ANTIMICROBIAL RESISTANCE OF BACTERIAL AGENTS OF THE UPPER RESPIRATORY TRACT AMONG HOSPITAL PATIENTS IN ASEER REGION, SAUDI ARABIA

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ABSTRACT

Introduction: Antimicrobial resistance (AMR) is an internationally recognized threat to health. Microbial resistance to antibiotics has increased alarmingly over recent decades prompting the world health organization to declare this is a global public health crisis. The contribution of primary healthcare is particularly important as this is where almost 80% of all antibiotics used within the health service are prescribed. **Objectives:** Upper respiratory tract infection (URTI) is considered as one of the major public health problems and it is recognized as the leading cause of mortality and morbidity in many developing countries. The objectives of the study were to study the resistance of the bacteria causing upper respiratory tract infection to antimicrobial drugs in children. To study the type and frequency of antibiotic prescription for Upper respiratory tract infection (URTI) without apparent bacterial infection. To investigate the type and frequency of antibiotic prescription for URTI without apparent bacterial infection in Aseer region based on both visits and facilities. **Methods**: Saudi Arabia has several challenges that can stimulate the emergence and spread of multi drug resistant bacteria. Cross-sectional analysis of the drug utilization study was conducted to evaluate the pattern of antibiotics use in Pediatric Hospital, in Aseer region, Saudi Arabia. From a total of 200, subjects were analyzed, antibiotics were prescribed in 77% of these visits. **Results:** Stenotrophomonas maltophilia has emerged as an important nosocomial pathogen capable of causing respiratory infections. According to the table 5 of prevalence of antimicrobial susceptibility, the treatment of nosocomial infections by S. maltophilia is difficult, as this pathogen shows high levels of intrinsic or acquired resistance to different antimicrobial agents, drastically reducing the antibiotic options available for treatment. Amikacin (30 %), Gentamicin (35%), Ertapenem (44%), Imipenem (51%), Meropenem (37%), Cephalothin (54%) and Cefuroxime (48.6 %) show the highest resistance. **Conclusion**: In general, visits to physicians were more likely to result in an antibiotic prescription than visits to hospital outpatient clinics. Their increasing inappropriate consumption leads to the development of bacterial resistant strains. Such resistance to antibiotics is likely to lead to reduction in the effectiveness of many antibiotics.

KEYWORDS: Antibiotics, Upper respiratory tract infection (URTIs) – pharyngotonsillitis – antibiotic resistance – microorganisms.

INTRODUCTION

Antimicrobial resistance (AMR) is an internationally recognized threat to health. Microbial resistance to antibiotics has increased alarmingly over recent decades prompting the world health organization to declare this is a global public health crisis. The contribution of primary healthcare is particularly important as this is where almost 80% of all antibiotics used within the health service are prescribed[1].

Bacterial infections resistant to antibiotics can limit the availability of effective treatment options, rendering some commonly encountered bacterial infections difficult to treat, including those of the respiratory tract. Antibiotic resistant infections are also twice as likely to be associated with greater morbidity and mortality and are associated with increased healthcare costs[2].

In low income countries, affordability of second line drugs and reduced access to healthcare can restrict the use of newer broad spectrum antibiotics, resulting in growing concerns for increased morbidity and mortality from antibiotic resistant infections in these countries[3].

Respiratory tract infections have a significant impact on health on worldwide. The great majority of respiratory

infections are of viral origin. Respiratory tract infections (RTIs), which involve the upper or lower respiratory tract, frequently occurs after birth[4,5,6]. Upper respiratory tract infection (URTI) has been recognized as one of the most common medical problems in the daily lives of people worldwide and is the leading cause of morbidity and mortality- in critically ill patients in developing countries[4,7]. Acute viral infections predispose children to bacterial infections of the sinuses and middle ear[8] and aspiration of infected secretions. For developing countries the greatest problem is the mortality from URTI in children less than five year of age.

OBJECTIVES

The objective of the present study is to focus on the trends in the antibiotic utilization in upper respiratory tract infections. This information is not disease specific but reflects overall rates and illustrates trends in utilization of antibiotics in the treatment of upper respiratory tract infection.

