Bacterial Isolates and Antibiotic Sensitivity in Community Acquired Pneumonia

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SUMMARY

Objective: The objective of the study was to determine bacterial causes of community acquired pneumonia and their antibiotic sensitivity pattern amongst patients admitted into medical wards in Aminu Kano Teaching Hospital, Kano, Nigeria

Methods: The study incorporated patients aged fifteen years and above admitted into the Accident and Emergency unit, Medical wards, and Intensive care unit of AKTH with a provisional diagnosis of Community-Acquired Pneumonia between June 1, and November 30 2006.Those who have been on antibiotics two weeks prior to presentation were excluded from the study. Each patient had collection of sputum samples for gram and ziehl-Neelson (ZN) staining and bacteriological culture. Blood culture was also done for all cases and antibiotic sensitivity testing was done on isolates.

Results: During the six month period, 50 patients (mean, age 43.2 range18-76, were evaluated. All patients had single conventional bacterial isolates. *Streptococcus pneumoniae* was the commonest isolate, found in 32 cases (64%). *Klebsiella pneumoniae* was the second, found in 7 cases (14%), others isolates found were *Pseudomonas aeruginosa* in 5 cases (10%), *E coli* 3cases (6%), *Staphylococcus aureus* in 2 cases (4%) and *Proteus spp* in 1 case (2%). 2 patients (4%) were sputum smear positive for acid- fast bacilli (AFB).The isolates showed good sensitivity to the newer and more expensive antibiotics (quinolones and cephalosporins), with resistance to the older and cheaper ones except gentamycin.

***Conclusion*:** Streptococcus pneumoniae is the most prevalent pathogen isolated in cases of community acquired pneumonia in Kano and the newer antibiotics; cephalosporins and quinolones showed good sensitivity profile.

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INTRODUCTION

Community acquired pneumonia was described as being the commonest cause of hospital admission in Zaria, Nigeria; this same trend was documented from other African countries like Ethiopia and Kenya.[1-3] Community Acquired Pneumonia is caused by a variety of viral bacterial and fungal pathogens, however bacterial pathogens account for the majority of cases.[4] *Streptococcus pneumoniae* accounted for over 80% of cases of CAP in the pre-penicillin era, surprisingly it is still the most common identified pathogen in nearly all studies, be it community or hospital based.[5] Other groups of pathogens responsible for community-acquired pneumonia are the bacterias causing atypical pneumonia.[6]Atypical pneumonia is an uncommon diagnosis in sub-Saharan Africa; nevertheless, lack of response to penicillin in some cases of pneumonia alludes to the fact that atypical bacteria may be responsible for some of these infections.[7]

However, studies in Nigeria, Kenya and Ethiopia have found *M pneumoniae* as the pathogen responsible for a good number of the cases. *Legionella pneumophilia* seems not to be an important cause of pneumonia in Africa.[1-3] A number of studies in Africa found *Mycobacterium tuberculosis* as a cause of CAP, often co-existing with other bacterial pathogens.[1-3] Even with state of the art laboratories in the developed countries, a microbiological diagnosis of CAP is only confirmed in 50-70% of cases.[8] It is therefore easy to understand why in resource constrained countries, a lower yield is often found.

If it were possible to know the pathogen responsible for CAP within a very short period, it would have been easy to start treatment with an antibiotic to which the organism is susceptible; however, most often a therapeutic decision has to be taken without such a privileged knowledge. In many instances, an empirical treatment is initiated knowing neither the pathogen responsible nor its antibiotic sensitivity profile. The clinician has to rely in most instances on knowledge of local epidemiological profile of common bacterial isolates in CAP and their sensitivity pattern. Despite remarkable advances in the identification of new microbial and anti-microbial agents, the world over, there is still a paucity of data on common causes and susceptibility pattern of CAP in Kano. This is further compounded by the increasing emergence of antibiotic resistant organisms. This study sets out to fill in this gap, and to form a basis for comparing antibiotic susceptibility pattern over time.

