EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 5
Issue: 1
106-112
Year: 2018

SUSCEPTIBILITY PATTERN OF EMPIRICAL THERAPY FOR UPPER RESPIRATORY INFECTIONS AT PIGG'S PEAK GOVERNMENT HOSPITAL

Siphesihle C. Mhlanga[1], Alemayehu L. Duga[2]*, Admire T. Makunde[3], Sifundo Zwane[4] and Sebenta Menon[5]

[1,5]Swaziland Christian Medical University Pharmacy Department.
[2]Management Sciences for Health Swaziland.
[3]Swaziland Christian Medical University Medical Laboratory Department.
[4]Pigg's Peak Government Hospital.

***Corresponding Author: Alemayehu L. Duga**
Management Sciences for Health(MSH)-Swaziland.

Article Received on 09/11/2017 **Article Revised on 30/11/2017** **Article Accepted on 21/12/2017**

ABSTRACT

Background: The utilization of empirical antimicrobial therapy for the treatment of upper respiratory tract infections (URTIs) has the potential of affecting the susceptibility of URTIs. **Methods:** A quantitative prospective cohort study was done from 4th until the 23rd of July 2017 at the Pigg's Peak Government Hospital Out Patient Department where bacteria samples were collected from 33 patients with URTIs. Amongst the bacteria that were obtained 28 samples produced the most prevalent of pathogenic bacteria klebsiella pneumoniae and they were tested for susceptibility amongst four antimicrobials including ampicillin, penicillin-G, erythromycin and co-trimoxazole. The zones of inhibition produced by the disks were used to generate results for the susceptibility tests and were analysed using the Statistical Package of Social Sciences software version 20. **Results:** Amongst the four antibiotics that were tested ampicillin was 25.0% susceptible, 32.1% intermediate susceptible and 42.9% resistant. Penicillin G was 10.7% susceptible, 17.9% susceptible and 71.4% resistant. Erythromycin was 46.4% susceptible, 21.4% intermediate susceptible and 32.1% resistant. Lastly, co-trimoxazole was 75.0% susceptible, 14.5% intermediate susceptible and 10.7% resistant. **Conclusions:** This study has shown that Klebsiella pneumoniae has shown some resistance to erythromycin, Pennicilin G and ampicillin respectively. On the other hand, this bacterium showed to still be susceptible to cotrimoxazole. Recommendations are made to the hospital that it undertakes more surveillance in monitoring susceptibility patterns of antimicrobials, substitution of more resistant antimicrobials and also following strict policies on prescribing antimicrobials.

KEYWORDS: Empiric therapy, antimicrobial, upper respiratory infections, antimicrobial resistance.

INTRODUCTION

Upper Respiratory Tract Infections (URTIs) are basically infections of the superior part of the respiratory system. They are caused by bacteria and/or viruses. Bacteria that may cause these infections include; K. pneumoniae, S. pyogens, S. pneumoniae, H. influenzae, M. catarrhalis, and S. aureus.[5,1] URTIs can be transmitted by breathing in contaminated air, cigarette smoking, overcrowded places and contact with infected person. These infections include; bronchitis, rhinitis, sinusitis, pharyngitis, tonsillitis, epiglottitis, common cold and naso-pharyngitis.[11]

To treat URTIs a combination of drugs are used. URTIs drug treatment is aimed at alleviating pain, decrease congestion, arresting cough as well as eradicating and/or inhibiting the growth of the targeted microorganism(s). The classes of drugs used may include; Non-Steroidal Anti Inflammatory Drugs (NSAIDS), anticholinergic, antihistamine first generation, antitussives, corticosteroids, decongestants, antivirals and antibiotics.[8][13] Antibiotics used to treat bacterial URTIs include: amoxicillin, erythromycin, clindamycin, benzathine benzyl penicillin and phenoxymethylpenicillin.[14]

Most UTRIs are caused by viruses and these are mostly misdiagnosed and treated as bacterial infection hence contributing to the increased chances of microbial resistance.[2] A study by Zoorob et. al. (2012) explained that antibiotics were prescribed to 65% of 52, 000 URTI outpatients cases of ambulatory network. Zoorob further explained that this overuse and also inappropriate use of antibiotics may lead to; increase microbial resistance, increased cost and increase adverse effects such as anaphylactic shock.[16]