MATERIALS AND METHODS

Patients between the age group 3 months to 15 years suffering from acute respiratory tract infection were selected for the study during April to October 2016 from the Microbiology department of Maternity and children hospital in Khamis Mushayat and Aseer hospital in Abha. Acute tonsillitis and pharyngitis in the patient presenting with fever and sore throat were considered as symptoms to select the subjects.

Data for children with diagnosis of URTIs from the outpatient record of each patient was collected in a separate proforma. The form included the following domains: Socio demographic characteristics (Age, gender, nationality), Clinical data (Clinical diagnosis, Clinical manifestations, Examination findings), Laboratory data: (Culture and sensitivity data: Organism isolated, sensitivity and resistance pattern), Drug data: (Antibiotic agents prescribed, dose and duration of treatment, change of medication and response to treatment). Sputum specimens for bacteriological culture was subjected to Gram-staining and examined microscopically. Specimens were inoculated onto Mac-

conkey agar, blood agar and chocolate agar media. The inoculated plates were incubated at 37°C for 24-48 aerobically, except for chocolate agar, in which the plates were incubated for 24-48 h at 37°C in an atmosphere of 5-10% CO_2. After incubation, macroscopic and microscopic examinations of colonies on plates were carried out, and suspect colonies were sub cultured on appropriate solid culture media for purification. They were later sub cultured on appropriate slants and stored at 4°C for further analysis. Pure cultures were presumptively identified based on their cultural and morphological characteristics on selective and differential media. Standard microbiological techniques and biochemical tests were also employed to confirm isolates.

In most cases Bacteria were identified via phoenix automated phenotypic identification criteria (Becton Dickinson, Oxford, U.K) or with API 20 E strips. Minimum inhibitory concentrations (MCs) were established by micro broth dilution (phoenix,)British Society for Antimicrobial Chemotherapy (BSAC)agar dilution, or disc diffusion.

Antimicrobial susceptibility testing

The drug utilization data was retrieved from the medical records of patients using a specially designed data collection form. In vitro antimicrobial susceptibility tests for the isolates were performed by modified Kirby-Bauer Disk Diffusion Technique. In this technique a sterile cotton swab was dipped into the standardized solution of bacterial cultures and used for evenly inoculating Mueller-Hinton plates (Himedia, Mumbai) and allowed to dry. Thereafter, antibiotic discs with the following drug contents- were placed on the plates, spacing them well to prevent the overlapping of inhibition zones. These antibiotics were selected based on prescription practices for URTIs in our locality. The plates were incubated at 37°C for 24 hr, and the diameters were measured. The results were read as recommended by the National committee for clinical laboratory standards. The antibiotic sensitivity was tested for the following antibiotics presented in Table I.

Table I: Antibiotic sensitivity of antibiotics.

S.No.	Name of antibiotic	Symbol
1	**Amikacin**	AK
2	**Gentamicin**	GM
3	**Ertapenem**	ETR
4	**Imipenem**	IMI
5	**Meropenem**	MER
6	**Cephalothin**	KF
7	**Cefuroxime**	CTX
8	**Trimethoprim-sulfamethoxazole**	TRIM
9	**Colistin**	CS
10	**Ceftazidime**	CAZ
11	**Tigecycline**	TRIG
12	**Aztreonam**	ATM
13	**Cefepime**	CPM

14	**Piperacillin-Tazobactam**	PRL
15	**Levofloxacin**	LEVO
16	**Ceftriaxone**	CRO

Statistical analysis was carried out using Microsoft Excel. The data was loaded on to SPSS software 17 and the analysis for Chi square was completed.

RESULTS
During the six months study from (April 2016- October 2016)-bacterial strains were isolated from 200 patients having acute pharyngotonsillitis. The study monitored the antibiotic/s utilization pattern of the patients treated for upper respiratory tract infection in Maternity and children hospital in Khamis Mushyat and Asser hospital in Abha. Observations of the study are presented in the form of different figures and tables. Among the total of 200 children, (60%) were males and 40%were females. A significant difference has been found in the incidence of tonsillopharyngitis among different age groups.

