Emergence of panresistant superbugs is a serious threat to global public health security.

Panresistant infections are associated with prolonged hospitalization, disseminated infections and mortality.

Antimicrobial misuse leading to selection pressure, transfer of resistance, inadequate detection of panresistance and inadequate infection control measures may contribute to a “Microbial Holocaust” by panresistant pathogens.

Detection and characterization of panresistance requires specialized testing modalities.

Study confirms and characterizes panresistant phenotypes.

METHODS

Fifty isolates identified by conventional methods and found resistant to all empirical antimicrobials by Kirby Bauer method.

Vitek 2 compact was used for identification and interpretation.

PCDT for ESBL + AmpC, and Klebsiella pneumoniae carbapenemase (KPC) + MBL (Rosco Diagnostica, Denmark) were interpreted as per CLSI/EUCAST methods.

A ≥5mm increased zone of cefotaxime+clavulanic acid (CTX+C) against cefotaxime (CTX30) or cefotaxime+clavulanic acid+cloxacinil (CTXCC) against cefotaxime+cloxacinil (CTXCX) is indicative of ESBL. A ≥5mm increased zone of CTXCC against CTX30 or CTXCC against CTXCC is indicative of Amp C β-lactamase.

A ≥5mm increased zone of CTXCC against CTX30 or CTXCC against CTXCC is indicative of coexistent ESBL and Amp C.

A ≥5mm increased zone of meropenem+dipicolinic acid (MRPDP) against meropenem (MRP10) confirms MBL.

A ≥5mm increased zone of meropenem+boronic acid (MRPBO) against MRP10 or meropenem+cloxacinil (MRPCX) confirms KPC/other Ambler class A β-lactamase.

A ≥5mm increased zone of both MRPBO and MRPCX against MRP10 confirms Amp C hyperproduction with porin loss/efflux.

RESULTS

Panresistant Klebsiella pneumoniae, Klebsiella oxytoca, Burkholderia cepacia, Pseudomonas aeruginosa, Acinetobacter baumannii and Escherichia coli were isolated from blood samples from oncology patients and transplant recipients; multiple injuries and burn wounds; and endotracheal aspirates from critical care patients.

27 (54%) were found resistant to all drugs.

23 (46%) were found susceptible to tigecycline and colistin.

Multiple resistant phenotypes were encountered such as ESBL+ carbapenemases (metallo or KPC), resistance to carbapenemases (impermeability) and aminoglycoside resistance (AAC 6’+) were frequently seen in Klebsiella pneumoniae and Klebsiella oxytoca.

Carbapenemase (metallo or oxa), acquired penicillinase + resistance to carbapenemases (impermeability) and high level resistance + resistant carbapenemases (impermeability) were seen in Pseudomonas aeruginosa.

Resistant carbapenemases (impermeability), carbapenemase (metallo or oxa) and high level resistance + resistant carbapenemases (impermeability) were seen in Acinetobacter baumannii.

ESBL+ carbapenemases (metallo or KPC) were seen in E. coli.

Phenotypic combined disk tests (PCDT) for ESBL + Amp C; KPC + MBL interpretations revealed coexistent ESBL, Amp C and MBL alongwith resistance to polymyxins and tigecycline.

DISCUSSION

Emergence of panresistant superbugs in cancer, burns, wounds, critical care and transplant recipients can cause significant morbidity and mortality.

Multiple resistance phenotypes may surpass routine identification and result in treatment failures.

Molecular methods such as DNA hybridization, 16s rDNA amplification with species specific primers and pulsed-field gel electrophoresis are highly specific for identification, resistance characterization, strain typing and outbreak investigation.

Comprehensive diagnosis by phenotypic methods & systems is may also form the only available modality for identification of panresistant pathogens for medium sized laboratories.

The increasing transmission of formidable panresistant pathogens, rising population of immunocompromised populace and failure if antimicrobial therapy forms a lethal triangle.

Clinical correlation of panresistance is mandated as in vitro resistance may not corroborate to clinical picture.

Coexistent ESBL, AmpC and MBL along with resistance to Tigecycline and Colistin leaves no viable options.

Uncontrolled infection and ongoing transmission can lead to outbreaks and epidemics which may have long term effects on furtherance of pathogenicity and drug resistance.

Colistin + rifampin and colistin + antipseudomonal penicillins have been found promising in panresistant infections.

Panresistant pathogens can be exploited as bioweapons.

CONCLUSION

Panresistant superbugs can cause significant morbidity and mortality.

A greater emphasis on infection control and antimicrobial stewardship policies and practices in primary as well as intensive care settings is mandated.

While rapid response to outbreaks may help control their emergence and transmission, grave issue of their exploitation as bioweapons remain at large.