In 2016 Swaziland OPDs of all Health centres had 424 965 cases of URTIs. Amongst these cases Manzini region had the highest prevalence of URTIs where amongst these cases Ngculwini Nazarene Clinic had 15 185. In Hhohho region, Mbabane Government Hospital had the highest number of cases which was 10 700 and Pigg's Peak Government Hospital had 11 016 cases. In the Lubombo region, Ubombo sugar hospital had 9 748 cases. In the Shiselweni region Nhlangano health center had 4 878 cases.[4]

They are quite a number of studies that have been done in different parts of the world which were investigating the susceptibility patterns of antimicrobial drugs that are used to treat URTIs. A retro prospective study that was done in the United States of America by Sanchez et al. (2013) illustrated that from the year 1998 until 2010 there has been an increasing resistance of the bacteria (K. pneumoniae) which mostly causes URTIs. This pathogen was resistant by over 15% to antibiotics which included trimethoprim/sulfamethoxazole, tetracycline, ceftazidime, aztreonam, ciprofloxacin and tobramycin.[12]

In India there was also an antimicrobial susceptibility study that was done where various antimicrobial drugs were tested for effectiveness against K. pneumoniae and some of these antimicrobial drugs are part of the STG/EML URTIs antibacterial drugs. In this study the most effective drugs were imipenem and amikacin by (86%). These were followed by tobramycin and gentamycin with (80.6%), Ofloxacin (79.2%) and ciprofloxacin. Some drugs were quite resistant and they included Amoxicillin (88.9%), Ampicillin (83.3%) and cotrimoxazole (70.8%).[6]

A retro prospective study which done in Sydney Australia from January 2013 to December 2015 on the susceptibility patterns of drug resistant bacteria causing UTRIs and other infections illustrated that some of the drugs that are used in Swaziland are ineffective. In the study K. pneumoniae was the most prevalent bacteria and in the three years the resistance of antibacterial drugs towards it was 89% in 2015, 74% in 2014 and 51% in 2013 which was remarkably increasing over the years.[3]

In Africa they were also studies that were done on the susceptibility patterns of empiric therapy for URTIs and other infections. In Kampala, Uganda a study by Kyabaggu et. al. (2007) which was testing for susceptibility patterns of these infections and it illustrated that K. pneumoniae was 24% or less resistant to cotrimoxazole, meaning it was more effective, 24% of ciprofloxacin was effective meaning most of it was resistant, for amoxicillin it was 7.7% susceptible meaning it was mostly ineffective, and lastly erythromycin was 23.1% susceptible meaning it was also mostly ineffective.[5] In Swaziland there were no studies that were done related to this cases but studies in other countries even some in Africa illustrate a growth in antimicrobial resistance even in drugs that are used to treat URTIs in the Kingdom of Swaziland.

MATERIALS AND METHODS

Study area and period

The study was conducted at Pigg's Peak Government Hospital located in the Northern Hhohho region of Swaziland. From 4th to 23th of July 2017 throat swabs were collected from patients presenting with a diagnosis of URTIs after consultation at the OPD of the hospital. These samples were taken for susceptibility testing at the Swaziland Christian University Microbiology Laboratory.

Study design

The study was a quantitative prospective cohort study where bacteria samples from patients with URTIs were collected for microbial susceptibility testing.

Population

Source of population

The source of population were patients that came for treatment at the OPD of Pigg's Peak Government Hospital from the 4th to 23th of July 2017 with bacterial UTRIs. The study population were patients of all ages and gender presenting at the OPD of Pigg's Peak Government Hospital with an URTIs mainly caused by bacteria. These infections included; bronchitis, rhinitis, sinusitis, pharyngitis, tonsillitis, epiglottitis, naso-pharyngitis and any other non-specific URTIs.

Inclusion and exclusion criteria

Patients of all ages and gender that presented at the hospital's OPD and were diagnosed by a medical doctor of having any form of URTIs caused by bacteria. Excluded from this study were patients who were on antibiotic therapy for 8 hours, patients that had used mouth washes (gargles) on the day of diagnosis, patients that presented signs and symptoms of viral URTIs and Children that presented with symptoms of acute heamophilus epiglottitis.

Sample size and sampling procedures

Sample Size

The sample size was calculated using Raosoft online calculator where:
The margin error was: 5%
The confidence level was: 95%
The population size was: 5750 people
The response distribution was: 50%
Then the final sample size that was calculated was: 361

Sampling procedures

Random systemic sampling method was employed in this study. With this method one in every thirteen patients was selected to represent each group of thirteen patients in the 361 sample size.