On the basis of age, most cases of pharyngotonsillitis occurred in the 3-15 yrs of age. A significant difference has been found in the incidence of URTIs among different age groups.

In **1995 Dajani**[9] reported that the incidence of tonsillitis was 30% in children and 10 % in adults. In the present study, 48 % of patients affected by upper respiratory tract infections were below 15 yrs of age. It is thought to be due to lowered immunity, which has proved statistically significant.

Table II: Percentage occurrence of URTIs on the basis of age.

Age group	Number of patient	Percentage
Below 15 years	116	58
15 -30 yrs	84	42

A majority (58%) of the selected subjects with URTIs were below 15 years of age, followed by forty two percent between 15 and 30 years of age.

Table III: Percentage occurence of URTIs on the basis of sex.

Sex	Number of patient	Percentage
Male	120	60
Female	80	40

Sixty percent of the selected subjects were males and forty percent were females.

Table IV: Percentage occurrence of bacterial isolates responsible for URTIs.
(N = 200)

Name of Organisms	Total No.	Percent
Stenotrophomonas maltophilia	52	26
Stanphylococcus aureus	9	4.5
Pseudomonas aerugunosa	40	20
Klebiella pneumonia	12	6
E.coli	17	8.5
Acenitobacter	14	7
Others	16	8
Normal flora	40	20
Total	200	100

Table IV shows that Stenotrophomonas maltophilia is the most common (26%) pathogenic organism responsible for pharyngotonsillitis followed by P.aerugunosa (20%), E.coli(8.5%).,K.pneumonia(6%), Acinetobacter (7 %) and S.aureus (4.5%).

Table V: Percentage

S.No.	Name of antibiotic	Symbol	Percentage of Resistance
1	**Amikacin**	AK	30
2	**Gentamicin**	GM	35.7
3	**Ertapenem**	ETR	44.3
4	**Imipenem**	IMI	51.4
5	**Meropenem**	MER	37.1
6	**Cephalothin**	KF	54.3
7	**Cefuroxime**	CTX	48.6
8	**Trimethoprim-sulfamethoxazole**	TRIM	1.4
9	**Colistin**	CS	
10	**Ceftazidime**	CAZ	2.9
11	**Tigecycline**	TRIG	
12	**Aztreonam**	ATM ATM	4.3
13	**Cefepime**	CPM	2.9
14	**Piperacillin-Tazobactam**	PRL	4.3
15	**Levofloxacin**	LEVO	
16	**Ceftriaxone**	CRO	1.4

Resistance of antibiotics
The above table indicates that Cephalothin (54.3 %), Imipenem (51.4 %) Cefuroxime (48.6 %), Ertapenem (44.3 %), Gentamicin (35.5 %) and Amikacin (30 %) show more resistance to the microorganisms.

DISCUSSION
During this study it has been found that Stenotrophomonas maltophilia is the most common pathogenic organism responsible for pharyngotonsillitis followed by P.aerugunosa,S.aureus, K.pneumonia, Acinetobacter and E.coli.It has been observed in the general population[10] and in ICUs[11] alike that *S. maltophilia* is most frequently associated with respiratory tract infections (RTIs).The prevalence of RTIs due to *S. maltophilia* is generally higher than that of other infections caused by that pathogen, but varies widely among countries and continents, ranging from 1.6 to 6.3% during the period 1997–2012[12, 13, 14].

Stenotrophomonas maltophilia has emerged as an important nosocomial pathogen capable of causing respiratory infections. According to the table 5 of prevalence of antimicrobial susceptibility, the treatment of nosocomial infections by S. maltophilia is difficult, as this pathogen shows high levels of intrinsic or acquired resistance to different antimicrobial agents, drastically reducing the antibiotic options available for treatment. Amikacin (30 %), Gentamicin (35%), Ertapenem (44%), Imipenem (51%), Meropenem (37%), Cephalothin (54%) and Cefuroxime (48.6 %) show the highest resistance.

Staphylococcus aureus, Citobacter and Acinetobacter and streptococcus pyogenes found during this study are also an important nosocomial pathogen capable of causing respiratory infections. These pathogens also show high levels of intrinsic or acquired resistance to different antimicrobial agents,[14] found that beta haemolytic streptococcus in 46% cases. Looney et al.,[15]

reported an incidence of 13%. But in the present study the percentage of beta haemolytic streptococcus was found to be less.

