AN INVESTIGATION OF ANTIBIOTIC PRESCRIBING IN PATIENTS WITH UPPER RESPIRATORY TRACT INFECTIONS (URTIs) AT KATUTURA HEALTH CENTRE

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DECLARATION

I, Mwape Kunda, hereby declare that this study is a true reflection of my own research and that this work has not been submitted for a degree at any other educational institution.

Mwape Kunda   Date

DEDICATION

To my late mother, **Alice Chilufya,** thank you for encouraging me to exhale high in my education. I have made it this far because of your encouragement and spiritual guidance during the time you were here on earth. Rest in peace.

To my father, **Mr Kenneth Kunda**, you taught me to work hard and always gave me support in every way. I believe you will be proud of this work.

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ABSTRACT

Upper Respiratory Tract Infections (URTIs) are viral in 80% of the cases (Mazur, 2010) but antibiotic prescribing in these illnesses still remains a problem in many places, where about 60% of patients with URTIs receive antibiotics inappropriately (WHO, 2010).This makes URTIs important targets for strategies aimed at reducing irrational antibiotic use because irrational use of antibiotics leads to the emergence and spread of bacterial resistance, which is a growing global public health concern. Other consequences of irrational use of antibiotics are wastage of resources and adverse effects. The purpose of this study was to explore antibiotic prescribing in patients with URTIs at Katutura Health Centre (KHC).

A descriptive, cross sectional, quantitative design based on patients' prescriptions was used. Data was analysed using Epi info version 7.1.1.14 and SPSS version 22.0 statistical packages. Microsoft office excel 2010 was also used for graphical presentation of the results.

The rate of antibiotic prescribing for patients with URTIs at KHC was 78% (95% CI, 74% - 82%). Further analysis with the chi-square test of antibiotic prescribing (response variable) and illness, age, gender and profession (exposure variables) showed that age and illness were significantly associated with antibiotic prescribing ($p < 0.05$) while gender and profession rank were not. Compliance to treatment guidelines was 47% (CI, 40%-54%). The total cost of antibiotic prescribing in this study was N$ 2406.98, of which non-specific URTIs accounted for 48% (N$ 1150.45). Irrationally prescribed antibiotics accounted for 44 % (N$ 1052.07) and those that were rationally prescribed, 8% (N$ 204.46). The total cost of antibiotic

treatment of illnesses assessed for rationally was N$ 1256.5 of which N$ 1052.07 (84%) was the cost of irrationally prescribed antibiotics and N$ 204.46 (16%) for rationally prescribed antibiotics. This showed that the cost of irrational prescribing was costing five times more than that of rational prescribing.

Antibiotic over prescribing is a problem in patients with URTIs. The Ministry of Health and Social Services need to develop or adopt international strategies that deliver proven efficacy in reducing antibiotic prescribing in URTIs. These include developing or adopting antibiotic policies that are specific to URTIs, patient education through literature and media campaigns, and implementing and enforcing continued education for health workers on the judicial use of antimicrobials. Further research is also needed to determine the factors that contribute to antibiotic over prescribing in URTIs.

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LIST OF ABBREVIATIONS

AOM	Acute Otitis Media
CDC	Centre for Disease Control and Prevention
CMS	Central Medical Stores
CSOM	Chronic Suppurative Otitis Media
GABHS	Group A β –hemolytic streptococcus
GP	General Practioner
HF	Health Facility
KHC	Katutura Health Centre
NSTG	Namibia Standard Treatment Guidelines
PHC	Primary Health Care
PMIS	Pharmaceutical Management information system
STG	Standard treatment Guidelines
URTI	Upper Respiratory Tract Infection
USAID	United States Agency for International Development
WHO	World Health Organisation

CHAPTER 1

INTRODUCTION

1.1 Background

URTIs are a group of disorders that include common cold, sore throat, tonsillitis, sinusitis, acute otitis media, epiglottitis, rhinitis, tonsillitis and nasopharyngitis (Jones, 2005).

Patients with Upper Respiratory Tract Infections (URTIs) constitute a major portion of the primary health care practitioners' workload, particularly during winter (Bauman, 2000) and as indicated by Kontarakis et al. (2011), primary health care practitioners' account for the majority of antibiotic prescribing, in Greece. Mazur (2010) indicated that these infections are viral in 80% of the cases and do not respond to antibiotic therapy. In spite of this, physicians continue to prescribe antibiotics even though they know that antibiotics are not effective against viral infections (Shlomo, Adi & Elizier, 2003). A study done in Turkey showed that antibiotics were prescribed for 91.8% of patients with URTIs. The same study also showed that antibiotics were prescribed for 41.9% of patients with a common cold, 94.7% of patients with acute pharyngitis, 94.1% of patients with acute sinusitis and 100% of those with acute otitis media (Leblebicioglu, Canbaz, Peksen & Gunaydin, 2002). The World Health Organization (2010) also states that up to 60% of people with viral upper respiratory tract infection receive antibiotics inappropriately.

Considering these figures, it is clear that antibiotic prescribing in URTIs, among others, is alarmingly high and contributes to the emergence and spread of bacterial resistance, which is a major global public health problem (Togoobaatar et al., 2010). Other consequences of inappropriate use of antibiotic prescribing in URTIs include: wastage of resources, side effects, eroded patient confidence, among others.

A number of studies support the relationship between antibiotic use and the resistance rate. This worldwide epidemic of antibiotic resistance is a danger of ending the golden age of antibiotic therapy (Gould, 2009). It leads to increased mortality, morbidity, increased cost of health care and ultimately with time decrease in the rate of successful treatment (Hashemi, Nasrollah & Rajabi, 2013). For instance, the rapid increase in drug-resistant *Streptococcus pneumoniae* infections are of particular concern in pediatrics since pneumococci is the leading cause of bacterial meningitis, pneumonia, bacteraemia and otitis media in children (Togoobaatar et al., 2010). Furthermore, infections caused by antimicrobial-resistant bacteria are associated with substantially higher rates of morbidity and mortality compared to infections caused by antimicrobial-susceptible bacteria (Erika, Myrielle, Pierre, Damien & Shigui, 2008). In the United States, for example, it was estimated that there were 18,650 deaths in patients with invasive methicillin-resistant *Staphylococcus aureus* in 2005, exceeding the total number of deaths due to HIV/AIDS in the same year (Klevens et al., 2007). Additionally, it has been estimated that antimicrobial resistance annually costs US$4000–5000 million in the USA and €9000 million in Europe (Holloway & Van Dijk, 2011). This shows that antimicrobial resistance impacts on all areas of medicine, and makes successful empirical therapy much more difficult to achieve. Even though the problem of antimicrobial resistance cannot be prevented, its development and spread can be slowed (Gould, 2009).

Apart from the emergence and spread of bacterial resistance, antibiotic over prescribing results in an unnecessary financial burden on the patient and society, as well as unnecessary adverse effects (Butler, Rollnick, Kinnersley, Jones & Stott, 1998).

Some of the factors or attitudes that are known to influence antibiotic prescribing are fear, complacency, insufficient knowledge, external responsibility of the pharmaceutical industry, over-the-counter antibiotics (Vazquez-Lago, et al., 2012), physicians perceived parental expectations (Ciofi et al., 2006),unrealistic patient expectations, patient pressure to prescribe antibiotics, and insufficient time to educate patients about the effectiveness of antibiotics (Macfarlane, Holmes, Macfarlane & Britten, 1997). Younger age and a diagnosis of tonsillitis and otitis media have also been reported to be associated with antibiotic prescribing (Senok, Ismaeel, Al-Qashar and Agab, 2009).

Some of the proven ways of reducing antibiotic overuse include: the use of treatment guidelines such as the newly launched Namibian Standard Treatment Guidelines (NSTG), the Centre for Disease Control and Prevention (CDC) guidelines as well as campaigns such as the GET SMART-know when antibiotics work of 2010. In addition, identifying knowledge related to inappropriate antibiotic prescribing among prescribers can enable specific interventions to be designed that can help improve antibiotic use and reduce the spread of microbial resistance (Vazquez-Lago, et al., 2012).