The following procedures were followed during sample collection.

1. Samples were collected by prescribing nurses and doctors at the hospital's outpatient department (OPD), these were then transported to the Pigg's Peak hospital laboratory for storage. When collecting the sample

a) The health professionals depressed the tongue using a tongue depressor to examine the inside of the mouth, looking for any membrane exudate or pus, and inflammation.
b) After identifying the affected area, he/she swabbed it using a cotton swab.
c) The sample swab was then sealed and labelled.
d) After labelling the collected swabs was then placed in a cooler box and taken to the hospital laboratory for appropriate storage.

2. Storage of samples in Pigg's Peak hospital laboratory

a) The samples in the cotton swabs were stored in a refrigerator at the laboratory at a temperature of (4-10^{o}C) for a period of 3 days before their transportation to Mbabane at the Swaziland Christian Medical University for analysis.

3. Transporting of the samples from Pigg's Peak Government Hospital to Swaziland Christian Medical University Laboratory.

a) The samples in a closed tube were transported in cooler box.
b) The transportation was done after 3 days of storage.

4. Processing of the samples in the microbiology laboratory at Swaziland Christian University. This part was divided into 3 days.

a) Day 1:
The bacteria samples were cultured on blood agar and Macconkey culture media and incubated overnight.
b) Day 2:
There was identification and isolation of bacteria colonies through microscopy and biochemical tests and they were then standardized and inoculated in Mullar Hinton media plates and then antibiotic disks were inserted and incubated overnight. Both for the control bacteria strains and the samples
c) Day 3:
There was generation of the susceptibility results using an interpretative chart Both for the control bacteria strains and the samples.

Data collection instruments

The instrument for collecting data included

- Pen and a paper with tables for recording sample labels, as well laboratory results.
- Laptop which has SPSS software for capturing the data.

Data collection process

Two stages were crucial for the generation of data and they were as follows:

a) Using the table to capture the gender and age of patient and label of the sample collected at the hospital, the very same data was entered in a same table in a MS excel as backup just in case the hardcopy get lost or ruined.
b) Using another table the diameter of the zones of inhibitions was recorded and also the results from the zone of inhibition table was also recorded and this data was also recorded using a excel programme in a computer and then stored as backup just in case the hardcopy becomes ruined and also to analyse it easily.

Data processing and analysis

The data was processed and analysed using the statistical Package for Social Sciences (SPSS) version 22.0 statistical package. In the SPSS software various variables were be entered and the number of cases per variable were entered. The Data was further analysed and graphical presentation of the data was generated using the software. To create an appropriate backup for the data it was entered in a laptop, tablet and then saved into an external hard drive. The tablet and the laptop had security codes in order to access the data and for protection of the data these devices had antivirus software to prevent loss of the data.

Data quality assurance

The control strains of Staphylococcus aureus ATCC 25923 and E. coli ATCC 25922 were used to control the quality of the sensitivity test at the lab thus discouraging development of false susceptibility data. Results that were accepted were within the CLSI specified ranges.

RESULTS AND DISCUSSION

Demographic description of the sample

Among the patients that were part of the study they were more females that participated in the study compared to males the following pie chart illustrates the participation amongst the different genders.

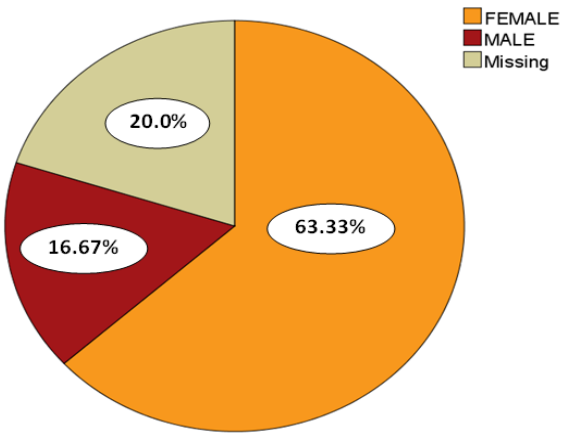

Figure 3: A Pie chart showing the participation of the different genders on the study.

The age amongst the patients was not evenly distributed even though there were less males that were part of the study, the eldest group among the participants were the males as illustrated in the bargraph below.