Reason may be as follows.
Streptococcus pyogenes is confined to fall and winter season[16] and the present study was carried out during summer season. This may be the reason for not finding this pathogen in the study samples. The study focused on the prevalence and antibiogram of bacteria causing URTIs among children in a Asser region. Respiratory tract infection is considered as one of the most important infectious diseases in developing and semi developed countries. Stenotrophomonas maltophilia is an increasingly deadly pathogen that is known to cause a variety of nosocomial and community-acquired infections. In our study, Stenotrophomonas maltophilia was the commonest pathogen seen in the majority of the population (26%). Stenotrophomonas maltophilia has shown a disconcerting propensity to develop resistance to antimicrobial agents and has become an important challenge for the clinicians. Hence, before selecting an antibacterial drug, the clinician must first consider the likely causative organism. Knowledge of the prevalent organisms and their current sensitivity are of great help in choosing an antibacterial drug.

The increasing frequency of antibiotic resistance has been reported first in infections at sites where penetration of the antimicrobial agent is restricted and the level of therapeutic concentrations is consequently more difficult to be achieved. It could also hinder the eradication of infections in respiratory tract infections treated using standard antibiotic therapy regimens[17]. Accurate information on local epidemiology and antimicrobial resistance patterns of pathogens is essential to select a clinically effective antibiotic therapy for the infection[18].

Based on age most cases of pharyngitis occurred in the 3-15 years of age. A significant difference has been found in the incidence of pharyngitis among different age group.

In 1995 Dajini[9] reported that the incidence of tonsillitis was 30 % in children and 10% in adults. The present study includes 43% of patients who were below 15 years of age for the incidence of tonsillitis. It is due to lowered immunity, which was proved statistically significant

Percentage occurence of pharyngotonsillitis based on sex - Among the 200 patients, 60% were male and 40 percent were females. This shows that males are more susceptible than females. The reason is unknown. More than one in 10 initial antibiotic monotherapies for the URTIs were associated with treatment failure.

CONCLUSION

Antimicrobial resistance (AMR) is a global issue that requires tremendous attention. International agencies have suggested recommendations and plans to combat AMR. It is now up to countries to take the lead and implement local action plans to limit AMR. Saudi Arabia faces several challenges that can stimulate the emergence and spread of multi drug resistance (MDR) bacteria. These challenges require cultivated efforts from different sectors to successfully achieve a significant control of AMR in the country**.** URIs are mostly caused by viruses. Penicillin is recommended for patients with GABHS pharyngitis and amoxicillin clavulanate for those with moderate or severe suspected acute bacterial rhinosinusitis. Patients with moderate or severe influenza, those with underlying medical conditions who develop influenza, and those hospitalized for management of influenza should be treated with a neuraminidase inhibitor.

Antibiotics misuse/overuse is an important public health issue that affects the community and the individual. Using antibiotics to treat children from upper respiratory tract infections is evidently inappropriate unless the infection was proven to be bacterial. This misuse of antibiotics, especially in children, will increase the risk of developing bacterial resistance which emphasis on the need to discover the contributing factors to this overuse of antibiotics.

Prevalence of resistance to commonly prescribed primary care antibiotics in URIs in children is high,. This could render some drugs ineffective as first line treatments for. URIs .Routine use of antibiotics in primary care contributes to antimicrobial resistance in children, which can persist for up to six months after antibiotic prescription.

