CHARACTERIZATION OF MULTIPLE DRUG RESISTANT *KLEBSIELLA* STRAINS ISOLATED IN KENYA.

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ABSTRACT

Klebsiella species cause a variety of infections and may serve as a reservoir of multiple resistance determinants that may be transferred to other bacteria. Since *Klebsiella* and the other bacteria share a common environment, it is probable that cross transfer of resistance determinants takes place between them. At the Kenyatta National Hospital, infections by *Klebsiella* species and other enteric bacteria have been shown to be prevalent.

The present study was undertaken to characterise Kenyan isolates of *Klebsiella* species isolated and identified at the Kenyatta National Hospital and the Centre for Microbiology Research of the Kenya Medical Research Institute (KEMRI). A total of 134 isolates were studied. Eighty six isolates were from urine while 48 isolates were from wounds, blood, cerebrospinal fluid, high vaginal swabs, stool or tracheal aspirate. One hundred and seventeen (117) isolates were identified as *Klebsiella pneumoniae* sub species *pneumoniae*, 2 isolates as *Klebsiella pneumoniae* subspecies *ozaenae* and 15 as *Klebsiella oxytoca.*

Resistance to antimicrobial agents was established by the disk diffusion technique and determination of minimum inhibitory concentrations (MICs) by the agar dilution technique. Disk diffusion tests revealed thirteen (13) different patterns among the 86 urinary isolates and sixteen (16) patterns among the 48 non-urinary isolates. Among the urinary isolates, resistance to individual drugs was in the rising order of nalidixic acid at 3.5%, nitrofurantoin 9.3%, gentamicin 66.3%, tetracycline 77.9%, streptomycin 90.7%, co-trimoxazole 96.5%, and sulphamethoxazole at 97.7%. Among the non-urinary isolates resistance to individual drugs rose in the order of kanamycin at 47.9%, gentamicin 52.1%, chloramphenicol 66.7%, tetracycline 68.8%, co-trimoxazole and streptomycin

72.9 % each, sulphamethoxazole 85.4%, and ampicillin at 97.7%. Determination of MICs for nine drugs against 86 isolates selected at random gave rise to twenty different resistance patterns. All isolates were susceptible to ciprofloxacin. Thirty isolates (34.9 %) were resistant to all other drugs except ciprofloxacin. Only one isolate (1.2 %), *Klebsiella pneumoniae* sub species *ozaenae* was susceptible to amoxycillin. Based on the MIC results, the isolates exhibited resistance to individual drugs in the rising order of amoxycillin-clavulanic acid at 53.5%, gentamicin 61.6%, chloramphenicol 72.1%, tetracycline 75. 6%, co-trimoxazole and trimethoprim, 77.9% sulphamethoxazole, 88.4%, and amoxycillin 98.8%.

Plasmid DNA was isolated from all the 86 isolates for which MICs had been determined. Analysis of the plasmid DNA by agarose gel electrophoresis produced a diversity of plasmid profiles which did not correspond to any resistance patterns determined by either disk diffusion or MICs.

Conjugation of *Klebsiella* strains with *Escherichia coli*-K-12 resulted in 12 successful instances of transfer of resistance to co-trimoxazole, tetracycline, gentamicin and amoxycillin. Analysis of plasmid DNA of transconjugant *E.coli* showed that resistance transfer was mainly effected by large plasmids. Transformation of *Escherichia coli* SURE strain by plasmid DNA from *Klebsiella* resulted in the transfer of both small and large plasmids. Resistance to amoxycillin, trimethoprim and sulphamethoxazole was transferred in three transformations.

Digestion of plasmid DNA from *Klebsiella* strains, *E.coli* K-12 transconjugants and transformed *E.coli* SURE strain was done using the restriction enzyme H*ind* III. Similar restriction patterns emerged for two *Klebsiella* donors and their transformed SURE strain recipients.

Both the disk diffusion technique and the determination of MICs, showed a high prevalence of resistance to the commonly prescribed drugs: ampicillin, co-trimoxazole, tetracycline, chloramphenicol, and gentamicin while resistance to the less commonly used kanamycin and the urinary antiseptics nalidixic acid and nitrofurantoin was comparatively less prevalent. MIC results showed 98 % of the isolates were resistant to amoxycillin but use of amoxycillin- clavulanic acid resulted in the reduction of resistant isolates to 54.8 %. The isolates were however susceptible to the third generation cephalosporins, except for two isolates which were resistant to ceftriaxone. Resistance to the more commonly prescribed drugs including chloramphenicol, gentamicin sulphamethoxazole and tetracycline occurred so often as to exclude them as reliable effective therapeutic agents in treating infections caused by these isolates. Resistance was transferable by both conjugation and transformation. This shows that there is a likelihood of spread of resistance determinants from *Klebsiella* to other organisms within Kenyatta National Hospital.

Based on the results of this study there is need to rationalize the use of antimicrobial agents through improved prescribing habits and continuing education for health personnel.