1.2 Problem statement

As indicated in the background section, antibiotic prescribing in patients with URTIs is common in primary health care settings. To date, no studies have been conducted in Namibia on antibiotic prescribing in URTIs but the third national survey on drugs in 2001 reported by Lates and Shiyandja showed an increasing trend in antibiotic prescribing. That is, 39% was reported in 1997, 43% in 1999 and 51% in 2001. According to the authors, this rising trend could be attributed to polypharmacy and non-adherence to standard treatment guidelines (STGs). Recent reports indicate that there has been a reduction of antibiotic prescribing in the last 2.5 years, but there was a slight increase in outpatient prescriptions with an antibiotic to 45.6% in the reporting period July to September 2011. In addition, only Oshikoto and Oshana regions achieved the acceptable result for the health facility indicator (HF13) for monitoring antibiotic prescribing. That is, 20% and 26%, respectively (Phulu, Sumbi & Lates, 2011).

Irrational use of antibiotics leads to the emergence and spread of bacterial resistance, wastage of resources, adverse effects which need more resources to be treated and patient misconception of these medicines, among others. The emergence and spread of bacterial resistance are a worldwide public health concern that calls for action in order to maintain the efficacy of these vital medications.

Harris et al. (2003) indicated that URTIs are important targets for strategies aimed at reducing excess antibiotic use because antibiotics are frequently prescribed in these illnesses that are predominantly of viral etiology.

It is against this background that this study aimed to explore antibiotic prescribing in patients with URTIs in order to develop strategies and make recommendations that will promote judicious use of these important medicines, promote quality patient care and avoid wastage of scarce resources.

1.2 Purpose of the study

The purpose of this study was to explore antibiotic prescribing in patients with URTIs at Katutura Health Centre (KHC).

1.3 Objectives

1. To determine the rate of antibiotic prescribing in patients with URTIs.
2. To assess the rationality of the treatment of URTIs.
3. To compare the cost of rational and irrational antibiotic use in URTIs.

1.5 Significance of the study

This study contributed to the knowledge of the magnitude of antibiotic prescribing in URTIs, the magnitude of irrational prescribing of antibiotics and the associated cost. Furthermore, assessment of treatment appropriateness helped in assessing prescribers' adherence to treatment guidelines, which are aimed at promoting rational prescribing, avoiding wastage of resources and providing patients with the most cost-effective treatment. The findings of this study could be significant in making appropriate recommendations and interventions to promote judicious use of antibiotics in order to preserve their efficacy, reduce wastage of scarce resources and optimise patient care.

1.6 Definitions of Key Concepts

Investigation - Refers to carrying out a systematic or formal inquiry into something. (Oxford Dictionaries, 2013)

Antibiotic - Antibiotics are substances derived from various species of microorganisms such as bacteria, fungi, actinomycetes, etc., including synthetically derived antibiotics such sulphonamides and quinolones that suppress the growth of other microorganisms and may eventually destroy them (Seth & Vimlesh, 2009). The term antibiotic is used as synonym for antibacterial, a substance that acts against bacteria (Kourtis, 2011). In this study, the term antibiotic means antibiotics prescribed for all patients with a diagnosis of the URTI by GPs or nurses during the study. Data on the antibiotics was extracted from patients' prescriptions “health passports” as the patients collected their medication from the pharmacy.

Prescribe- means to recommend or advise and authorize the use of a medicine or treatment for someone, especially in writing (Oxford Dictionaries, 2013). In this study prescribe means the recommended medicines in writing, that is, antibiotics and other medicines, by GPs or nurses during the study of patients with URTIs.

Upper Respiratory Tract Infections (URTIs) - Any infectious disease of the upper respiratory tract. These include common cold, laryngitis, pharyngitis or tonsillitis, acute rhinitis, acute rhinosinusitis and acute otitis media (Ramachandra et al., 2012). For this study, the URTIS that were purposely selected are non- specific URTIs, the common cold, pharyngitis/tonsillitis and acute otitis media.

Compliance – means conforming to a regulation, such as specifications, policy, standard or law**.** In this study, it refers to conforming to NSTGs (2011) and WHO (2001) guidelines with respect to the recommended treatment for the illnesses that were included in this study. That is, the choice of antibiotic (if recommended), dose, frequency and duration.

Rational prescribing – refers to patients receiving medications appropriate to their clinical needs (right drug), in doses that meet their own individual requirements, for an adequate period of time, and at the lowest cost to them and their community (WHO, 2013).

Failure to prescribe in accordance with guidelines, inappropriate self-medication (often of prescription – only medications) and non – adherence to dosing regimens are examples of irrational use of medicines (WHO, 2013).

In this study, rational prescribing means choosing the right antibiotic, right dose, right frequency and right duration as prescribed by both the Namibian and WHO guidelines. A prescription by GPs or nurses for a patient with an URTI was considered irrational if one or more of these conditions were not satisfied. Rationality was assessed using the Namibian standard treatment guidelines (2011) and the WHO recommendations.

Standard treatment guidelines- these are systematically developed statements to help practitioners or prescribers to make decisions about appropriate treatments for specific clinical conditions. They include information on diagnostic criteria, treatment of first choice, important side effects, contraindications, referral criteria and also medicine information for patients (Managing drug supplies as cited by Walley & Wright, 2010). In addition, they briefly identify and summarize the most current data about prevention, diagnosis and therapy of particular diseases and sometimes define all relevant decision options with their respective health outcomes including a risk-benefit and cost analysis. By helping professionals in deciding which treatment to use, guidelines aim to improve the quality of care delivered, standardize medical care and enhance cost efficiency (Kirch, 2008). In this study, guidelines refer to the Namibian Standard Treatment guidelines (NSTGs) and the WHO guidelines. These guidelines were used to assess the rationality of antibiotic prescriptions by GPs and nurses for all patients diagnosed with an URTI during the study. Every prescription except for those with a diagnosis of URTIs was assessed. This was done after collecting data from the prescriptions that were included in the study whether or not an antibiotic was prescribed. If an antibiotic was prescribed, then all aspects of interest were assessed.

1.7 Ethical considerations

Permission to conduct the study was granted by the University of Namibia postgraduate committee and also by MoHSS research committee prior to the commencement of the study, as indicated in Annexure A and B respectively.

The study focused on the review of patients' prescriptions. Therefore, in order to ensure confidentiality and anonymity of both the prescribers and the patients, no names were recorded on the data collection tool, instead, all the data collection forms were allocated an identification number from 1 to 385. In addition, only the profession of the prescribers was recorded.

1.8 Summary

This chapter covered the background to the study and its significance, including research problem, research purpose and objectives and definitions of main concepts. The next chapter will discuss the literature review related to this study.

CHAPTER 2

LITERATURE REVIEW AND CONCEPTUALISATION

2.1 INTRODUCTION

The purpose of this chapter is to introduce to the reader the concept of the study, provide an overview of the URTIs under study, state the recommended treatment of the World Health Organization and the Namibia standard treatment guidelines, provide an overview of the rate of antibiotic prescribing in these conditions and describe problems associated with inappropriate antibiotic prescribing.

2.2 CONCEPTUALIZATION OF THE STUDY

URTIs are viral in 80% of the cases (Mazur ,2010) but antibiotic prescribing in these illnesses still remains a problem in many places where about 60% of patients with URTIs receive antibiotics inappropriately (WHO, 2010).To date, there has been no study conducted in Namibia to determine the rate of antibiotic prescribing in URTIs, but results from PMIS (2011) by Phulu, Sumbi & Lates , show that many facilities in Namibia (KHC inclusive) do not achieve the target of the indicator HF13 that monitors antibiotic prescribing in outpatients. This problem could be attributed to antibiotic prescribing in URTIs because they constitute a major part of the primary health care practitioners' workload (Bauman, 2000). Irrational antibiotic prescribing is a global public health problem and according to Harris et al. (2003), URTIs are important targets for strategies aimed at reducing excess antibiotic use because antibiotics are frequently prescribed in these illnesses that are predominantly of viral etiology.

Assessment of medicines use can be made by extraction of the required information from patient's prescriptions (Suttajit, Wagner, Tantipidoke, Ross-Degnan & Sitthi-Amorn, 2005). In this study, patients' prescriptions were used to obtain the required data which was entered on a data collection form (Annexure A). This form was developed to contain all variables of interest. The variables being, patient age and gender, diagnosis, antibiotic prescribed, quantities of antibiotics dispensed, compliance to STGs of antibiotic prescriptions, other medicines prescribed and prescriber rank or profession.

