Antimicrobial susceptibility of organisms isolated from sputum culture of Karachi, Pakistan

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Abstract: Our study aims to contribute to developing antibiotics prescription guidelines at a national and a regional level directed by the antibiotics susceptibility patterns and rapidly emerging resistant organisms. This study is designed to observe the antimicrobial susceptibility in sputum culture isolates and drug resistance patterns against various antimicrobials. This was a retrospective cohort study; data was collected from two laboratories from 1st Jan to 15 July 2007. All laboratory reports were analyzed using SPSS version 19.0.The sputum culture was found positive for microbial growth in 217 reports out of 864 total (25.11%). The leading organisms were 25.8% Klebsiella pneumoniae, 23.5% Streptococcus pneumoniae, 18% Pseudomonas aeruginosa and 12.9% Staphylococcus aureus. S.pneumoniae and S.aureus were sensitive to the combination of beta lactam antibiotics and anti-beta lactamase while K.pneumoniae and P. aureginosa were susceptible to fluoroquinolones, macrolides and aminoglycosides. The total yield of sputum culture was 25.11%. The gram positive cocci which were isolated were mostly resistant to beta lactam antibiotics alone i.e. only 45% of S. pneumoniae and 33% of S.aureus were sensitive to Amoxicillin alone. Sensitivity to Co-amoxiclav was still high. 90% and 85% of S. pneumonia and S.aureus respectively were sensitive to Co-amoxiclav. The P.aeruginosa resistance to Amikacin in our study is 10%.

Keywords: Sputum culture, antimicrobial susceptibility, drug resistance.

INTRODUCTION

Contemporary knowledge of an organism's sensitivity directs the correct choice of antibiotics. The appropriate use of the correct antibiotic against susceptible bacteria will not only cure the disease but will also potentially save us from the use of unnecessary antibiotic prescriptions and thus help us control the increasing resistance to antibiotics. The accelerated resistance developing to antibiotics by the common pathogens is one of the most concerning global problem of this century. According to a study, the use of antibiotics has increased a lot from the years 2000 to 2008 in Pakistan (Tanwir and Khan, 2011). Along with that, Respiratory tract infections (RTIs) are amongst the most prevalent and deadly infections that are responsible for over 50 million deaths globally each year (Zafar *et al*., 2008). Respiratory tract infections are also the most common reason of physician's visits and antibiotic prescription (WHO Burden of Disease Project, 2005) (Mogyoros, 2001). Respiratory infections continue to be a major health problem despite identification of etiologic organism and the availability of potent antimicrobial drugs (Pennington, 1994). Although the most common cause of these infections is viral in nature but bacterial and fungal causes still account for an enormous burden (Pennington, 1994). In Pakistan, RTI is the second most common cause of death in children less than 5 years of age (Pakistan Demographic Health Survey 1998). In a resource limited country such as Pakistan, antibiotic resistance is one of the common issues which is further fuelled by irrational antibiotic prescription (WHO Burden of Disease Project, 2005). Apart from this, empirical treatment is carried out pertaining to the high cost of laboratory services or their unavailability which requires surveillance studies to define regional patterns of antimicrobial resistance. While it is well established that the rate of antibiotic resistance has been increasing for past several decades and it is a serious matter of concern, there is still insufficient data to delineate the trend of specific antibiotic resistance to specific organism (GARP 2011). We therefore based our study on a 7 year old data from now to establish culture sensitivities of different microbes to commonly used antibiotics and set forth the outline of its comparison with latest trend of microbial resistance patterns.

MATERIALS AND METHODS

It was a retrospective cohort study; data was collected and analyzed from two laboratories in Karachi from 1st Jan to 15 July 2007. The permission has taken from both the laboratories. The lab A, situatedin Saddar, Karachi (linked with a Private Hospital) while the Lab B was located in Nazimabad, Karachi. After addressing all the ethical considerations, review by the institutional review board and ensuring the data confidentiality, all the culture reports were collected for the respective study duration. There were 864 culture reports. 217 were found positive for bacterial growth. All the reports irrespective of

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clinical condition were included in the study conducted during 1st January -15th July 2007. Others which did not fall under the respective dates were excluded. The data was collected retrospectively from the laboratory records and entered in the electronic software SPSS for analysis. The standard operation protocols of the two laboratories were the same: The samples were transferred to microbiology laboratory and were analyzed within 30 min to 1 hour of collection. Nutrient agar, Mac Conkey agar and blood agar were used for streaking of sample and then incubated at 37°C for 24 hours as described by chessborough.