METHODS

The study was conducted at Aminu Kano Teaching Hospital; a tertiary health centre, established in Kano in 1988. It has a bed capacity of 310 beds. Ethical clearance was obtained

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from The Ethical Committee of Aminu Kano Teaching Hospital and written consent was obtained from recruited patients/their relation.The study was a descriptive prospective study incorporating 50 consecutive patients 15yrs and above admitted with a diagnosis (based on clinical and radiological findings as well as positive pathogen culture) of Bacterial Community-Acquired Pneumonia necessitating admission into the Accident and Emergency unit, Medical wards and Intensive care unit of AKTH between June 1, and November 30 2006. Patients who have been on antibiotics two weeks prior to presentation were excluded from the study as this is likely to affect the yield of pathogen culture. Upon admission; before antibiotics are administered; sputum specimens were collected from eligible patients, in sterile sputum bottles, and delivered to the microbiology laboratory for immediate processing. These was done for three consecutive days, for purpose of Ziehl-Neelson (ZN) staining for AFB (acid fast bacilli)

Gram staining was done on initial sputum sample. The sputum specimens were inoculated in blood agar chocolate agar and MacConkey agar. Culture plates were incubated for 24hrs at 37^0C. Thereafter smears were obtained from each for gram staining and standard biochemical testing, to determine the bacterial species of the isolate. All isolates had antibiotic sensitivity determined by the standard disc diffusion technique, against commonly available antibiotics.[9]

Disc of the following antibiotics were used: penicillin G (10 units), ampicillin (25mg), amoxicillin (10ug), amoxyclav (30ug), cloxacillin (5ug), tetracycline (10ug), erythromycin (10ug), chloramphenicol (10ug), gentamicin (10ug), cefuroxime (30ug), ceftriaxone (30ug), ceftazidime (30ug), pefloxacin (10ug), ciprofloxacin (5ug), ofloxacin (5ug), sparfloxacin (10ug). A diagnosis of *Mycobacterium tuberculosis* infection was made based on at least two samples of sputum testing positive for acid-fast bacilli by ZN staining. Blood cultures were done aerobically on thioglycolate broth , and preparations were sub-cultured every 2days, on chocolate agar, MacConkey agar, and blood agar for up to 7 days. The agar plates were examined for pathogenic bacteria and biochemical test carried out to determine specie type.[10]

Anaerobic blood cultures were done on chocolate agar plate, which where incubated for 72hrs in oxoid anaerobic jar following standard procedure of oxygen evacuation, using gas generating kits (UNIPATH LIMITED HAMPSHIRE ENGLAND). Data obtained were analyzed using the statistical package SPSS version12. Means, ranges and standard deviations were computed for quantitative variables and proportions for qualitative data. Two tailed t-test was used for comparison of group means, while the significance of observed differences in proportions was determined by chi-square test. A p-value of <0.05 was considered statistically significant.

RESULTS

During the study period 612 hospitalised patients were screened, 67 had clinical features suggestive of pneumonia but only 50 patients, who satisfied the inclusion criteria for bacterial community acquired pneumonia with positive pathogen culture were studied. This translated to a relative incidence of 8.17%. All patients were admitted via the Accident and Emergency Unit of the hospital into either the Medical wards or ICU. Only 3 of the patients were managed in the ICU. The ages of the patients ranged from 18-76 years, with a mean age of 43.2 (standard deviation 15.24). The peak age groups were 45-54 years. There were 33 males and 17 females, giving a male: female ratio of 1.9:1. There was no significant difference in the age distribution between males and females (Figure 1).There was no organism isolated from blood cultures after 1 week of incubation.

All patients had single conventional bacterial isolates in sputum. *Streptococcus pneumoniae* was the commonest isolate, found in 32 cases (64%). *Klebsiella pneumoniae* was the second, found in 7 cases (14%), others isolates found were *Pseudomonas aeruginosa* in 5 cases (10%), *E coli* 3cases (6%), *Staphylococcus aureus* in 2 cases (4%) and *Proteus spp* in 1 case (2%). 2 patients (4%) were sputum smear positive for acid- fast bacilli (AFB). All 32 (100%) isolates of *Streptococcus pneumoniae* were sensitive to cerftriaxone and ceftazidine, 23 (72%) isolates were sensitive to cefuroxime and sparfloxacin. 18(56%) were sensitive to Amoxycillin and ofloxacin. 16(50%) were sensitive to gentamicin and ciprofloxacin. All the 32 isolates were resistant to penicillin, amipicillin, cloxacillin, tetracycline erythromycin, chloramphenicol and co-trimoxazole. The isolates generally showed good sensitivity to the newer and more expensive antibiotics (quinolones and cephalosporins), with resistance to the older and cheaper ones except gentamycin (Table1).

