EXTENDED SPECTRUM β-LACTAMASE MEDIATED RESISTANCE TO THIRD GENERATION CEPHALOSPORINS AMONG MULTI DRUG RESISTANT *KLEBSIELLA PNEUMONIAE* IN NAIROBI, KENYA.

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ABSTRACT

This study focused on the prevalence molecular biology of extended-spectrum beta-lactamase (ESBL)-positive *Klebsiella pneumoniae* isolates. Extended-spectrum beta-lactamase (ESBL)-producing strains of *Klebsiella pneumoniae* have caused major therapeutic problems worldwide since the majority are resistant to various antibiotics. In this study, an investigation was conducted regarding antibiotic-resistant patterns of 80 *Klebsiella pneumoniae* isolates consisting of 32 isolates from the Centre for Microbiology Research KEMRI and 48 isolates from the Kenyatta National Hospital microbiology laboratory. Strains were identified by standard identification procedures and API 20 E kit. The susceptibility of isolates to commonly available antimicrobial agents was determined using the disk diffusion method and the minimum inhibitory concentrations. Based on the disk diffusion results, resistance to the individual drugs was as follows in the ascending order; augmentin (11.25%), tetracycline (25%), sulfamethoxazole (27.5%), gentamicin (27.5%), cefepime (33.75%), cefoxitin (35%), chloramphenicol (353%), streptomycin (36.25%), ciprofloxacin (37.5%), kanamycin (47.5%), cotrimoxazole (55%), aztreonam (62.5%), amikacin (70%), piperracillin (80%) and ampicillin (87.5%). All the isolates were sensitive to imipinem. Determination of M.I.Cs for thirteen antibiotics, showed slightly different resistant patterns. The MIC results showed that the isolates exhibited resistance to the individual antibiotics in the following ascending order; augmentin (12.5%), tetracycline (26%), gentamicin (31%), Sulphamethoxazole (33%), cefoxitin (38%), chloramphenicol (38%), streptomycin (40%), ciprofloxacin (45%), kanamycin (48%), trimethoprim (58%), co-trimoxazole (60%), amikacin (73%), amoxicillin (85%) and ampicillin (87.5%). Disks containing

ceftazidime, cefotaxime, ceftazidime/clavulanic acid and cefotaxime/clavulanic acid were used in the phenotypic confirmatory disk diffusion test (PCDDT) method to detect ESBL isolates. A comparison between the confirmatory method and double-disk synergy test (ceftazidime, ceftriaxone, cefotaxime, and amoxicillin/clavulanic acid) was also made to assign the appropriate method of detection for ESBLs. The E-test was used to determine the susceptibility of isolates to cefepime. ESBL-negative isolates showed high susceptibility to all tested antibiotics (76-99%). Using the interpretative guidelines of the NCCLS, 25% to 30% of the ESBL isolates would have been reported to be susceptible to the third generation cephalosporins by routine antimicrobial susceptibility methods. The double disk synergy test (DDST) was found to be a useful, simple and cost effective test for the detection of ESBL producing strains. The results indicated a high prevalence (37.5%) of ESBL production in *Klebsiella pneumoniae* isolates in Nairobi and have major implications concerning the clinical use of third generation cephalosporins. Resistance to ciprofloxacin and gentamicin were found in 37% (n=30) and 28% (n=22) of isolates, respectively. Production of ESBL was detected in 37.5% of isolates. Resistance to cefepime was found in 33.75% of isolates. Conjugation experiment of the *Klebsiella pneumoniae* strains with *Escherichia coli*-K-12 resulted in successful transfer of resistance to cefotaxime.

Based on the laboratory results obtained, the prevalence of ESBL strains among the *Klebsiella pneumoniae* isolates is relatively high. More importantly, 33% of ESBL strains were also resistant to ciprofloxacin while the resistance to aminoglycosides was quite prevalent. Continuous surveillance and review of the *Klebsiella pneumoniae* treatment guidelines is therefore recommended. Polymerase chain reaction (PCR)

results indicated that, seven (23.3%) of the ESBL producing *Klebsiella pneumoniae* isolates had the CTX-M gene, eight (26.7%) isolates had the SHV gene and six (20%) of the ESBL producing isolates had the TEM gene.