By disk diffusion technique, antibiotic susceptibility pattern of isolates on commonly used antibiotics was performed on Mueller-Hinton agar medium according to Clinical Laboratory Standard Institute (CLSI) guidelines (NCCLS 1995). Paper disk was impregnated with antibiotics (Sigma chemicals): Amoxicillin (10µg), Co-amoxiclav (20/10µg), Cefixime (5µg), Clarithromycin (15µg), Ciprofloxacin (5µg), Amikacin (30µg) respectively and incubated at 37°C for 24 hours in 5-10% CO_2 enriched environment. The medium containing antibiotic disks were quality controlled daily by standard culture. After defined incubation period, the diameter of zone of inhibition was measured and interpretation of result based on CLSI guidelines was performed (NCCLS 1995).

Reporting results

Susceptible (S): Implies that the isolated organism is inhibited by usually achievable concentration of the antimicrobial when recommended dosage of it is used. Intermediate (I): Implies that the response rate of the isolated organisms is lower than for susceptible organism by usually achievable concentration of the antimicrobial when recommended dosage of it is used. Resistant (R): Implies that the isolated organism is not inhibited by usually achievable concentration of the antimicrobial when recommended dosage of it is used.

STATISTICAL ANALYSIS

Data is analyzed for description i.e. for the categorical variables, frequencies and percentages were calculated. Confidence limit (95%) was calculated using standard error of a mean and standard error for continuous and categorical variables respectively. The *Chi-Square* test is used to identify the association and significance difference between categorical variables. SPSS Version 19.0 was used to statistically analyze the data.

RESULTS

Percentage of organisms on sputum culture

25.11% of the sputum cultures were positive for the presence of microorganisms. of these, 25.8% had *Klebsiella pneumoniae*, 23.5% had *Streptococcus pneumoniae*, 18% had *Pseudomonas aeruginosa*, 12.9% had *Staphylococcus aureus*, 4.1% had *Moraxella catarrhalis*, 3.7% had *Escherichia coli*, 0.9 % had Proteus, 0.5% had Salmonella while the remaining 10.60% were positive for other organisms.

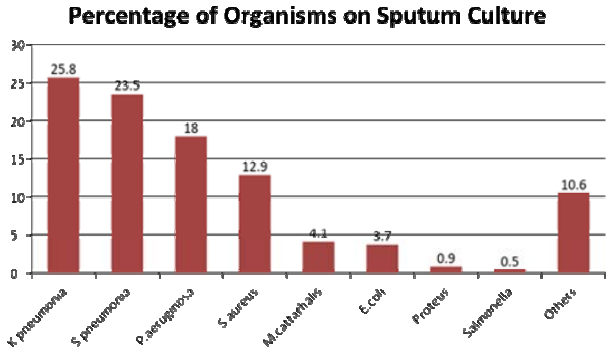

Fig. 1: Percentage of organisms on sputum culture.

Demographic data Age and sex distribution of patients for pneumoniae

Twelve and a half percent of the patients were of the age (1-20 years), 39.29% were of (21–40) years, 14.3% were of 41-50 years, and 33.9% were of the age (>50 years). Over all 58.9% of *K. pneumoniae* was isolated from males and 41.1% from female patients.

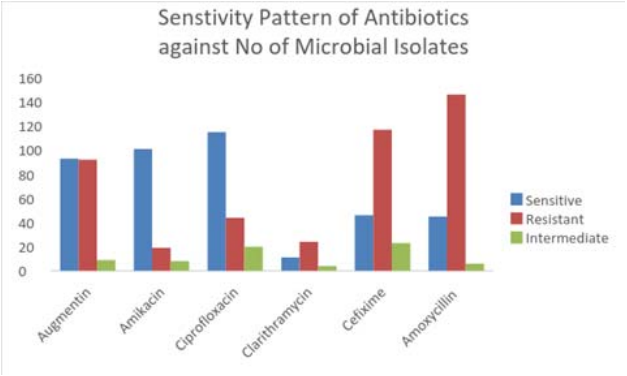

Fig. 2: Sensitivity pattern of Antibiotics against total number of microbial isolates.

Age and sex distribution of patients for S. pneumoniae

17.65% of the patients were of the age (1-20 years), 33.33% were of (21-40) years, 7.8% were of 41-50 years, and 41.18% were of the age (>50 years). Over all 60.8% of *S. pneumoniae* was isolated from males and 39.2% from females.

Age and sex distribution of patients for P.aeruginosa

5.13% of the patients were of the age (1-20 years), 28.21% were of (21-40) years, 17.9% were of 41-50 years, and 48.72% were of the age (>50 years).Over all 69.2% of *P. aeruginosa* was isolated from males and 30.8% from females.