Although URTIs are viral in most cases, rational prescribing is important in some of the cases that are bacterial and require antibiotic treatment, in order to avoid development of resistance and treatment failure. According to WHO (2013), rational prescribing refers to patients receiving medications appropriate to their clinical needs (right drug), in doses that meet their own individual requirements, for an adequate period of time and at the lowest cost to them and their community. Therefore, this study was based on the NSTGs (Table 2.2 & Annexure D) and WHO (Table 2.2) recommendations. These STGs recommend antibiotic prescribing in all the conditions that were included in the study except for the common cold. STGs are systematically developed statements to help practitioners or prescribers to make decisions about appropriate treatments for specific clinical conditions. They include information such as diagnostic criteria, treatment of first choice (drug choice, dose and duration), important side effects, contraindications, referral criteria, and also medicine information for patients (Managing drug supplies as cited by Walley & Wright, 2010). In this study, the aspects that were assessed were the choice of antibiotic, dose, frequency and duration of treatment.

2.2 UPPER RESPIRATORY TRACT INFECTIONS

URTIs can be characterized by a group of disorders that include common cold, pharyngitis, tonsillitis, sinusitis, acute otitis media, epiglottitis, rhinitis, tonsillitis and nasopharyngitis (Jones, 2005) which significantly occur in the upper respiratory tract. These infections have been regarded as non-specific, a term that is used to describe acute infections involving the nose, paranasal sinuses, pharynx, larynx, trachea and bronchi. Hence, proper judgement is required in determining the affected respiratory mucosal part. URTIs are and remain contagious for a few hours to 2-3 days of exposure and the symptoms are known to last for 7 to 10 days or longer. The symptoms include stuffy nose, fever, vomiting, and irritability, loss of appetite, watery eyes, runny nose, sneezing, coughing and sore throat. Although they are known to be mild and self-limiting, they could lead to life threatening conditions. URTIs are caused by viruses in most cases, but they can also be bacterial in etiology (Rohilla, Sharma & Kumar, 2013). They occur in both children and adults and are a major cause of mild morbidity which has a high cost to society, being responsible for missed work and unnecessary medical care (Cotton, 2008). The viruses that cause these infections include rhinovirus, coronavirus, parainfluenza, respiratory syncytial virus, adenovirus, Human metapneumovirus and Influenza. Occasionally the enterovirus is implicated in summer (Cotton, 2008). While the bacteria are: *Group A* *β –hemolytic streptococcus* (GABHS), *Neisseria gonorrhea*, *Arcanobacterium haemolyticum*, *Mycoplasma pneumoniae* and *Chlamydophila pneumoniae* (Ferri, 2012). The types of the URTIs that were included in this study are discussed as follows:

2.2.1 The common cold

The common cold is an acute self–limiting syndrome, accompanied by other URTI symptoms and signs. It occurs worldwide with peak incidence occurring in winter in temperate regions, whereas in the tropical regions its most common in the rainy season (Elliot, Casey, and Lambert & Sandoe, 2011). This illness is common during the winter season, probably due to overcrowding and staying indoors (Jones et al. , 2005). Although the common cold is mild, self -limiting and of a short duration, it is the leading cause of acute morbidity, making it the most infectious condition seen in ambulatory care. In addition, it is known to be the leading cause of industrial and school absenteeism. In the United States for example, it accounts for 170 million days of restricted activity, 23 million days of school absence and 18 million days of work absence (Sloane, Slatt, Ebell, Jacques & Smith, 2008). Everyone suffers from the common cold each year, both in developing and developed countries (WHO, 2001). On average, young children have 6 episodes per year and adults have 1 to 2 per year (Jones et al., 2005). Elderly people do not have colds more often than young adults, but their colds are complicated more frequently by lower respiratory tract infections (Jones et al. 2005).

This self-limiting viral infection of the upper respiratory tract is caused by a number of viruses, the most common of these being rhinoviruses, parainfluenza viruses, respiratory syncytial virus and adenoviruses. The season of the year, the person's age and prior exposure are important factors in the type of virus causing the infection and the type of symptoms that occur. For instance, outbreaks due to adenoviruses are common in early fall and late spring, those caused by respiratory syncytial virus peak in the winter and spring months, whereas infections due to the adenoviruses and coronaviruses are most frequent during winter and spring months. Infections resulting from the respiratory syncytial virus and parainfluenza viruses are common and severe in children less than 3 years of age. However, these infections occur less frequently and with milder symptoms with increasing age. Parainfluenza viruses often produce lower respiratory symptoms with first infections but, less sever upper respiratory with reinfections. Rhinoviruses are the most common cause of colds in ages 5 to 40 years. There are more than 100 serotypes of rhinoviruses and people acquire lifetime immunity to an individual stereotype, but it would take a long time for one to be immune to all the stereotypes (Porth, 2011).

Transmission of the common cold viruses is by aerosol or large droplets or via virus-contaminated hands. This is facilitated by the nasal discharge which causes irritation and results in sneezing (Elliot et al., 2011). Fingers are known to be the greatest source of spread and the nasal mucosa and conjunctival surface of the eyes are the most common portals of entry of the virus. The most highly contagious period is during the first 3 days of the onset of symptoms and the incubation period is approximately 5 days. Cold viruses can survive for more than 5 hours on the skin and hard surface such as plastic countertops. The aerosol spread of colds through coughing and sneezing is much less important than the spread by fingers picking up the virus from contaminated surfaces and carrying it to the nasal membranes and eyes (Porth, 2011). In addition, it can also be transmitted via direct hand to hand contact (Sloane et al., 2008). This makes hand washing one of the important preventive measures for avoiding the common cold (Porth, 2011).

The viruses responsible for the common cold infect the nasal respiratory cells, causing increased mucus production and edema. Rhinoviruses and coronaviruses have a tropism respiratory epithelium and optimally reproduce at temperatures well below 37^{o}C. So the infection remains limited to the cooler passages of the upper respiratory tract. Infected cells release chemical mediators, such as bradykinin, which is responsible for most of the symptoms associated with the common cold, namely increased mucus production, nasal congestion and eustachian tube obstruction. The resulting stasis of secretions may predispose to secondary bacterial infection and lead to bacterial sinusitis and otitis media (Ruben & Reinsner, 2009).

The common cold usually begins with a sore and scratchy throat, followed by profuse and water rhinorrhea, nasal congestion, sneezing and coughing. Other symptoms include malaise, fatigue, headache, hoarseness, sinus congestion and myalgia. Fever is common in children, but is infrequent in adults (Porth, 2011). Nasal blockage is common and sinusitis is part of the common cold symptoms. Nasal discharge may become purulent. The common cold, should resolve in 7 to 10 days. Pharyngitis and conjunctivitis may also occur, with enterovirus infection and as earlier mentioned it can complicate into bacterial sinusitis and bacterial otitis media (Elliot et al., 2011).

2.2.2 Acute pharyngitis and tonsillitis

Pharyngitis or tonsillitis is inflammation of the pharynx and / tonsils (Ferri, 2012) caused by an infection or irritation (Buttaro, 2012). Sore throat is used as a synonym for this condition. Acute pharyngitis is known to account for 1.3% of outpatient visits to health care providers in the United States of America and it affects persons of all ages (Ferri, 2012).

Acute pharyngitis and tonsillitis are caused by both viruses and bacteria. Acute pharyngitis is most often caused by a virus and depending on the season and patients age, 70 to 90 % of acute episodes are viral and involve a wide array of common viruses (Jong & Stevens, 2012). The viruses implicated in these infections are Rhinovirus, Respiratory syncytial virus, influenza A and B, Epstein – Barr virus, Adenovirus, Herpes simplex virus (Ferri, 2012). Rhinovirus is the most common virus associated with pharyngitis especially during spring, followed by adenovirus in both adults and children, which accounts for 20% of pharyngitis cases in late winter and early spring especially among children younger than 5 years of age. Enteroviruses are a common cause in late summer and fall months (Jong & Stevens, 2012). As earlier mentioned, pharyngitis and tonsillitis are also caused by bacterial pathogens of which *Group A β –hemolytic streptococcus* (*Streptococcus pyogenes* or GABHS) is not only the common bacterial pathogen that causes pharyngitis but also most likely to result in complications of pharyngitis (Ferri, 2012). About 5-10% of the population carries Streptococcus pyogenes in the pharynx; carriage rates are higher among children especially during winter (Elliott et al., 2011). In children, GABHS causes 10-30% of cases of pharyngitis with children aged 5 to 15 years at the greatest risk for infection and complications, whereas in adults, it accounts for 5 to 10 % of the instances. Winter months are associated with an increase in GABHS pharyngitis in people of all ages, though it accounts for 50% of the cases in children (Jong & Stevens, 2012). Others bacteria that cause pharyngitis are *Neisseria gonorrhea*, *Arcanobacterium haemolyticum*, *Mycoplasma pneumoniae* and *Chlamydophila pneumoniae* (Ferri, 2012).