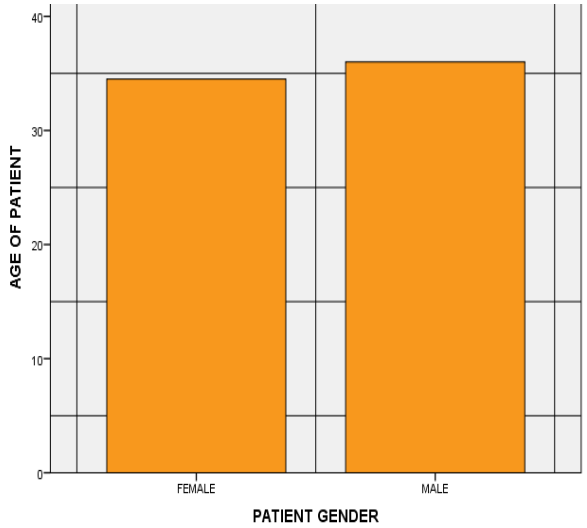

Figure 4: A graph showing the distribution of age amongst both gender groups that participated.

The overall distribution of age amongst the participants is that the participants were all between the ages of 20 to 50 years. Within this group the youngest participants were between the ages of 20 and 50 years old and the following bar charts illustrate this:

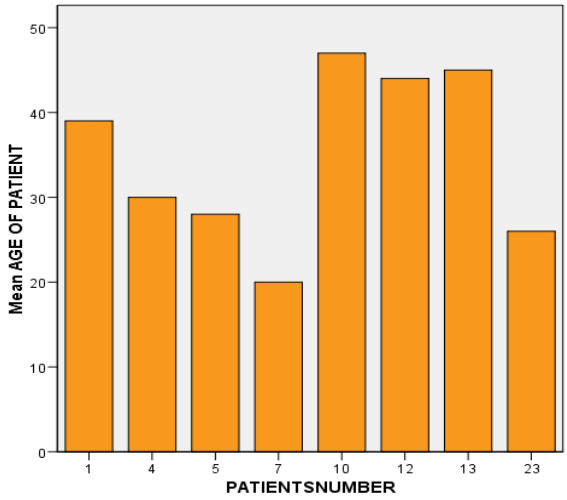

Figure 5: A graph presenting the age distribution of the participants of this study.

Antimicrobial susceptibility

33 Samples were collected and out of all this samples only 28 samples were processed. Since there was limited time and resources to perform susceptibility tests on all pathogenic bacteria isolated from the patients the tests were only done on one gram negative bacteria (Klabsiela pneumoniae) and was done using four different antimicrobials and these results are presented below.

The presentation of the results are mainly three and they include resistant (ineffective), intermediate (almost effective but not ineffective) and susceptible (effective).

Ampicillin susceptibility results were as follows:

Ampicillin Susceptibility

Table 1: Presenting the sensitivity results for ampicillin.

	Frequency	Percent	Valid Percent	Cumulative Percent
Resistant	12	42.9	42.9	42.9
Intermidiate	9	32.1	32.1	75.0
Susceptible	7	25.0	25.0	100.0
Total	28	100.0	100.0	

Penicillin susceptibility results were as follows:

Penicillin Susceptibility

Table 2: Presenting the sensitivity results for penicillin.

	Frequency	Percent	Valid Percent	Cumulative Percent
Resistant	20	71.4	71.4	71.4
Intermidiate	5	17.9	17.9	89.3
Susceptible	3	10.7	10.7	100.0
Total	28	100.0	100.0	

Erythromycin susceptibility results were as follows:

Erythromycin Susceptibility

Table 3: Presenting the sensitivity results for erythromycin.

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Resistant	9	32.1	32.1	32.1
	Intermidiate	6	21.4	21.4	53.6
	Susceptible	13	46.4	46.4	100.0
	Total	28	100.0	100.0	

Cotrimoxazole susceptibility results are as follows:

Cotromoxazole Susceptibility

Table 4: Presenting the sensitivity results for cotrimoxazole.

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Resistant	9	32.1	32.1	32.1
	Intermidiate	6	21.4	21.4	53.6
	Susceptible	13	46.4	46.4	100.0
	Total	28	100.0	100.0	

The distribution of effectiveness of each and every antibacterial agent amongst the patients are represented as follows.

