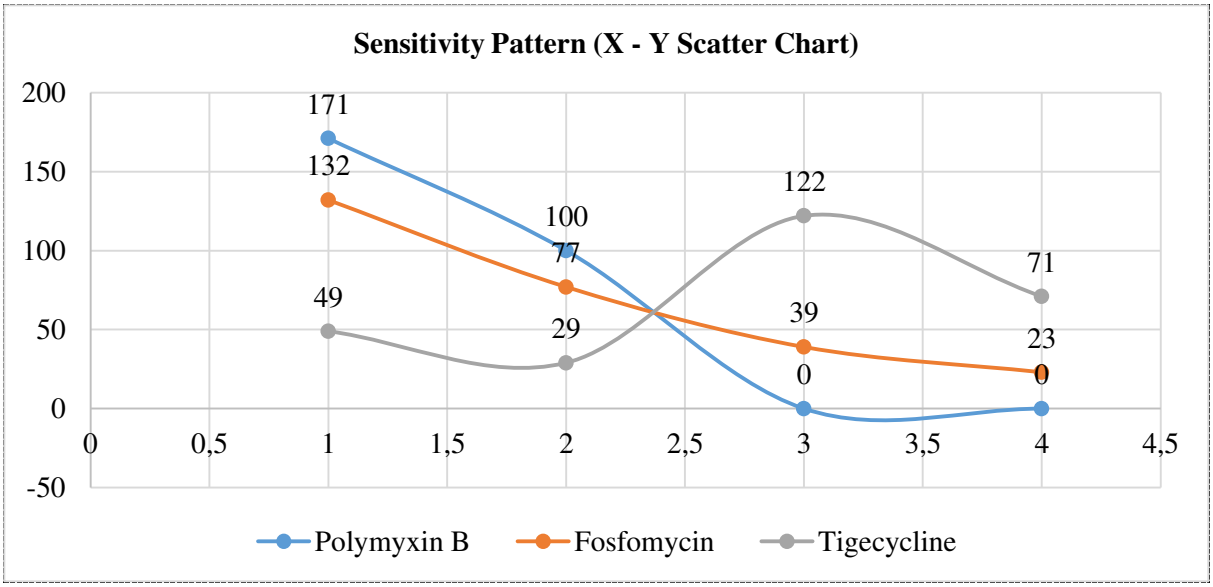
RESULTS

The 171 collected clinical specimens of those participants who comply with the criteria of the research. The age was calculated in Mean ± SD as (42.02 ± 22.367) with Confidence Interval value as (38.65 – 45.40). In the total sample of 171 patients, a total of 110 were male 64%; whereas, 61 were female 36%. According to research results, males dominated the females in number. The result of the research shows that in the total research sample 49 CPE isolates 29% were observed as susceptible to Tigecycline; whereas, in the total of 122 isolates resistant cases were 71%. In the same way, 132 CPE isolates susceptibility to Fosfomycin was observed in 77.2%; whereas, in the total of 39 isolates resistant cases were 22.8%. All the cases were observed susceptible to Polymyxin–B as shown in the given tabular data.

Table: Group Wise Sensitivity Pattern

Group	Antimicrobial susceptibility			
	Sensitive		Resistance	
	No	%	No	%
Polymyxin B	171	100	0	0
Fosfomycin	132	77	39	23
Tigecycline	49	29	122	71





DISCUSSION:

The provision of a significant issue in the course of treatment of the infections of nosocomial type by MDR (Multidrug-resistant) emergence of gram-negative bacilli. The strongest antibiotic class against resistant of the bacteria is Carbapenems, a threat serious in nature to the world's healthcare system is isolated by global CPE spread poses [5]. Isolation of CPE is non-susceptible in vitro to the β-lactams, such as β lactam/β-lactamase combination of the inhibitors, Carbapenems, Fluoroquinolones and amino glycol sides which are frequent [6]. The selected therapeutic options against Carbapenems infections causing the bacteria production are restricted to Tigecycline, Colistin and Fosfomycin. Polymyxin – B susceptibility in the global perspective the clinical isolates of CPE are in the range of 80 to 100 [7]. Though, the resistance incidence is high among few of the regions because of the resistance strains clonal spread. According to results of our research that there was 100% susceptibility of colistin to isolates of CPE [8]. Spain and India respectively 97.5 and 100 % susceptibility results are observed, which are similar to our research results. The research results held at the United Kingdom the susceptibility rate was 92% as isolates of CPE were susceptible to Polymyxin – B. Because of less availability and high-cost factors our research shows better vitro colistin efficacy against CPE, the reason behind may be the restricted use of antimicrobial. In the vitro Fosfomycin activity against isolates of CPE isolates research shows 74% isolates of CPE to antimicrobial. Comparable results have been observed in the research held at the United Kingdom in 2011 as susceptibility rate was 60.5%. German research through the method of agar dilution shows that 72% isolates of CPE were Fosfomycin susceptible. In a research of United States of America, the Fosfomycin activity was assessed as in opposition to 68 KPC were creating isolates of pneumonia, out of which non- susceptible to Colistin and Tigecycline was 23. The valuation shows that the rate of susceptibility was 93% in the overall group and 87% in the case of the non-susceptible group to Tigecycline and colistin. An extreme resistant to drug subgroup non-susceptible to colistin and Tigecycline was observed as 83%. Whereas in the setting, our research 29% isolates of CPE were Tigecycline susceptible, other observed at various other countries were varying. We witnessed the involvement of both Fosfomycin and colistin is potent to be used for the management of the CPE infection. The requirement of time is that healthcare facilities and policies should be implemented and extended the restriction of infection spread. For the management of the threatening disease and infections, it is necessary to the microbiologists, and clinicians to observe closely the Carbapenems use and also monitor antimicrobials use for the preservation of precious antimicrobials. The focus and emphasis are to be put on the combined-therapy instead of mono-therapy for the restriction of the progression of resistance.