It is normally not easy to differentiate viral from bacterial pharyngitis based on clinical signs and symptoms, but they are a few distinct characteristics of each. In viral cases, patients typically describe the sudden attack of sore throat, fever, malaise, cough, headache, myalgias, and fatigue, rhinitis, conjunctivitis which is generally associated with adenovirus, congestion and a cough with sputum production can also be present. On physical examination, findings include mild erythema with little or no pharyngeal exudate, although the pharynx may appear swollen. Painful or tender lymphadenopathy is not typically present. In bacterial pharyngitis, patients may report a sudden onset of sore throat, painful swallowing, fever (temperature higher than 38.5^{O}C) chills, headache, nausea, vomiting and abdominal pain. Rhinitis, cough, conjunctivitis and myalgias are not typically present in bacterial pharyngitis. In GABHS infection, the physical examination reveals marked erythema of the throat and tonsils, patchy, discrete, white or yellowish exudate, pharyngeal petechiae and tender anterior cervical adenopathy. Pressure on the tonsillar pillars may produce purulent drainage. The uvula may also be edematous and temperature higher than 38.3^{o}C. On occasion, GABHS may be seen with erythematous, persistent sore throat with a little fever and no exudate (Buttaro, 2012). Bacterial pharyngitis can complicate into peri-tonsillar and retropharyngeal abscesses, GAS post infective rheumatic fever and glomerulonephritis (Locke, Keat, Walker & Mackinnon, 2012).

The diagnosis of acute pharyngitis is complicated by the 10% to 30 % of the cases caused by bacterial pathogens, particularly GABHS, as well as the lack of clinical features that readily distinguish viral and bacterial infections. Furthermore, concerns over the risk of suppurative and nonsuppurative complications associated with GABHS pharyngitis, have fueled the widespread practice of empirical antibiotic therapy, which has led to overuse of antibiotics and consequences such as unnecessary cost, adverse events and bacterial resistance (Jong & Stevens, 2012).

2.2.3 Acute Otitis Media (AOM)

Otitis media (OM) is an acute upper respiratory tract infection that affects the respiratory mucosa of the middle ear cleft. In developed countries, OM is the commonest indication for antibiotic prescribing and surgery in young children.

AOM is a common condition, especially in children under the age of 5 years. The recurrence rate is at 10-20% in this age group which usually experience at least three episodes in the first year of life. The probability of recurrence is greater if the first episode occurs in the first year of life and becomes a rare condition after puberty. The condition has a generally natural course and the most severe symptoms resolve within two or three days. Children with bilateral AOM have a greater chance of persistent fever and pain. Perforation of the eardrum occurs in approximately 4 to 8% of the cases, causing the discharge which is sometimes present in this condition.

Severe complications including, mastoiditis and meningitis, are very rare. Approximately 50% of the children develop otitis media with effusion (OME) four to six weeks after an episode of AOM and approximately 25% still have this condition after three months (Blijham, 2011).

The different types of otitis media include acute otitis media, otitis media with effusion, chronic suppurative otitis media (CSOM), acute otitis media with perforation, acute otitis media without perforation. Complications of AOM include CSOM, mastoids, labyrinths, facial palsy, meningitis, intracranial abscess and lateral sinus thrombosis. (Morris & Leach 2009). Furthermore, OM with effusion can cause complications such as conductive hearing loss that can have an impact on a child's speech and language development (Locke et al., 2012).

Pneumococci are the most common pathogens causing AOM in 30- 40% of the cases. Even though *the Haemophilus influenza* and *Moraxella catarrhalis* are also most cultured, there are usually no bacteria in approximately 40% of middle ear cultures (Blijham, 2011). Other bacterial causes include *Streptococcus pneumoniae*, Streptococcus pyogens and *Staphylococcus aureus* (Locke et al., 2012). Episodes of AOM usually follow URTI. The viruses responsible for these infections can cause AOM themselves (Biljhan, 2011) of which in 50% of cases are caused by Respiratory syncytial virus (Locke et al., 2012). URTIs may result in edema and blockage of the eustachain tube, with subsequent impaired drainage of middle –ear fluid, predisposing bacterial infection (Elliott, et al). Hence, the postulation that bacterial infections often develop following ' viral population' of the mucous membranes (Blijham, 2011).

AOM is characterized by a rapid and short onset of signs and symptoms of inflammation in the middle, such as, otalgia (ear ache), fever and sometimes otorrhoea. These are the primary symptoms and signs of AOM .Other symptoms that are associated with it are general illness, sometimes purulent discharge , general symptoms such as, irritability, night-time restlessness or gastrointestinal symptoms (abdominal pain, diarrhoea, vomiting, loss of appetite) (Blijham, 2011), crying, itching ears, poor feeding, pain upon drinking and eating (Namibia standard treatment guidelines, 2011) which can also be suggestive of AOM in children even if there is no earache or otorrhoea (Blijham, 2011). Adults could also complain of headache, malaise and weakness (Namibia standard treatment guidelines, 2011). On physical examination, the ear drum appears reddened and bulging and, if untreated, drum perforation with subsequent purulent discharge may occur (Elliot et al., 2011).

The bacteria most implicated in AOM are *Streptococcus pneumonia* and *Haemophilus influenza.* Bacterial infection is suggested by the presence of acute onset of pain in the ear, fever, and redness and decreased mobility of the tympanic membrane. Patients presenting with these signs require antimicrobials because meningitis can be a complication (WHO, 2001).

2.3 TREATMENT OF UPPER RESPIRATORY TRACT INFECTIONS

Treatment of URTIs is mostly symptomatic. However, antibiotics are indicated in some cases.

Antibiotics are substances derived from various species of microorganisms such as bacteria, fungi, actinomycetes, etc., including synthetically derived antibiotics such sulfonamides and quinolones that suppress the growth of other microorganisms and may eventually destroy them (Seth & Vimlesh, 2009). The term antibiotic is used as synonym for antibacterial, a substance that acts against bacteria (Kourtis, 2011).

Antibiotics can be classified based on their chemical structures. Alternatively, they can also be classified on the basis of their target specificity. That is narrow spectrum antibiotics, which target particular types of bacteria, such as gram negative or gram positive bacteria, whereas broad spectrum antibiotics can be effective against a wide range of bacteria. Furthermore, antibiotics can be classified as either being bactericidal or bacteriostatic. Bactericidal agents typically kill bacteria directly, whereas bacteriostatic agents prevent cell growth and division. Antibiotics can also be classified based on their mechanism of action. There are five major mechanisms by which an antibiotic exerts its pharmacological action. These are inhibition of bacterial cell wall synthesis, inhibition of bacterial protein synthesis, alteration of bacterial cell wall, inhibition of bacterial nucleic acid synthesis, and antimetabolite activities. Inhibition of bacterial cell wall formation is probably the most common mechanism by which an antibiotic kills bacteria or inhibits their growth. Examples of antibiotics that interfere with cell wall formation are beta-lactam antibiotics including penicillins, cephalosporins, vancomycin, etc. Those that interfere with protein synthesis of bacteria by binding to the 50S ribosomal unit include, clindamycin, chloramphenical, lincomycin and macrolides and those that bind to the 30S ribosomal unit are tetracycline and aminoglycosides. Sulphonamides and trimethoprim kills bacteria by inhibiting folate synthesis. Metronidazole and quinolones exert their action by interfering with bacterial DNA synthesis, while rifampicin interferes with bacterial RNA synthesis (Dasgupta, 2012).