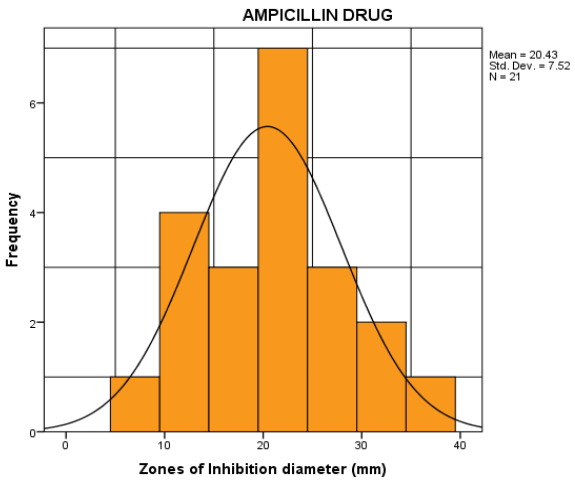

Figure 6: A graph showing the distribution of the zones of inhibition diameter among the samples when using ampicillin antibacterial drug.

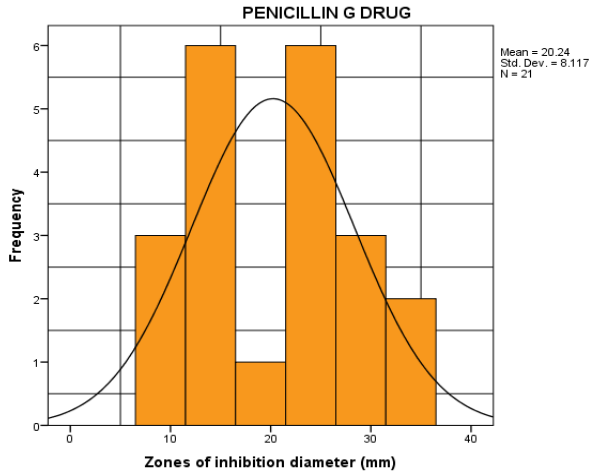

Figure 7 A graph showing the distribution of the zones of inhibition diameter among the samples when using penicillin G antibacterial drug.

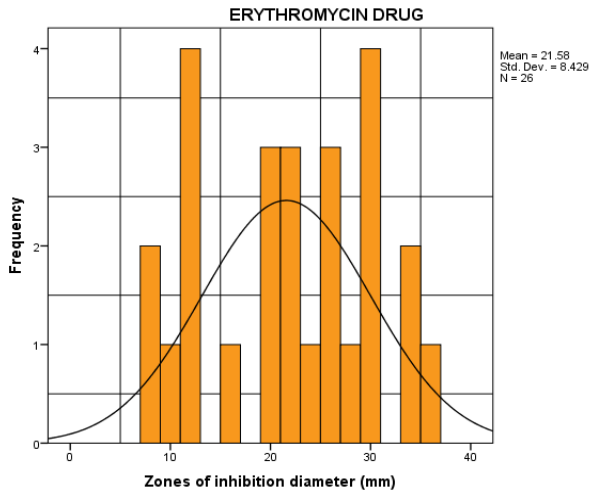

Figure 8: A graph showing the distribution of the zones of inhibition diameter among the samples when using Erythromycin antibacterial drug.

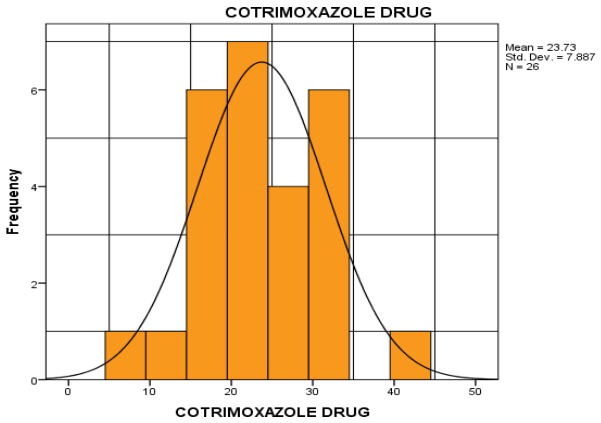

Figure 9: A graph showing the distribution of the zones of inhibition diameter among the samples when using ampicillin antibacterial drug.

Since the study was carried out to investigate the susceptibility patterns of upper respiratory tract infections. Four antibacterial drugs were used to test the susceptibility and it was against one most prevalent gram negative bacteria causing URTIs (Klebsiella pneumoniae). This antibacterial drugs were ampicillin, penicillin G, erythromycin, and cotrimoxazole.