Table 1: Sensitivity pattern of *K. pneumoniae* to antibiotics

Antibiotic	Sensitive	Intermediate	Resistant
Amoxicillin	3	47	2
Co-amoxiclav	8	40	4
Cefixime	29	18	4
Clarithromycin	3	10	1
Ciprofloxacin	37	4	5
Amikacin	38	4	1

Table 2: Sensitivity pattern of *S. pneumonia* to antibiotics

Antibiotic	Sensitive	Intermediate	Resistant
Amoxicillin	3	47	2
Co-amoxiclav	47	5	0
Cefixime	4	31	12
Clarithromycin	1	7	2
Ciprofloxacin	37	4	5
Amikacin	9	13	2

Table 3: Sensitivity pattern of *P. aeruginosa* to antibiotics

Antibiotic	Sensitive	Intermediate	Resistant
Amoxicillin	6	30	1
Co-amoxiclav	6	31	1
Cefixime	1	32	1
Clarithromycin	2	3	0
Ciprofloxacin	25	7	1
Amikacin	27	1	3

Table 4: Sensitivity pattern of *S. aureus* to antibiotics

Antibiotic	Sensitive	Intermediate	Resistant
Amoxicillin	9	18	0
Co-amoxiclav	22	4	0
Cefixime	2	25	0
Clarithromycin	3	2	0
Ciprofloxacin	12	7	7
Amikacin	8	1	1

Age sex distribution of patients for S.aureus

17.86% of the patients were of the age (1-20 years), 17.86% were of (21-40) years, 21.4% were of 41-50 years, and 42.86% were of the age (>50 years). Over all 64.3% of *S. aureus* was isolated from males and 35.7% from females.

Antibiotic susceptibility

The gram positive rods i.e. *S. pneumoniae* and *S. aureus* responded very well to the combination of beta lactam antibiotic and anti-beta lactamase while the gram negative rods like Klebsiella, Pseudomonas were best susceptible to fluoroquinolones, macrolides and aminoglycosides. The sensitivity patterns of these microorganisms are given in tables.

Sensitivity patterns of antibiotics against no of microbial isolates was determined. Statistically significant relationship by chi-square test was done keeping the significance value <0.05 identified for Amoxicillin, Co Amoxiclav, Ciprofloxacin, Cefixime and Amikacin against different bacterial isolates for differences which were found in sensitivity patterns. No significant correlation was identified against clarithromycin.

DISCUSSION

The study was conducted in order to evaluate the susceptibility of different microorganisms, isolated from sputum culture of patients with respiratory tract infections, to different antibiotics. The main differences cited in the two laboratories were that lab A mostly had data which was predominantly from hospitalized patients and lab B from out patients. The clinical condition of the patient or the reason for the test was not mentioned in reports from both the laboratories. So these findings

cannot be generalized to patients with lower respiratory tract infections.

Klebsiella was the leading organism in our study followed by *S. pneumonia* and *P. aeuroginosa* whereas *S. pneumoniae* was the most common pathogen isolated from sputum culture of AECOPD (Patel AK *et al*., 2015) and CAP patients (Resmi *et al*., 2013) in two different states of India. The only difference being that our study included reports irrespective of clinical condition of the patients unlike the study done in Gujarat which specifically included patients with AECOPD and the latter done in Kerala with CAP patients.

In our study, only 45% of *S. pneumoniae* and 33% of S. aureus were sensitive to amoxicillin alone which is in contrast to a study conducted from 1998-2000. According to the study, the only oral agents to which over 90% of *S. pneumoniae* isolates were susceptible were amoxicillin (95.1%) and co-amoxiclav (95.5-97.9%) but it can be explained by the continued evolution and geographical variation in bacterial resistance over the years (Jacobs *et al*., 2003).The main reason for this high bacterial resistance seems to be a liberal use of amoxicillin as a first line antibiotic for infections. The second highest prescriptions among Swedish dentists were noticed of amoxicillin according to a study (Tanwir *et al*., 2012). In our study, sensitivity to Co-amoxiclav was still highas 90% and 85% of S. pneumonia and S. aureus respectively are sensitive to Co-amoxiclav. S. pneumoniae was found to be most sensitive to linezolid, followed by amoxicillin-clavulanate, cloxacillin and ceftriaxone according to a relatively recent study (Resmi *et al*., 2013)but since Linezolid was not tested in our study, we were unable to determine its efficacy compared to co-amoxiclav.A study in which the efficacy of co-amoxiclav was determined in bacterial exacerbation of chronic bronchitis in which the leading pathogens were S. pneumonia and Haemophilus, the co-amoxiclav eradication rate was 82.2% and 81.2% for ciprofloxacin group (Cazzola *et al*., 1995), while the S. pneumonia we isolated in our study, 90% were sensitive to co-amoxiclav, and 59% to ciprofloxacin. However,a strong association between fluoroquinolone usage and a dramatic rise inciprofloxacin-resistant S. pneumonia has been found according to study done in Canada from 1997- 2006 (Adam *et al*., 2009). This shows that there has been a significant increase in the ciprofloxacin consumption over the past few years and subsequent decrease in efficacy of this particular antibiotic. In another study of microorganisms susceptibility, isolates from patients with community acquired respiratory tract infections in Pakistan, showed that 100% of *S. pneumoniae* is sensitive to Co-amoxiclav and 72% to Clarithromycin (Zafar *et al*., 2008). A study done in 2005 on *S. aureus* strains from patients with high risk of endocarditis showed that 53.3% were resistant to Amoxicillin, 13.3% to Co-amoxiclav and 27.6% to clarithromycin (Groppo *et al*., 2005).This is much higher than our study.