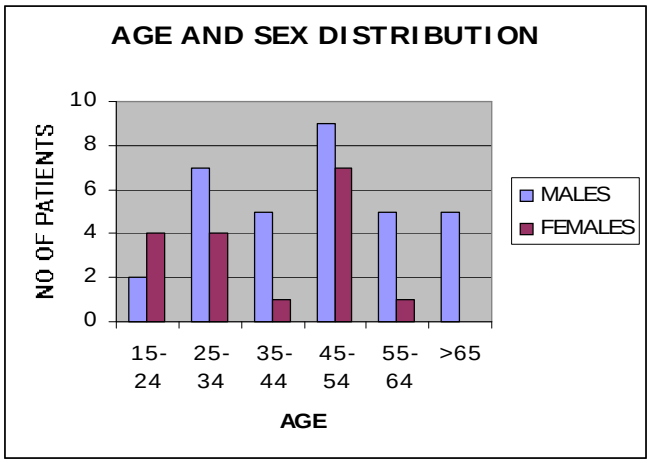

Figure 1: Age-sex distribution of patients with CAP

Table 1: Antibiotics susceptibility pattern of bacterial isolates

Bacterial isolate	*S pnuemoniae*	*K pnuemoniae*	*P aeruginosa*	*E coli*	*S aureus*	*Proteus spp*
No of isolates (%)	32	7	5	3	2	1
Penicillin	6(19)	1(14)	-	0(0)	0(0)	-
Ampicillin	5(16)	2(29)	0(0)	1(33)	0(0)	0(0)
Amoxycillin	17(53)	5(71)	0(0)	1(33)	1(50)	0(0)
Clavulanated Amoxycilllin	23(72)	4(57)	1(20)	3(100)	1(50)	0(0)
Cloxacillin	6(19)	2(29)	0(0)	0(0)	2(100)	0(0)
Tetracyclin	2(2)	1(14)	0(0)	1(33)	0(0)	0(0)
Erythromycin	11(34)	1(14)	0(0)	0(0)	0(0)	0(0)
Chloramphenicol	5(16)	0(0)	0(0)	1(33)	0(0)	0(0)
Cotrimoxazole	8(25)	0(0)	-	0(0)	-	-
Gentamycin	16(50)	3(43)	4(80)	2(66)	-	1(100)
Cefuroxime	21(66)	5(71)	2(40)	2(66)	1(50)	1(100)
Ceftriaxone	32(100)	7(100)	3(60)	2(66)	1(50)	1(100)
Ceftazidimez	32(100)	7(100)	5(100)	2(66)	2(100)	1(100)
Pefloxacin	18(56)	3 (43)	3(60)	1(33)	0(0)	0(0)
Ciprofloxacin	16(50)	3(43)	1(20)	0(0)	0(0)	0(0)
Ofloxacin	17(53)	2(29)	2(40)	1(33)	1(50)	0(0)
Sparfloxacin	21(66)	6(86)	3(60)	1(33)	1(50)	1(100)

Keys: 0: Indicates resistance - : Indicates not tested

DISCUSSION

Microbiological evidence of pneumonia is not found in up to 50% of patients in most studies, depending on the diagnostic methodology used. This finding cuts across geographical, economical and technological devices. In our study only patients with suggestive clinical and culture isolate of a pathogenic bacteria were included. This precludes the possibility of including patients with pneumonia like states like bronchitis and Bronchial asthma. *Streptococcus pneumoniae* was the commonest isolate from patients with CAP in keeping with most other studies all over the world.[11, 12] It is likely that those cases that were excluded due to inability to culture a pathogenic organism might be due to *S Pneumoniae* as was alluded to by several studies. [12-14]

Klebsiella pneumonia was the commonest gram-negative organism found in this study, which is in keeping with another study from Ibadan.[15] Other studies have implicated *Haemophilus infuenzae* as the commonest gram-negative organism isolated in CAP as well as being second to *S pneumoniae* as a cause of pneumonia. The 2nd ranking of *K pneumoniae* in our study may be due to the fact that *H influenzae* is a fastidious organism that is not isolated commonly in this environment.[14,15] It is easily overgrown by other organism in sputum culture especially if there is delay in processing the sample.[16]

Pseudomonas aeruginosa was isolated in 5 (10%) cases in this study. Its finding is commoner among patients with immunosuppression, cystic fibrosis and bronchiectasis.[17] It may be that the finding of this isolate may suggest the presence of some underlying lung disease, however, this would require some further studies to prove.