Amongst these antibacterials, cotrimoxazole was the only antibiotic with a susceptibility of 75.0% which was the highest compared to all the antibacterial drugs. This shows that this antibacterial is most effective and it has shown very low resistance (10.7%). This further shows that this antibacterial when given to patients has quite slim chances of not being effective. When its susceptibility and intermediate susceptibility is added a total of 89.3% effectiveness is produced and this is quite impressive when compared to that of the other antibiotics. The improved effectiveness might be due to the synergistic effect of the two compounds, trimethoprim and sulfamethoxazole, that make up this antibacterial.

These findings agree with the findings of a study that was done in Germany by Stock and Wiedemann (2001) where cotrimoxazole was found susceptible to all the Klebsiella species including Klebsiella pneumonia and another study that was done in Lebanon by Moghnieh et. al. (2002) which also showed that this drug was effective as well On the other hand a study that was done in Tanzania by Marwa et al. (2015) showed that cotrimoxazole was 74.1% resistant which shows that over the years there has been an increasing resistance of this antibacterial drug.

Other outstanding results that were observed was the 71.4% resistance of penicillin G which was the highest among all the antibacterial drugs investigated. Its susceptibility or effectiveness was 10.7% which was the smallest amongst these antibacterial drugs. This shows that this antimicrobial has very slim chances of working when given to patients and this may be mainly because

the strain of Klebsiella pneumoniae that is common in the patient population was resistant to penicillin G and its mechanism of resistant might had been producing beta-lactamase enzymes that breakdown the antibacterial beta-lactam ring structure preventing it from eliciting its therapeutic effect. These findings actually agree with study that was done in German by Stock and Wiedemann (2001) where this drug was resistant to all the various strains of Klebsiella bacteria including Klebsiella pneumoniae. On a study that was done in Nigeria by Nkang et. al. (2009) penicillin G was susceptible or effective to quite a number of gram negative bacteria including Klebsiella pneumoniae.

Ampicillin was the second highest antimicrobial in terms of resistance or ineffectiveness following penicillin G. This shows that these penicillins are quite ineffective on Klebsiella pneumoniae. After these analysis it is quite possible that any penicillin drug that is expected to have an effect to this bacteria might be ineffective, hence Patients maybe exposed to ineffective treatment. Findings by Manikandan and Amsath (2013) in India agree with these findings.

Erythromycin had more cases of resistance compared to cases of effectiveness. This could be due to the bacteria developing efflux resistance mechanism which expels the drug molecule from the bacteria preventing it from yielding its therapeutic effect. This results also shows that using erythromycin may not be suitable as well, as just like most of the antibacterial drugs that were tested in this study, less treatment successes can be yielded by using it. These results are also in line with a study that was done in Germany by Stock and Wiedemann (2001) and another in Uganda by Kyabaggu et. al. (2007) which showed resistance of erythromycin towards klebsiella pneumoniae and other klebsiella bacteria In contrast though a study by Nkang et. al. (2009) in Nigeria showed that erythromycin was effective towards klebsiella pneumonie.

CONCLUSION

This study has shown that Klebsiella pneumonia has shown some resistance to erythromycin, Pennicilin G and ampicillin respectively. On the other hand, this bacterium showed to still be susceptible to cotrimoxazole. Worldwide a number of retrospective studies on susceptibility of these very same drugs have shown an increasing bacteria developing resistance to these antimicrobial drugs. This therefore shows that there is need for consistence monitoring of antimicrobial resistance of the drugs we use. Furthermore, there is need to promote rational use of antimicrobials in order to safeguard the pool of effective antibiotics we currently use.

ACKNOWLEDGEMENTS

The author and the editor of this research would like to thank individuals and institutions who helped in the organisation of information sources, suggestions, editing, advices and opinions towards making this research successful like Swaziland Christian Medical University, National Emergency Response Council on HIV and AIDS, Mankayane Government Hospital and Pigg's Peak Government Hospital.