The gram negative rods K. pneumonia and *P. aeruginosa* were mostly susceptible to the fluoroquinolones, macrolides and aminoglycosides. K. pneumonia species isolated from a tertiary care hospital in Pakistan showed 12.5% were resistant to Co-amoxiclav and 55% to Ciprofloxacin (Amin *et al*., 2009). Amikacin is still shown to have a high sensitivity pattern for Klebsiella at 92.7% according to a 2013 study done in Gujarat, India by Asati Rakesh Kumar. The *P. aeruginosa* resistance to Amikacin in our study is 10% which is consistent with a survey undertaken in Italy in 1995, in which lack of susceptibility to Amikan was 10.6% (Bonfiglio *et al*., 1998). In a previous hospital study, resistance rate among *Pseudomonas aeruginosa* was only 5–9% against Amikacin (Bouza *et al*., 1999) while in studies performed in the year 2012 in Pakistan showed resistance of 35%.Thus the resistance of *P. aeruginosa* to Amikacin is continuously on a rise(Fatima *et al*., 2012).Nevertheless, Amikacin was found to be the most effective antibiotic, followed by Co-trimoxazole and Quinolones against *P. aeruginosa* with 90% of its isolates sensitive to this particular antibiotic, according to a recent study done in Karachi (Fouzia *et al*., 2014) and another study done in South India showed 95% susceptibility to Amikacin (KV Ramana *et al.*, 2013). Resistance exhibited by *P. aeruginosa* against ciprofloxacin in one study was 100% (Vincent *et al*., 2010) which is in contradiction with our results and with the results shown by KV Ramana *et al* with 75% susceptibility to Amikacin. Similarly, another study claimed a resistance of 87% (Gill *et al*., 2011). A study done in Tehran exhibited a similar pattern of sensitivity to ciprofloxacin which was 87.5% (Maryam *et al*., 2014)

Our study also demonstrated that more men than women are prone to respiratory tract infections which is in accordance with a previous study done by Falagas *et al.* (2007) and another study by Jensen *et al*.(2004). However, *Mycoplasma pneumoniae*, the main pathogen of atypical community-acquired pneumonia that is often found in adolescents and young adults, shows a clear predominance in females, from studies in Japan (Eshima *et al.*, 2012) but our study was not able to determine it as *Mycoplasma pneumoniae* was not one of the leading organisms found in our sputum culture.

CONCLUSION

In a developing country like Pakistan where multiple socioeconomic constraints are one of the major factors contributing toward the increasing burden of drugs resistance as explained by Okeke *et al.* (1999), there is a dire necessity of guidelines on the controlled use of antibiotics with efforts focusing towards health staff and

patients education regarding the liberal use of antibiotics. The differences in the behavioral and socio-economic factors affecting both genders in Pakistan may be one of the cause of differential prevalence of respiratory tract infections among males and females. The need of the hour is to establish our national and regional guidelines for antibiotics use in various conditions. The council for Appropriate and Rational Antibiotic Therapy (CARAT) criteria, as well as the World Health Organization recommendations, emphasize the importance of choosing the best possible susceptible drug for the optimal duration to prevent the further emergence of resistant bacterial strains (WHO report on infectious diseases 2000). Antibiotics should be prescribed only when needed and used in the appropriate doses for recommended period of time so that the increasing resistance to antibiotics is not further accelerated. We recommend the use of Co-amoxiclav instead of Amoxicillin alone against the gram positive rods S. pneumonia and *S. aureus* while the gram negative rods like K. pneumonia and *P. aeruginosa* should be treated with a Fluoroquinolone or an aminoglycoside. Our study serves as a bench mark for motivating other researchers to address the persistently increasing antimicrobial resistance. The study also urges for development of newer and more potent antimicrobials in combating the issue of drug resistance. According to a study, multifaceted interventions have been demonstrated to be useful in controlling antimicrobial resistance (Cédric and Philippe, 2007).

Limitations

Our study had few limitations owing to limited time and resources. As this was a retrospective case based analysis, we have our doubts on the sampling methods and how accurately did the laboratories adhere to their standard operation protocols. Our study did not take into account the clinical parameters of the patients and their referral methods so we cannot accurately generalize it to patients with lower respiratory tract infections. As this study was conducted in 2007, it cannot be generalized to current resistance patterns. In literature there have been very scarce data in our study population in last decade especially on these antibiotics sensitivity patterns.

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