CONCLUSION:

We observed CPE as (100%) Polymyxin – B susceptible; whereas, in the case of Fosfomycin it is 77% and Tigecycline susceptibility as 29%. These antimicrobials are potent to be utilized for the CPE infection treatment and management.

REFERENCES:

1. Fan, B., et al., Activity of colistin in combination with meropenem, Tigecycline, Fosfomycin, Fusidic acid, Rifampin or Sulbactam against extensively drug-resistant Acinetobacter baumannii in a murine thigh infection model. PloS one, 2016. 11(6): p. e 0157757.
2. Bergen, P.J., et al., Polymyxin combinations: pharmacokinetics and pharmacodynamics for rational used. Pharmaco therapy: The Journal of Human Pharmacology and Drug Therapy, 2015.35(1): p. 34-42.
3. Abid, M., et al., antimicrobial susceptibility pattern of polymyxin b, tigecycline and Fosfomycin against carbapenems producing Enterobacteriaceae (CPE). Pakistan Armed Forces Medical Journal,2017(6): p. 1026-1029.
4. Bradford, P.A., et al., Correlation of β-lactamase production and colistin resistance among Enterobacteriaceae isolates from a global surveillance program. Antimicrobial agents and chemotherapy, 2016. 60(3): p.1385-1392.
5. Betts, J.W., et al., In vitro and in vivo activities of tigecycline-colistin combination therapies against carbapenem-resistant Enterobacteriaceae. Antimicrobial agents and chemotherapy, 2014. 58(6): p. 3541-3546.
6. Kaye, K.S. and J.M. Pogue, Infections Caused by Resistant Gram-Negative Bacteria: Epidemiology and Management. Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy, 2015.35(10): p. 949-962.
7. Doi, Y. and D.L. Paterson. Carbapenems producing Enterobacteriaceae. in Seminars in respiratory and critical care medicine. 2015.NIH Public Access.
8. Rizek, C., et al., In vitro activity of potential old and new drugs against multidrug resistant gram-negatives. Journal of Infection and Chemotherapy, 2015. 21(2): p.114-117.
9. Rodríguez-Baño, J., et al., Treatment of

Infections Caused by Extended-Spectrum-Beta-Lactamase-, AmpC-, and Carbapenems Producing Enterobacteriaceae. Clinical microbiology reviews, 2018. 31(2): p. e00079-17.
10. Ni, W., et al., Efficacy of polymyxins in the treatment of carbapenem-resistant Enterobacteriaceae infections: a systematic review and meta-analysis. Brazilian Journal of Infectious Diseases, 2015. 19(2): p. 170-180.
11. Karaiskos, I., A. Antoniadou, and H. Giamarellou, Combination therapy for extensively-drug resistant gram-negative bacteria. Expert review of anti-infective therapy, 2017. 15(12): p. 1123-1140.
12. Zusman, O., et al., Polymyxin mono therapy or in combination against carbapenem resistant bacteria: systematic review and meta-analysis. Journal of Antimicrobial Chemotherapy, 2016. 72(1): p. 29-39.
13. Morrill, H.J., et al. Treatment options for carbapenem-resistant Enterobacteriaceae infections. in Open forum infectious diseases. 2015. Oxford University Press.
14. Garnacho-Montero, J., et al., Optimum treatment strategies for carbapenem-resistant Acinetobacter baumannii bacteremia. Expert review of anti-infective therapy, 2015.13(6): p. 769-777.
15. Perez, F., et al., Treatment options for infections caused by carbapenem-resistant Enterobacteriaceae: can we apply "precision medicine" to antimicrobial chemotherapy? Expert opinion on pharmacotherapy, 2016.17(6): p. 761-781.
16. Bergen, P.J., et al., Optimizing polymyxin combinations against resistant gram-negative bacteria. Infectious diseases and therapy, 2015. 4(4): p. 391-415.