REFERENCES

1. Bosch, A., Biesbroek, G., Trzcinsi, K., Sanders, E., Bogaert, D. Viral and Bacterial Interactions in the Upper Respiratory Tract. PLoS Pathog, 2013; 9(1): e1003057. doi:10.1371/journal.ppat.1003057.
2. Brink A. J., Cotton M. F., Feldman ., Finlayson H., Friedman R L., Green R., Hendson W., Hockman M H., Maartens G., Madhi S A., Reubenson G., Silverbauer E J., Zietsman I L. Updated recommendations for the management of upper respiratory tract infections in South Africa, 2015; 105: 5. Butler 2010.
3. Hall, L., Gardner, A., Mac Beth, D. and Mitchell, B. Using A Clinical Governence Framework To Identify Barriers To Infection Control Practice. Institute of Biomedical Innovation, Queensland University Of Technology, Brisbane, Australia, 2016.
4. Health Management Information System Data base (HIMS). Upper Respiratory Infections Out Patient Department (OPD), 2016.
5. Kyabaggu, D., Ejobi, F. and Olila, D. The sensitivities to first-line antibiotic therapy of the common urinary tract bacterial infections detected in urine samples at a hospital in metropolitan Kampala (Uganda). Veterinary Medicine, Makerere University, P.O. Box 7062, Kampala, African Health Sciences, 2007; 7(4): 214-222.
6. Manikandan, C. and Amsath, A. Antibiotic susceptibility pattern of Klebsiella pneumoniae isolated from urine samples. Internationa; Journal of Current Microbiology and applied Sciences. ISSN: 2319-7706, 2013; 2(8): 330-337. From http://www.ijcmas.com, [12 January 2017].
7. Marwa, K, J., Mushi, M, F., Konje, E., Alele, P, E., Kidola, J. and Mirambo, M, M. Resistance to Cotrimoxazole and Other Antimicrobials among Isolates from HIV/AIDS and Non-HIV/AIDS Patients at Bugando Medical Centre, Mwanza, Tanzania, Hindawi Journal; Article ID 103874, 2015; 8. From: www.himdawi.com /journals/art/2015/103874 [22 January 2017].
8. Meneghetti, A. (2016, June 6). Upper Respiratory Tract Infection Medication. Retrieved January, 2017, from Medscape: http;//www.emedicine.medscape.com/article/302460 medication.
9. Moghnieh, R., Musharrafieh, U., Husni, R., Abboud, E., Haidar, M. and Abou Shakra, D. (2014). E. Coli, K. pneumonia and K. oxytoca community-acquired infections susceptibility to cephalosporins and other antimicrobials in Lebanon. Retrieved, 2017. from Medscape:

https://www.ncbi.nlm.nih.gov/m/25011373/?i=4&from=/11339246/related

10. Nkang, A., Okonko, I., Mejeha, O., Adewale, O., Udeze, A., Fowotade, A., Fajobi, E. Adedeji, A. and Babalola, E. Assessment of antibiotics susceptibility profiles of some selected clinical isolates from laboratories in Nigeria. Journal of Microbiology and Antimicrobials, 2009; 1(2): 019-026. Available online http://www.academicjournals.org/jma [14 January 2017].
11. Rohilla, A., Sharma, V. and Sonu, K. UPPER RESPIRATORY TRACT INFECTIONS: AN OVERVIEW. International Journal of Current Pharmaceutical Research, 1 to 3, 2013; 5(3): ISSN- 0975-7066.
12. Sanchez, V, G., Mastre, N, R., Clark, B, R., Fyyaz, M., Duvvuri, P., Ekta, G. and Bordon, J. Klebsiella pneumonia Antimicrobial Drug Resistance, United States, 1998. Emerging Infectious Diseases, 2010; 19(1): Available at www.cdc.gov/eid [29 January 2017].
13. Shulman, S., Bisno, A., Clegg, H., Gerber, M., Kaplan, E., Lee, G., Martin, J. and Van Beneden, C. Clinical Practice Guideline for the Diagnosis and Management of Group A Streptococcal Pharyngitis: Update by the Infectious Diseases Society of America. Clinical Infectious Diseases, 2012; 55(10): e86-e102.
14. Standard Treatment Guidelines and Essential Medicines List of Common Medical Conditions in the Kingdom of Swaziland. Copyright © 2012 Ministry of Health, 1st Edition.
15. Stock, I., and Wiedemann, B. Natural antibiotic susceptibility of Klebsiella pneumonia, K. oxytoca, K. planticola, K. ornithinolytica and K. terrigena strains. The Pathological Society of Great Britain and Ireland. J. Med. Microbiol, 2001; 50: 396-406.
16. Zoorob R, Sidani MA, Fremont RD, et al. Antibiotic use in acute upper respiratory tract infections. Am Fam Physician, 2012; 86(9): 817-822.