Staphylococcus aureus was isolated in 2 (4%) cases which is similar to findings in other studies. [15,18] and would ideally require an intensive care unit (ICU) management. Other common aetiological finding in most studies include: *Mycoplasma pneumoniae* and *Chlamydia pneumoniae*, however the evidence for these atypical organisms can only be obtained by serially following pre-treatment and convalescent 1gG serological assay specific to these organisms. The technology for these was not available in our setting during the study. Two of the patients studied had a positive sputum smear for acid fast bacilli (AFB). This finding is consistent with findings in other studies,[19, 20] the implication is that; patients with pulmonary tuberculosis could be traced if screening for it is initiated early. Blood cultures were all-negative. Blood culture is particularly useful in detection of *S pneumoniae* in patients that have started therapy with antibiotics prior to presenting to hospital. The patients studied had no prior usage of antibiotics for their pneumonia before they were admitted.

It is also likely that delay in processing samples of blood culture may be responsible for lack of isolation of isolates. Antibiotic susceptibility of causative agents of infection has far reaching public health implications, so much so that several international bodies and societies have put in place mechanism to study the trend of global antibiotic resistance. The usage of antibiotics in Africa is one of immense intrigue, in spite of having a very high burden of community infections. The pattern of prescription of drugs by non-qualified personnel under dosing and outright fake drug racketeering has become profound. These factors lead to development of resistance by bacterias to drugs that otherwise would have been helpful in treating infections.[21] This study has found high level of resistance to commonly prescribed and relatively cheap antibiotics like Amoxycillin, Ampicillin, chloramphenicol and co-trimoxazole, which are often the first line drug in most African settings. Furthermore, with the high prevalence of HIV infection and an attendant prophylactic usage of co-trimoxazole in AIDS patients, there is fear that the drug will be opened to further pressure. This finding is similar to an earlier report from Habib et al. from Kano.[22]

This study has found low susceptibility to Ciprofloxacin and Ofloxacin but a relatively good susceptibility to Sparfloxacin and Pefloxacin. *Staphylococcus aureus* was found to be sensitive to Ofloxacin and Sparfloxacin and resistant to Ciprofloxacin and Pefloxacin, which is in line with an earlier report by Ikeh from Jos where 85% of *Staphylococcus* were sensitive to Ofloxacin and 45% were sensitive to Pefloxacin.[23]

The natural history of these events is that with increasing usage of these antibiotics indiscriminately, the resistance level will continue to increase as such there is a need for a quick legislation to turn the tide of inappropriate usage of antibiotics in Nigeria. Amoxycillin/Clavulanic acid (Amoxiclav) has faired well in this study with 32 (64%) of the isolates being sensitive to it. This may be due to the protective property of the clavulanic acid in the drug. Furthermore the availability of cheap generic forms of quinolones has shifted the attention of prescribers away form it, being relatively expensive and having few generic preparations. In spite of the long tradition of using gentamicin as first line drug all over Nigeria, for many infections this study has found a fairly good susceptibility, 52% for it. It is likely that this drug will have many more years of useful usage in rationale antibiotic prescription, bearing in mind that it is cheap, readily available and not subject to much counterfeiting. It is also worthy of note that it is effective against a significant percentage of *S pneumoniae* (50%) and has strong anti *Pseudomonal* activity 80%. This potential will allow its usage in rural hospital setting as first line parenteral drug in CAP, in patients who do not have underlying kidney disease.

Cephalosporins are relatively expensive, compared to other antibiotics and as such are not commonly used except in specialized situations like secondary and tertiary care centers. This study has found high susceptibility to cephalosporins by both gram positive and gram negatives bacterials isolated. This is in keeping with report by Habib et al from Kano.[22] It is also the trend that has been documented globally.[24.25.] It appears to be the last line of antibiotic defence in Nigeria, as such efforts should be made to ensure appropriate and proper utilization. Patients enrolled into this study were started empirically on any of amoxycillin – clavulonic acid, quinolones or cephalosporins before antibiotic susceptibility results are available. In conclusion, this study demonstrated that *S pneumoniae* was the commonest pathogen cultured in cases of CAP, while *K pneumoniae* was the commonest gram negative isolate. High level of resistance to conventional antibiotics including ciprofloxacin and ofloxacin was found while susceptibility was established for the newer & more expensive cephalosporins and quinolones

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