Table 2.1 Classification of Antibiotics Based on Chemical Structure

Chemical structure	Example of drugs
Aminoglycoside	Amikacin, gentamicin, kanamycin, neomycin, streptomycin, tobramycin
Glycopeptides	Vancomycin
Beta-lactam	Penicillin G, penicillin V, ampicillin , carbenicllin , dicloxacillin , nafcillin , oxacillin, piperacillin, temocillin , ticarcillin
Cephalosporins	Cefadroxil , cefazolin , ceflatonin , cephalexin , cefixime,cefdinir , ceditoren , cefotaxime, cefepime , cefoperazone
Carbapenem	Ertapenem , doripenem , meropenem
Macrolide	Azithromycin , clarithromycin, dirithromycin, erythromycin , roxithromycin , troleandomycin
Monobactum	Aztreonam
Polypeptides	Bacitracin , colistin , polymyxin B
Oxazolidinones	Linezolid , quinupristin /dalfopristin
Quinolones	Ciprofolxacin , enoxacin , gatifloxacin , lomefloxacin, ofloxacin , norfloxacin , levofloxacin
Sulphonamides	Mafenide , sulfacetamide , sulfadiazine, sulfamethoxazole, sulfanilamide , sulfisoxazole, trimothoprim

(Dasgupta, 2012)

In cases where antibiotics are indicated, treatment is and must be based on the treatment guidelines of a particular setting. In this study, the NSTG (2011) was used as reference as well as WHO recommendation for which Namibia and many other countries use as a reference will be discussed.

Standard treatment guidelines are systematically developed statements to help practitioners or prescribers to make decisions about the appropriate treatment for specific clinical conditions. They include information on diagnostic criteria, treatment of first choice, important side effects, contraindications, referral criteria also medicine information for patients (Managing drug supplies as cited in Walley & Wright, 2010). In addition, they briefly identify and summarize the most current data about prevention and sometimes define all relevant decision options with their respective health outcomes including a risk-benefit and cost analysis. Furthermore, guidelines aim to improve the quality of care delivered, standardize medical care and enhance cost efficiency (Kirch, 2008).

2.3.1 Treatment of the common cold

Treatment of the common cold is symptomatic in both immune competent patients and immunocompromised patients. However, antiviral agents are available for use in immunocompromised patients (Elliot et al., 2011).

A. WHO recommendations

Antibiotics are not indicated in the management of the common cold and neither does their empirical use provide any benefit. The WHO (2001) further states that according to several randomized trials carried out in both industrialized and developing countries, antibiotic treatment does neither prevent complications, nor reduce the duration of the sickness. Thus, the common cold must be treated symptomatically with antihistamines and sympathomimetics. Even though this gives clinical relief it does reduce the incidence of OM following a cold.

B. Namibia standard treatment Guidelines

The NSTG recommends a general symptomatic management with the use of analgesics, antihistamines, ascorbic acid, though its value is doubtful. Antibiotics are reserved for secondary infections. Use of locally acting agents such as saline drops and vasocontrictors (oxymetazoline nasal spray or drops) that give quick, temporary relief is also recommended.

2.3.2 Treatment of acute pharyngitis and / tonsillitis (sore throat)

A. WHO recommendations

Distinguishing between streptococcal and viral pharyngitis on clinical grounds is usually difficult. However, tender, enlarged cervical lymph nodes and a scarlet fever-like rash are considered specific for *S. pyogenes*, but uncommon. The presence of the three major signs, that is, fever > 38^{o}C, intense pharyngeal pain, and absence of rhinitis and cough has a high positive-predictive value of *Streptococcal* pharyngitis. When these three signs are not all present, streptococcal etiology is unlikely. For a more specific diagnosis and therapy, a rapid antigen test or culture can be done if resources are available.

For streptococcal pharyngitis, the following are the treatment recommendations:

- Benzathine benzylpenicillin 1.2 million IU i.m. in a single dose for adults and children > 30 kg (children ≤ 30 kg: 30000 IU / kg, maximum 1.2 million IU i.m in a single dose.

  OR

- Phenoxymethylpenicillin 500 mg (children 10-20 mg/kg; maximum 500 mg) orally every 6 hours for 10 days.

  OR

- Amoxicillin 500 mg (children 15 mg/kg; maximum 500 mg) orally every 8 hours for 10 days.
- Patients allergic to penicillin: Erythromycin 500 mg (children: 10-15 mg / kg; maximum 500 mg) orally every 6 hours for 10 days. OR cefalexin 500 mg (children: 15 mg / kg: maximum 500 mg) orally every 6-8 hours for 10 days (WHO, 2001).

B. Namibian standard treatment guidelines

Patients < 15 years of age with sore throat, dyphagia, fever, red and inflamed tonsils, follicles on the tonsils, or enlarged lymph glands need active treatment. For symptomatic relief, paracetamol, salt water or chlorhexidine gargle and local antibiotic spray if available, are recommended. The antibiotics of choice are:

- Phenoxymethylpenicillin:

  Adults: 500mg PO four times daily for 5 days and in children: 250mg/5ml PO four times daily for 5 days OR

- Benzathine penicillin: Adults, 1.2 million units stat and children: 0.6 million units stat OR
- Azithromycin: Adults, 1 g PO daily for 3 days and children: 10mg/ kg per day PO for 3 days.

2.3.3 Treatment of Acute Otitis Media

A. WHO recommendations

The treatment of AOM involves the use of antibiotics even though in most cases it can resolve on its own. This is because of the complications that result if inadequately managed. The WHO (2012) states that there is no evidence for the safety of not giving antibiotics for AOM in settings where the prevalence of AOM and its complications are high. It furthur states that in developing countries where there could be a high rate of serious acute complications, such as mastoiditis, and where short-term and long-term complications of untreated AOM can lead to death or severe disability, antibiotic use is therefore beneficial.The benefits of antibiotic treatment for AOM include reduced pain in acute ear infection, reduced risk of acute, serious complications, possible reduced risk of long-term sequelae, including chronic suppurative otitis media (CSOM) and mastoiditis. The recommendations are as follows:

- Children with acute otitis media should be treated with oral amoxicillin at 40 mg/ kg twice per for 7–10 days. OR
- Where pathogens causing acute otitis media are known to be sensitive to co-trimoxazole, this antibiotic could be used as an alternative given twice per day for 7–10 days (WHO, 2012), at a dose of sulfamethoxazole 400mg +

trimethoprim 80mg (children 20mg / kg + 4 mg /kg; maximum 400 mg + 80 mg) orally every 12 hours for 5 days (WHO, 2001).

Studies have also shown that even though children treated with amoxicillin have a higher incidence of adverse effects such as diarrhea, vomiting and rash compared to those treated with placebo, it's still clear that its beneficial to give antibiotics rather than to withhold them (WHO, 2012).

B. Namibia standard treatment guidelines

The Nambian Standard Treatment Guidelines also recommend the use of antibiotics in treating AOM.

- For Adults: amoxicillin 500mg every 8 hours for 5 days and Children: phenoxymethylpenicillin 25-50 mg/kg per day in four divided doses; amoxicillin is recommended for use in children less than 20kg at the dose of 40mg/kg per day divided in 3doses every 8 hours for 5 to 10 days.

If no improvement in signs and symptoms after 1 to 2 days or there is frequent recurrence, that is, more than 4 episodes within 6 months, culture and sensitivity is recommended. If such services are not available, second line antibiotics such as cloxacillin or erythromycin antibiotics should be started.