REFERENCES

1. Majeed A, Moser K. Age- and sex-specific antibiotic prescribing patterns in general practice in England and Wales in 1996.Br J Gen Pract 1999; 49: 7356.10756619.
2. Holmberg SD, Solomon SL, Blake PA. Health and economic impacts of AMR. RevInfectDis 1987; 9: 1065-78. doi:10.1093/clinids/9.6.1065. 3321356.
3. Planta MB. The role of poverty in antimicrobial resistance. J Am BoardFam Med 2007; 20: 533-9.doi:10.3122/jabfm.2007.06.070019. 17954860.
4. Hayden FG. Respiratory viral threats. Curropininect Dis 2006; 19: 169-78 Medline Web of Science Google Scholar.
5. Ronceviæ N, Popadiæ J., Stojadinoviæ A. Treatment of acute infections of the lower respiratory tract in children. Med. Pregl. 2002; 22: 299–304.
6. Kumari H.B.V., Nagarathna S., Chandramuki A. Antimicrobial resistance pattern among aerobic gram negative bacilli of lower respiratory tract specimens of intensive care unit patients in a neurocentre. Indian J. Chest Dis. Allied Sci. 2007; 49: 19–22.
7. Navneeth B.V., M.R., Sandhya B. Antibiotic resistance among gram negative bacteria of lower respiratory tract secretion in hospitalized patients. Indian J. Chest Dis. Allied Sci. 2002; 44: 173–176.
8. Berman S. Otitis media in Children. New England Journal of Medicine. 1995a; 332(23): 1560–65.]
9. Dajani, A. Taubert and Ferrieri, P.Treatment of pharyngitis and prevention of rheumatic fever: a statement for health professionals. The American Pediatrics (Oct). 96 (4pt 1): 758-764. (1930).
10. Gales A. C., Jones R. N., Forward K. R., Liñares J., Sader H. S., Verhoef J. (2001a). Emerging importance of multidrug-resistant *Acinetobacter* species and *Stenotrophomonas maltophilia* as pathogens in seriously ill patients: geographic patterns, epidemiological features, and trends in the SENTRY Antimicrobial Surveillance Program (1997-1999). Clin. Infect. Dis. 32(Suppl. 2), S104–S113. 10.1086/320183.
11. Fluit A. C., Verhoef J., Schmitz F. J., European S. P. (2001b). Frequency of isolation and antimicrobial resistance of gram-negative and gram-positive bacteria from patients in intensive care units of 25 European university hospitals participating in the European arm of the SENTRY Antimicrobial Surveillance Program 1997-1998. Eur. J. Clin. Microbiol. Infect. Dis. 20: 617–625.
12. Sader H. S., Jones R. N., Gales A. C., Winokur P., Kugler K. C., Pfaller M. A., et al. (1998). Antimicrobial susceptibility patterns for pathogens isolated from patients in Latin American medical centers with a diagnosis of pneumonia: analysis of results from the SENTRY Antimicrobial Surveillance Program. SENTRY Latin America Study Group. Diagn. Microbiol. Infect. Dis. 1997; 32: 289.

13. Sader H. S., Farrell D. J., Flamm R. K., Jones R. N. (2014a). Antimicrobial susceptibility of Gram-negative organisms isolated from patients hospitalised with pneumonia in US and European hospitals: results from the SENTRY Antimicrobial Surveillance Program, 2009-2012. Int. J. Antimicrob. Agents 43: 328–334. 10.1016/j.ijantimicag.2014.01.007

14. H. S., Jones R. N., Gales A. C., Silva J. B., Pignatari A. C., SENTRY Participants Group (Latin America). SENTRY antimicrobial surveillance program report: Latin American and Brazilian results for 1997 through 2001. Braz. J. Infect. Dis. 2004; 8: 25–79. 10.1590/S1413-86702004000100004

15. Markowitz, M. Culture of the respiratory tract in pediatric practice. Amer.J.Dis.Child, 21:103-105, (1973).

16. Looney W. J., Narita M., Mühlemann K. *Stenotrophomonas maltophilia*: an emerging opportunist human pathogen. Lancet Infect. Dis. 2009; 9: 312–323. 10.1016/S1473-3099(09)70083-0.

17. Evan, A.S., Dick, E.C. Acute pharyngitis and tonsillitis in University of Wisconsin students. JAMA, 1964; 190: 699-706.

18. Gonzalo C.R. What is the importance of bacterial eradication in the treatment of respiratory tract infections? An. Pediatr. (Barc). 2004; 60: 459–467.

19. Rosentein N, Phillips WR, Gerber MA, Marcy MS, Schwartz B, Dowell SF. Indian J Pediatric 1998; 101: 181-184.