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Antimicrobial Resistant Profile of Streptococcus Pneumoniae Isolated from Suspected Tuberculosis Patients in Ekpoma, Nigeria and its Environs.

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Abstract:

Seven isolates of Streptococcus pneumoniae were isolated from sputum samples of suspected tuberculosis patients and characterized. Kirby-Bauer disc diffusion technique was adopted in susceptibility testing of isolates. Isolates showed the highest resistance of 85.7% to norfloxacin and ampicillin –cloxacillin, while the lowest resistance of 14. 3% was to caftaxidime and pefloxacin. The difference in resistance observed between norfloxacin and pefloxacin discourages a common practice where one antibiotic is used for susceptibility test and another (from the same group) is used for treatment. S. pneumoniae is significantly resistant to most of the commonly available antibiotics in Ekpoma and its environs.

Key Words: Antimicrobial resistant, S. Pneumoniae.

Introduction:

Prior to the 1960's, *Streptococcus pneumoniae* were assumed to always be susceptible to the penicillin and routine antibiotic susceptibility testing were not performed in most hospitals. However by 1980, numerous reports were made about pneumococcal isolates with relative resistance to penicillin and some isolates with multiple antibiotic resistances ⁽¹⁾. *S. pneumoniae* remains an important pediatric pathogen causing respiratory infections, pneumonia, bacteremia, and meningitis ⁽²⁾.

The first group of resistant *S. pneumoniae* is penicillin non susceptible *S. pneumoniae* (PNSP) whose rapid spread has been well documented ⁽³⁾. Within a large city resistant pattern can also vary by region ⁽⁴⁾. More troublesome was the emergence of Multiple Resistant pneumococci (MRP), first widely publicized by Jacobs ⁽⁵⁾. They were reported to have shown resistance to erythromycin, lincomycin, chloramphenicol and penicillin.

While these multiple resistant organisms have been widely reported in the United States, they are much larger problem in South Africa, Australia and New Guinea ⁽⁶⁾. Clinical health care providers' needs information about the pattern of drug resistance among isolates in their localities to enable them to optimize empirical regimens and initial therapy for *S. pneumoniae* infections. Accurate laboratory information is needed at the local level to minimize the development of antibiotic resistance ⁽⁷⁾. Such data are few if available for the Ekpoma population. This study was therefore designed to determine antibiotic resistance pattern of *S. pneumoniae* isolated from patients attending tuberculosis clinics in Ekpoma with the hope of providing information that will help control and prevent the infection.

Materials and Methods:

A total of 110 sputum samples were processed at Search-Light Medical Diagnostic Center Ekpoma. Seven strains of *S. pneumoniae* were isolated and identified using standard methods ⁽⁹⁾, and in accordance with the scheme of Barrow and Feltham ⁽¹⁰⁾. Antibiotic susceptibility testing was done by the Kirby-Bauer disc diffusion technique ⁽¹¹⁾. The antibiotics used were: pefloxacin, ceftaxidime, gentamicin, chloramphenicol, oxacillin, erythromycin, ampicillin-cloxacillin, and norfloxacin.

Results:

The result of this survey reveals norfloxacin and ampicillin-cloxacillin as showing the highest resistance (85.7% each), whereas pefloxacin and ceftaxidime showed the least resistance (14.3% each). Erythromycin showed 71.4% resistance to isolates. Gentamicin and chloramphenicol each showed 28.6% resistance and oxacillin showed 28.6% resistance respectively (Table 1).

Table 1. Antimicrobial resistance profile of 7 strains of *S. pneumoniae* isolated from sputum samples.

Antimicrobial Agent	No (%) of Resistant Strains
Norfloxacin	1 (85.7)
Ampicillin	1 (85.7)
Erythromycin	2 (71.4)
Oxacillin	4 (42.9)
Chloramphenicol	5 (28.6)
Gentamicin	5 (28.6)
Ceftaxidime	6 (14.3)
Peflaxine	6 (14.3)

Discussion:

