From bad to worse: Emergence of extensively drug resistant Gram negative bacilli among Nigerian immunocompromised patients

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Humankind is beginning to lose the war against renewed threats posed by infectious agents and their resistance to available antibiotics. Previous mild infections are now turning into "monsters", killing hundreds of people globally with little or no options for cure. The number of affected patients in developing countries is higher than figures in developed nations due to overuse of antibiotics, poor hygiene, environmental pollution, poor infrastructure and possible effects of the weather and climate in such nations[8]. Habits such as coughing in public places, discharge of sputum on bare floors, indiscriminate discharge of sewage in the environment, open defecation and urination has made infectious agents such as *Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa* and *Salmonella* spp. *(*which are often obtained and acquired in hospitals), readily available on different environmental surfaces and has made dissemination of such bacteria much faster in the community setting.

Isolation of different bacterial species as well as antibiotic resistant bacteria (ARB) from different clinical and environmental samples such as restroom floors, door handles of rooms and schools, mobile phones, activated sludge, sewage, refuse dump sites, and also on vegetables, animals and humans has been documented in Nigeria[2,12,13]. In the last decade, the prevalence has been increasing with no sign of respite. Of high concern is the alarming rate of Gram-negative bacilli (GNB), which are resistant to commonly prescribed and reserved antibiotics[3,6,11]. The magnitude is so high now because of increasing isolation of multidrug resistant (MDR) GNB such as *Escherichia coli, Klebsiella pneumoniae, Salmonella sp, Proteus sp* etc that are resistant to last resort antibiotics that are not available for use in the community or healthcare facilities[9].

Group and individual research findings in Nigeria have indicated beta lactamase production as the main cause of GNB resistance to penicillins, cephalosporins and carbapenems[4,7,10]. However, routine microbiological laboratory investigations carried out in the majority of medical laboratories in Nigerian hospitals are not capable of screening for or identifying specific beta lactamases produced by GNB or of isolating and characterising resistant *Acinetobacter baumannii* known to cause serious infections that are very hard to treat. By virtue of this, these pathogens are not being identified and this, in turn, leads to sub-optimal antibiotic therapy in Nigeria.

The category of patients most affected by these unidentified superbugs are hospitalised immunocompromised persons such as HIV infected individuals, children, elderly, pregnant women, diabetic patients, cancer patients, the malnourished and those on steroids and other immunosuppressive drugs. Concern about increasing morbidity, mortality, hospital stay, and severe economic loss to the patient and nation due to exhaustion of antibiotic options has been raised.

> *"Out of 68 Gram negative bacilli isolated from hospitalised immunocompromised patients, 22% exhibited an extensively drug resistant profile."*

The latest results from a study carried out in a tertiary /referral hospital in the north western region of Nigeria showed a progression from MDR to Extensively Drug Resistant (XDR) status among GNB[5] (**Fig. 1**). Out of 68 GNBs isolated from hospitalised immunocompromised patients, 15 (22.1%) isolates exhibited an XDR profile. Conversely, no XDR was recovered from the hands of immuno-competent healthcare workers (HCW), but 5.9% of isolates from them were MDR. Preliminary investigation revealed that 53.3% of the XDR isolates from immunocompromised patients were ESBL producers, 13.3% were AmpC producers, 25% co-produced ESBL and AmpC and none of the isolates were phenotypically confirmed to be carbapenamase / metallo-beta lactamases (MBLs) producers. XDR *Escherichia coli, Klebsiella pneumoniae, Enterobacter aerogenes* and *Proteus mirabilis* express 100% resistance to Gentamicin, Piperacillin+Tazobactam, Aztreonam, Ceftriaxone, Amoxicillin, Amoxycillin/Clavulanic acid, Tetracycline and Ciprofloxacin. The organisms demonstrated a variable resistance pattern against meropenem, colistin and tigecycline.

Fifty percent of the XDR isolates were resistant to Colistin, 75% resistant to Tigecycline—leaving virtually no or very little antibiotics available for treatment. *Enterobacter aerogenes* also demonstrated total

resistance to Meropenem, Cefoxitin and Tigecycline. Antibiotics with favourable activities against some of the XDR GNB in the study were Colistin, Tigecycline, Meropenem and combinations of Piperacillin-Tazobactam with either Ceftriaxone or Ceftazidime (**Fig. 1**).

Apart from behavioural factors such as self-medication and abuse of antibiotics, other anthropogenic factors, especially in Nigeria, that are believed to drive AMR from MDR to XDR status and facilitate their spread from one community / hospital to another, are: inappropriate antibiotic prescribing by community HCWs; unavailability of funds to engage in AMR research; non-communication of research findings to appropriate stakeholders; lack of implementation of suggestions from research findings; adherence to obsolete laboratory procedures for investigation; use of counterfeit multiple antibiotic sensitivity discs; questionable practices in hospitals and health ministries; re-labelling/ packaging of expired drugs; and persistent crisis between HCWs (especially doctors and medical laboratory scientists) over hospital or unit leadership, which divert attention of HCWs away from patient safety.

Fig. 1: Resistance pattern and available antibiotics for treating Gram negative bacilli isolated from immune compromised patients attending a Nigerian Federal Medical Center. Key: PEN=penicillins, CAB= carbapenems, AMI=aminoglycosides, CEP= cephalosporins, MAC=macrolides, FLO=flouroquinolones, TZP=Piperacillin-Tazobactam, COL=colistin, TIG=tigecycline

Despite efforts of organisations such as WHO, CDC, APUA and other non-governmental organisations in combating AMR globally, it seems Nigeria is far from reaching the milestone. Even though XDR pathogens were only detected among immunocompromised patients, other environmental, social, and economic factors could drive its dissemination to HCWs, other patients and other community members.
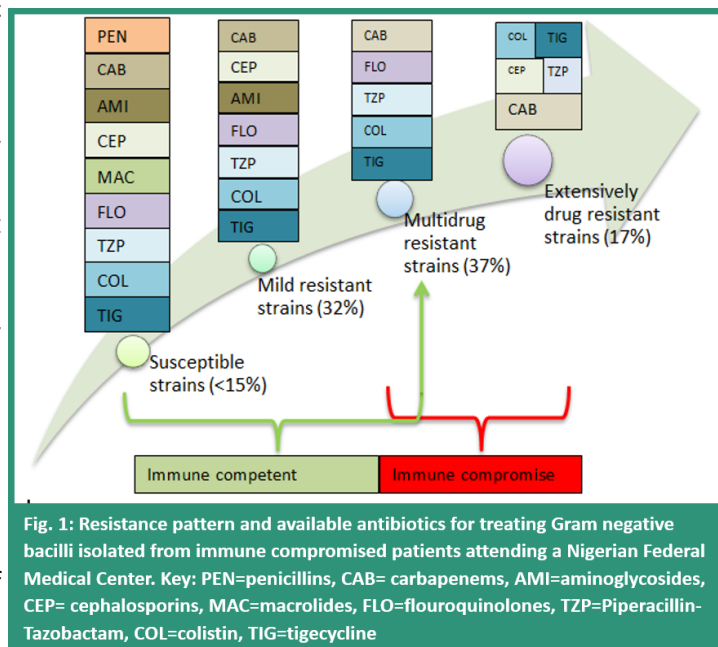
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