Table 2.2: Treatment of URTIs according to the Namibia standard treatment guidelines and the WHO guidelines

CONDITION	WHO GUIDELINES		NAMIBIAN GUIDELINES
Acute Pharyngitis or Tonsillitis	Children	Benzathine benzyl penicillin children > 30 kg 1.2 million IU i.m in a single dose Children ≤ 30 kg 30000 IU/Kg (maximum 1.2 m IU) as a single dose OR Phenoxymethylpenicillin 10-20 mg/ kg; max 500 mg orally every 6 hours for 10 days. OR Amoxicillin 15 mg /kg; maximum 500 mg orally every 8 hours for 10 days Patients allergic to penicillin: Erythromycin 10-15 mg / kg ; every 6 Hrs max 500 mg for 10 days OR cefalexin 15 mg /kg ; max 500 mg every 6 – 8 hrs. For 10 days	Benzathine penicillin 0.6 million units stat OR Phenoxymethylpenicillin 250 mg/5 ml PO 6 hourly for 5 days Or Azithromycin 10 mg/kg daily for 3 days
	Adults	Adults > 30 kg 1.2 million IU in a single dose IM OR Phenoxymethylpenicillin 500 mg orally every 6 hours for 10 days OR Amoxicillin 500 mg t.d.s for 10 days **Patients allergic to Penicillins:** Erythromycin 500 mg every 6 Hrs for 10 days OR cefalexin 500 mg 6-8 Hrs for 10 days.	1.2 million units stat Or Phenoxymethylpenicillin 500 mg PO QID for 5 days Or Azithromycin 1 g daily for 3 days
Common cold		Antibiotics are not recommended	Antibiotics are not recommended
Acute otitis media	Children	Amoxicillin 40 mg/kg; every 12 hours For 7 -10 days (WHO. 2012) OR Sulfamethoxazole 400mg+ trimethoprim 80 mg (20mg/kg +4mg/kg; max 400mg +80mg) orally every 12 hours for 5 days Allergic to penicillin: cefuroxime 250-500 mg orally every 12 hours for 5 days (WHO, 2001: Model for prescribing)	Phenoxymethylpenicillin 25-50 mg /kg per day in 4 divided doses for 5 – 10 days OR Amoxicillin < 20 kg, 40 mg/kg per day in divided in 3 doses every 8 hours for 5 to 10 days. >20 kg, 250-500 mg every 8 hours for 5 to 10 days

Even though guidelines are available for the optimal management of these conditions, compliance is a problem and use vary from setting to setting. This is evident in the World Health Organization's rational use of medicines fact sheet of 2010 which states that, more than 50% of all countries do not implement the basic policies to encourage rational use of medications. Furthermore, less than 40% of patients in the public sector and 30% in the private sector are treated according to clinical guidelines in developing countries. Non compliance to clinical guidelines can include inadequate doses, inappropriate choice of antibiotic or incorrect duration of treatment. For example, a study was done in Brazil by Del Fiol, Lopes, Barberto-Filho & Motta (2013) to assess the prescription and use of antibiotics for Brazilian children. The researchers monitored the use of antibiotics in 160 children two Primary Health Centers by using questionnaires administered to parents and caregivers that assessed the social, demographic and clinical conditions of the children.The antibiotic use pattern was then ascertained in these children and compared to the recommendations of the Brazilian and international guidelines. The study results showed a great variability in the amoxicillin doses used for URTIs ranging from 8.2 to 91.9 mg/Kg/day. In addition, the doses used in most treatments were far below the doses recommended in the Brazilian and international guidelines (50% and 97%, respectively). It was therefore concluded that compliance to guidelines was very low leading to under dosing and therapeutic failures**.** Likewise, in a retrospective electronic medical record review for veterans presenting to 1 of 3 primary care, outpatient veterans affairs clinic in Portland between July 1st, 2008 and June 30th, 2009 for acute respiratory symptoms, Logan, Yang & Forrest (2012) reported that, 5.4% of patients received antibiotic prescriptions. Of those antibiotics, 87.8% were not indicated and did not comply to the reccommendations of symptomatic treatment .On the other hand , a fairly higher compliance to antibiotic guidelines was reported in Norway where a retrospective examination of patients records in nursing homes who were prescribed with antibiotics was done to determine to what degree the prescribing was in accordance with the national guidelines for antibiotic prescribing.This study showed that a total of 714 antibiotic courses were prescribed to 327 patients yielding a prevalence of 6.6%. Compliant prescribing was 77% for urinary tract infections (UTI), 79% for respiratory tract infections (RTI), and 76% for skin and soft tissue infections (SSTI). Ciprofloxacin was responsible for 63% of non-compliant prescribing. Even though compliant prescribing in this study was higher than the earlier mentioned studies, the authors still recommended the need to actively implement antibiotic guidelines with efforts aimed at improving antibiotic prescribing in both nursing home and hospital physician (Fagan , Mæhlen, Lindbæk& Berild,2012).

2.4 ANTIBIOTIC PRESCRIBING IN URTIS

A study conducted in Bangkok, to measure patterns and assesses appropriateness of antibiotic prescribing for viral and bacterial URTIs using data from registration books and prescriptions. This study revealed that 91% of the patients probably had viral URTIs and 60% of viral and 89% of bacterial URTIs were prescribed an antibiotic. Other study findings included low adherence to national treatment guidelines, that is 36.4% for treatment of viral infections and 1.7% for treatment of bacterial URTIs. Amoxicillin was the drug of choice regardless of the diagnosis (Suttajit, Wagner, Tantipidoke, Ross-Degnan & Sitthi-Amorn, 2005).

A similar rate of antibiotic prescribing was also noted in Japan by Fukuhara & Higashi (2009) in a cross-sectional analysis of insurance claims submitted to an employer-sponsored health insurance plan for diagnoses of URI in order to investigate the type and frequency of antibiotic prescribing for URI without apparent bacterial infection based on both visits and facilities. 2,577 claims (non-bacterial URI, one visit per claim) were analyzed in relation to visits; antibiotics were prescribed in 60% of these visits. The study also showed that prescribers not only over prescribed antibiotics, but also opted for more expensive and broader spectrum antibiotics. These were: third-generation cephalosporins, which were the most commonly prescribed drug class (46%), followed by macrolides (27%) and quinolones (16%). The study had limitations such as lack of data on physical findings and laboratory results that may have led to antibiotic prescribing and selecting the sample based on diagnoses provided on insurance claims, listed for billing purposes. In spite of these limitations, the authors concluded that overuse of antibiotics existed because the rate of antibiotic use that was observed markedly exceeded the prevalence of bacterial URI shown in epidemiologic reports.

The types of URTI as well as patient factors such as age and presenting symptoms are frequently associated with antibiotic prescribing. For instance, of the 30% rate of antibiotic prescribing for viral respiratory infections, Nadeem et al (2010) observed that, the highest prescribing rate was for viral bronchitis, followed by pharyngitis and the common cold. Similarly, in a study done by Senok, Ismaeel, Al-Qashar and Agab (2009), diagnosis of tonsillitis and otitis media as well as younger age were observed to be regularly associated with antibiotic prescribing among pediatricians, general practitioners and emergency room physicians**.** Furthermore, symptoms such as fever, sore throat and earache increased the likelihood of antibiotic prescribing. Similar findings were observed by Teng, Leong, Aljunid and Cheah (2004) in a survey of 150 general practice clinics in three urban areas in Malaysia, to document the antibiotic prescribing rate for URTIs in general practice and its associated factors using a structured data encounter form on which participating general practitioners were requested to record demographic and process care data for or each of the 30 consecutive adult patients seen.The results of the study showed an overall 68.4% rate of antibiotic prescribing of the encounters with URTIs of which a significant proportion of the antibiotic choice was irrational. In addition, antibiotics were prescribed in 67.2% of acute respiratory infection encounters and 90.7% of acute tonsillitis encounters. Furthermore, antibiotics were prescribed in the following symptoms: fever (72.7%), cough (68.9%), sore throat (78.8%), runny nose (65.5%), phlegm (66.7%) and hoarseness (66.7%).The study showed that fever and sore throat were significantly associated with antibiotic prescribing.

Antibiotic prescribing can also be influenced by a physician’s specialty. For example, a retrospective case review study of child care visits coded as viral respiratory infections in primary care provider's office, convenient care clinic, or emergency room showed that children who were seen in the emergency room and by primary health care providers were more likely to receive antibiotics for viral infections than those seen by pediatricians (Nadeem et al., 2010).

2.5 CONSEQUENCES OF IRRATIONAL ANTIBIOTIC PRESCRIBING

Irrational use of antibiotics and other medicines cause harm to patients and leads to wastage of resources. The following are the consequences of irrational use of antibiotics.