Choice of antibiotics used include those commonly recommended for the management of *S. pneumoniae* in rural areas of developing countries ⁽¹²⁾ and the Kirby-Bauer disc diffusion technique adopted is in accordance with the recommendations of National Committee for Clinical Laboratory Standards ⁽¹³⁾. An interesting observation made in this survey is the difference in resistance between norfloxacin (85.7%) and pefloxacin (14%). They belong to the same generation of quinolone which appear to bind to several sites on the DNA gyrase enzyme. The nature of resistance showed by these two antibiotics discourages a common practice in some setting where sensitivity is done on one quinolone and another is used for treatment either due to cost implication or availability. This finding could be a pointer to emergence of quinolone resistant *S. pneumoniae* in Ekpoma and its environs. Antibiotic surveillance and multiple drug therapy if initiated in Ekpoma may help reduce resistance of drug used in the management of *S. pneumoniae* infections. While our isolate was 85.7% resistant to ampicillin-cloxacillin it showed 42.9% resistance to oxacillin. This is higher than 25% reported from 7 United States regions; 30% from Oklahoma; 10% from Calgary/Karachi and 0% reported from Thailand respectively ^(5, 2, 15, and 16). The

addition of oxacillin allows for greater chance in identifying penicillin resistant strains as seen in the difference in resistance between ampicillin-cloxacillin and oxacillin resistance to isolates (Table 1). The mechanism of penicillin resistance in *S. pneumoniae* is debated. It is not a beta-lactamase mechanism since a large enough beta-lactamase producing normal throat flora organism could prevent streptococcal eradication by destroying penicillin. Another hypothesis is based on antibiotic tolerance. Thus the growth of tolerant bacteria is inhibited by relatively low concentration of antibiotic, but extremely higher concentrations (> 32 times the MIC), are required to kill the organism. The most promising hypothesis centers on the alteration of the penicillin binding proteins found on the resistant pneumococci⁽¹⁷⁾.

Some of the isolates may be similar to those detected in recent nursing-home outbreaks involving a single clone of highly resistant organism⁽¹⁸⁾. An out-break clone or several resistant serotypes may have contributed to the observed 42.3% resistance to penicillin, in addition to the increasing local antibiotic prescribing practices in Ekpoma and other rural areas of some developing countries. Elaborate surveillance studies and a co-ordinated multidisciplinary approach is required to tackle the problem of high level penicillin resistance revealed by this survey.

Our findings further revealed 71.4% resistance to erythromycin. This is higher than 28% resistance reported by Chokephaibulkit (16), in Thailand and 4.2% reported by Harmish⁽¹⁹⁾, from non-invasive site in the Grampian Area. Resistance can result from mutation in chromosomal genes or plasmids transferred from resistance bacteria. Harmish⁽¹⁹⁾ reported two forms of erythromycin resistance in *S. pneumoniae*: The M and MLSB Phenotypes which are encoded by the *mef* (A) and *erm*(B) genes respectively.

Our isolates showed 28.6% resistance to chloramphenicol. This is similar to 26% resistance reported in Thailand⁽¹⁶⁾. Resistance to chloramphenicol is due to acquisition of plasmid that encodes the enzyme that chemically inactivates the drug⁽²⁰⁾. It's toxicity at higher dose and the complication of aplastic anemia have made the use of chloramphenicol reserved for life threatening infections for which no effective alternative treatment is available⁽²⁰⁾. Chloramphenicol is still being used in some developing countries due to its low cost.

Isolates showed 28.6% resistance to Gentamicin. This percentage of resistance showed by Gentamicin may be due to its ability to bind to several different sites on the bacterial ribosome, which lessens the likelihood of the development of mutational resistance and also due to it being less susceptible to enzymes that chemically inactivates the drug.

Isolates showed 14.3% resistance to ceftaxidine. This is lower than 42% reported in Thailand⁽¹⁶⁾. This pattern of resistance might be a pointer to

cephalosporin (caftaxidime) resistant *S. pneumoniae* in Ekpoma community and its environs.

Generally, as the prevalence of resistance increases, the public health response requires a multidisciplinary approach. Surveillance can increase awareness among clinicians and public health practitioners can assist in targeting areas for intervention. Clinical guidelines can improve management of clinical syndromes commonly attributable to pneumococcal infections⁽²⁰⁾. Adoption of intervention strategies including use of pneumococcal vaccines and campaigns to promote judicious use of antibiotics offer potential to prevent infections with drug resistant *S. pneumoniae*.

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