2.5.1 Antimicrobial resistance

Antimicrobial resistance (insensitivity) is the ability of a microorganism to prevent an antimicrobial for example from working against it. The use of an antibiotic for any infection, in any dose and over any period of time forces bacteria to either adapt or die in a phenomenon known as " selective pressure". The microbes that adapt and survive carry genes for resistance that can be transferred between individuals such that when an antibiotic is given, it only kills the sensitive bacteria but any resistant bacteria can survive and multiply. These microorganisms that are not killed are called antibiotic resistant. (Kirch, 2008). In other words, every time a person takes antibiotics, sensitive bacteria are killed, but resistant germs may be left to grow and multiply. Repeated and improper use of antibiotics are primary causes of the increase in drug-resistant bacteria. Therefore, decreasing inappropriate antibiotic use is the best way to control resistance (CDC, 2012).

Antibiotic resistance among common respiratory infection-producing bacteria such as *Streptococcus pneumoniae*, *Haemophilus influenzae* and *Moraxella catarrhalis* has become a major global public health problem. The use of antibiotics, whether or not medically justified for a particular illness, contributes to the development of these resistant bacteria (Jacobs, 2000). Teng, Leong, Aljunid and Cheah (2004) also stated that one of the main reasons that encourage the development of antibiotic resistance is the inappropriate use of antibiotics to treat viral URTIs. In addition, WHO (2013) states that, inappropriate use of antimicrobials often in inadequate dosage, for non-bacterial infections is one of the health hazards that lead to wastage of resources and encourage bacterial resistance. Furthermore, inappropriate antibiotic prophylaxis, errors in generic choice, route, dosing and duration of therapy or inappropriate combination therapy all contribute to this problem (Behera, 2010). Antibiotic resistance is a serious public health concern with economic and social implications in both developed and developing worlds, be it community acquired infections like *Streptococcal* infections, pneumonia, etc. or hospital acquired infections due to methicillin resistant *Staphylococcus aureus, etc.* These infections lead to higher rates of hospitalization, longer hospital stay, and increased cost of treatment and thus increased economic burden on the community (Behera, 2010). Overuse of antibiotics increases antimicrobial resistance and the number of medicines that are no longer effective against infectious disease. Many surgical procedures and cancer therapies are not possible without antibiotics to fight infection. In addition, antimicrobial resistance prolongs illnesses and hospital stays, and can even cause death, leading to costs of US$ 4–5 billion per year in the United States of America and €9 billion per year in Europe (WHO, 2010).

There are many factors that could be responsible for the increase in antibiotic resistance especially in developing countries. Some of which are: heavy burden of disease, huge populations, rapid spread of resistant bacteria through crowding and inappropriate use of available medicines. All this is further complicated by the availability of antibiotics on open markets sold without prescriptions and in most instances, antibiotics are given in inadequate amounts to treat serious infections due to poverty or lack of education. Overuse of abuse of antibiotics in clinical practice is also very common. Some of the reasons that influence abuse of antibiotics in clinical practice are patients' expectations and lack of uniformity among physicians to follow antibiotic policies (Behera, 2010).

Mechanism of resistance: Bacterial resistance can be natural, that is intrinsic to the microorganisms or it may be acquired. Acquired resistance can happen via "selective pressure" or mutation. Selective pressure occurs when use of an antibiotic for any infection, in any dose and over any period of time forces bacteria to either adapt or die. The microbes that adapt and survive carry genes for resistance that can be transferred between individuals (Kirch, 2008). Whereas as mutations occur spontaneously in bacteria which render them resistant to one antibiotic or another. Mutations lead to a change in a receptor or binding site, rendering the antibiotic ineffective. These changes are usually brought about by point mutations occurring at very low frequency on chromosomal DNA. Bacteria can also become resistant much more rapidly by acquiring the mutant resistance gene from another bacterium. This is known as transmissible antibiotic resistance which occurs mainly as a result of bacterial conjugation and is the cause of most of the current resistance problems. Fortunately several studies have shown that restricted use of certain antibiotics over several years can reverse resistance by selective pressure.

Antibiotic resistant bacteria are able to resist antibiotics through a diversity of ways. Some bacteria resist antibiotic action by denying it entry to the cell wall. For example, penicillin G is unable to penetrate the Gram negative cell wall. Other bacteria are naturally resistant to a particular antibiotic because they lack the target for its action, for example Mycoplasma do not posses peptidoglycan, the target for penicillin action. Bacteria may avoid action of an antibiotic by using or developing alternative biochemical pathways, so that its effect is cancelled out. Furthermore, many pathogens secrete enzymes that modify or degrade antibiotics, causing them to lose their activity, for example penicillins can be inactivated by enzymatic cleavage of their β-lactam ring. Similarly, cloramphenicol can be acetylated, while members of the aminoglycoside family can be acetylated, adenylated or phosphorylated, all leading to loss of antimicrobial activity (Hogg, 2005).

2.5.2 Wastage of resources

Improper use of medicines raises the cost of health services and increases the burden of chronic diseases. For example, the WHO (2010) documents that between 10–40% of national health budgets is spent on medicines and if medicines are not prescribed and used properly, billions of dollars of public and personal funds are wasted.

Aside from the obvious wastage of resources that occurs when medicines are used irrationally, treating viral URTIs with antibiotics with broad-spectrum antibiotics instead of the narrow spectrum antibiotics, further contributing to wastage of resources by increasing the overall price, since broad-spectrum antibiotics are more often than not more expensive than narrow spectrum antibiotics.

Studies have shown that patients with acute uncomplicated sinusitis when treated with broad-spectrum antimicrobial agents do not have better clinical outcomes than those treated with first line antibiotics. In other words, clinical outcomes are the same despite the class of antibiotic used, but the cost is higher in those treated with second line antibiotics (Piccirillo, Mager, Frisse, Brophy & Goggin, 2001). Despite the lack of superiority over first line antibiotics in terms of therapeutic benefits in the treatment of bacterial URTIs, broad spectrum antibiotic prescribing is a common occurrence in the management of acute respiratory tract infections. Steinman, Landefeld and Gonzales (2003) noted that broad-spectrum antibiotics such as quinolones, amoxicillin /clavulanic acid, second and third line cephalosporins, azithromycin and clarithromycin, were prescribed in 63% of patients with URTIs ranging from 46% of patients with the common cold to 69% of patients with acute sinusitis. Broad-spectrum antibiotics were chosen in 51% of patients with a common cold, 53% with acute sinusitis, 62% with acute bronchitis and 65% with acute otitis media.

A cross sectional study to examine the use and cost of the nonindicated treatment regimens of antibiotics for nonspecific upper respiratory tract infections (URIs) in a Medicaid population in the USA by Mainous & Hueston (1998) found that 23% of the total cost was for the unnecessary use of antibiotics and on average, the antibiotic cost for each episode of care was US$9. 91. In addition, the estimated cost of antibiotics for URTIs in a year for the Kentucky Medicaid program was US$1. 62 million. According to Pestotnik, Classen, Evans, & Burke (1996), antimicrobial agents is one of the costliest drug categories in hospital expenditures, accounting for approximately 20% to 50% of the total spending on drugs in the USA. The financial burden that is associated with antibiotic resistance has been observed to be significant. For example, it has been estimated that treating patients with antimicrobial resistance annually costs US$4000–5000 million in the USA and €9000 million in Europe (Holloway & Van Dijk, 2011). Therefore, reducing unnecessary prescribing of antibiotics can reduce on the cost of care and put to proper use the scarce health resources.

2.5.3 Side effects

Harmful reactions to medicines caused by incorrect use, or allergic reactions to medicines can lead to increased illness, suffering and death. Adverse drug reactions have been estimated to cost millions of dollars each year (WHO 2010).

Several side effects may occur from over consumption or inappropriate consumption of antibiotics. For instance, a risk of adverse gastrointestinal effects may be caused by antibiotics overuse (Irshaid, et al., 2004). According to Schroeder & Fahey (2002), drowsiness, diarrhea and hyperactivity are also significant side effects related to antibiotic use in children. These adverse effects are more significant in children. Side effects can also lead to poor adherence to medication which can further increase the risk of antibiotic resistance. A study by Arrol & Kenealy (2013) also showed that adults who were given antibiotics for common cold had a significantly greater risk of developing adverse effects that those treated with placebo.

2.5.4 Eroded patient Confidence

Exacerbated by the overuse of limited medicines, drugs may be often out of stock or become unaffordable, which could result in eroded patient confidence. Poor or negative health outcomes due to inappropriate use of medicines may also reduce patient confidence in the health care services (WHO, 2010).

2.6 SUMMARY

This chapter provided an overview of antibiotic prescribing in upper respiratory infections. It included a description of URTIs that were studied in terms of epidemiology, signs and symptoms and causative organisms, described the recommended treatments, that is both the Namibia standard treatment guidelines and the WHO recommendations, provided an overview of antibiotic prescribing in URTIs, the factors that lead to antibiotic overuse as well as the problems associated with inappropriate antibiotic prescribing. The following chapter will outline the design and research methodology of the study that was employed to attain the objectives of this study.

CHAPTER 3

RESEARCH METHODOLOGY

3.1 INTRODUCTION

The previous chapter focused on the literature review of the study. Chapter 3 will describe in detail the research methodology that was used to meet the study objectives. This chapter describes a descriptive, cross sectional quantitative study design, the population, sample size, research instruments, data collection methods, data analysis and ethical considerations that were applied in this study.

The purpose of this study was to describe antibiotic prescribing in patients with URTIs at Katutura Health Centre (KHC). This was attained through the steps delineated in this chapter.

3.2 RESEARCH DESIGN

A research design is a set of logical steps taken by the researcher to meet the purpose of the study. The design chosen should be the most appropriate to maximize the validity of the research findings (Van der Walt & Van Rensburg, 2011). In this study a quantitative, cross-sectional, descriptive, design was used to achieve the purpose of the study.

A descriptive study design is used in studies where more information is required in a particular field through the provision of the picture of the phenomenon as it occurs. This design only describes the phenomenon with no intention of establishing a cause – effect relationship (Van der Walt & Van Rensburg, 2006). In addition, descriptive studies answer basic questions about what is happening in a defined population or situation (Houser, 2012). These study designs can either be qualitative or quantitative. Since quantity was used to measure the phenomenon under study, a quantitative approach was used. Kumar (2008), states that quantitative research is based on the measurement of quantity or amount and is applicable to phenomena that can be expressed in numeric form.

This study design was appropriate because little is known about the use of antibiotics in URTIs at KHC and in Namibia and therefore, numeric data were collected to understand this phenomenon.

The data collection was done from May 2013 to July 2013 assessing the prevalence of antibiotic prescribing in URTIs, qualifying the study to be cross-sectional. Cross - sectional studies observe a sample population at a nominal point in time (Robertson & Williams, 2009). In other words, these studies basically are "snapshots" of the population status with respect to disease or exposure variables or both at a specific point in time mostly assessing disease prevalence (Rothman, 2002).

3.3 RESEARCH METHODS

3.3.1 Study setting

The study was conducted at KHC which is a public primary health care institution situated in Katutura, Windhoek. The health centre serves a population of more than 200, 000 people of the Katutura catchment area. It is currently staffed with 8 general practitioners, 30 nurses (enrolled and registered nurses), one pharmacist and 6 pharmacist assistants and other health workers.

The clinic is segmented into sections such as the parameter rooms or waiting area, radiography room, observation room, pediatric treatment room (where both nurses and doctors are assigned), doctors consulting rooms, nurses consulting rooms for adults, nurses dispensary room, main pharmacy, ART clinic, nurse dispensary and other rooms offering antennal, family planning, immunization, HIV counselling and testing services etcetra.

Upon arrival, patients are first registered in the outpatient register at the reception and pay a fee of N$ 8 (first consultation) or N$ 4 (follow-up consultation). These fees cover all services from consultation, diagnostics, pharmacy and so on. Those who are unable to pay still get their needed service.

From the reception, patients are sent to areas designated for parameters (blood pressure, temperature, weight etc.).

Adults have their parameters done before being sent to the nurse or doctor consultation in the parameter area designated for adults while pediatrics parameters are done by an assigned nurse in the pediatric area. After which Paediatric patients are seen by either nurses or a doctor to whom nurses refer some of their patients. After consultation, all patients treated by GPs collect their medications from the main pharmacy (children and adults), while those treated by nurses collect their medicines from nurses. That is, pediatrics seen by nurses receive their medication from the pediatric room, dispensed by each consulting nurse, while adult patients treated by nurses collect their medications from the nurse's dispensary room where a nurse is assigned on a daily basis to dispense medicine. During this study, nurses were requested to send patients with a diagnosis of an URTI to the main pharmacy so that data on antibiotic prescribing could also be collected from prescriptions by nurses that met the inclusion criteria.

3.3.2 Study population

A study population is a subset of the population with the characteristics of interest defined by the eligibility criteria. It is from this population that the sample to be studied is drawn (Friedman, Furberg & Demets, 2010). The study population comprised of all prescriptions of patients diagnosed with URTI, specifically diagnosed with the common cold, pharyngitis, tonsillitis and pharyngitis and tonsillitis at KHC in 2013. It is from this population that the sample was drawn. According to Health Information system (HIS), that is data from the outpatient department monthly report for June 2011, the number of URTI seen is as follows: patients under 5 years: nose and throat disease (=288), common cold (=219); for patients aged 5-17 years: nose and throat disease (=89), common cold (=115) and for patients aged 18 and over: nose/throat disorder (=314) and the common cold (=394). With an average of 1000 URTI cases per month, the total for 2013 was estimated to N = 12,000.

3.3.3 Sample size

Since it is usually not feasible to study a whole population, a sample of the population is drawn that is statistically representative of the population so that from the results based on the sample, inference to the population can be made.

By definition, a sample is a part or a fraction of a whole, or a subset of a larger set selected by the researcher to participate in a research study. It consists of a selected group of elements or units of analysis of a defined population (Van der Walt & Van Rensburg, 2006). The sample comprised of prescriptions of patients diagnosed with URTIs that met the eligibility criteria. The appropriate sample size was calculated as follows:

n = $z^2_{(1-\alpha/2)} \times p(p-1) \div d^2$ (Antonisamy, Christopher & Samuel 2010)

Where:

The value of $Z_{(1\text{-}\alpha/2)}$ is taken from the standard normal distribution table, *p* is the expected prevalence or proportion and *d* is the precision.

- For a confidence interval of 95%, the Z-value is 1.96

- Expected proportion (p). This is the proportion the investigator aims to estimate by doing the study. In many cases, this can be derived either from previous studies or by doing a pilot study. It is also suggested that if there was doubt about the value of 'p', it is best to err towards 50% as it would lead to a larger sample size.

- Precision (d), the level of precision, sometimes called sampling error, is the range in which the true value of the population is estimated to be. This range is often expressed in percentage points, (e.g., ± 5%). At the end of the study, the prevalence is presented with its 95% confidence interval. For example, if the prevalence is 20% and 95% CL is 10% to 30%. It means that the study has estimated the population prevalence is between 10% and 30%. The precision (d) for this estimate is 10% (i.e. 20% ±10%=10%-30%). It shows that the width of the confidence interval is two times the precision (cl=2d).

$$Sample\ size\ (n) = \frac{1.96^2 \times (0.5) \times (1 - 0.5)}{0.05^2} = 384.16$$

Therefore the calculated sample size was 385.

3.3.4 Sampling

Sampling is a process of selecting units from a population of interest so that by studying the sample, the results may be generalized to the population from which they were selected (Willium & Trochim, 2006). This is done because studying the entire population would be time consuming, costly and the population may be too large and widespread (Van der Walt & Van Rensburg, 2006). Therefore, a convenience sampling method was used to select 385 prescriptions of patients. Convenient sampling is a process of selecting subjects to be included in the study based on the ease of availability and meeting the eligibility criteria (Schuster & Powers, 2005). The study was conducted from the 18th of May 2013 to the 24th of July 2013. Accordingly, prescriptions of all patients that were seen at KHC during this period and met the eligibility criteria were consecutively enrolled into the study until the calculated sample size was reached on the 24th of July 2013 and enrollment officially closed. For this study, prescriptions of patients of all ages that met the eligibility criteria were included in the study. The pilot study revealed that practitioners sometimes wrote two diagnoses. This made it difficult to judge the basis upon which antibiotics were prescribed. Inaddtion, patients seen with a recurrent or non resolving URTI are more likely to have antibiotics prescribed. Based on these, the following inclusion criteria were applied.

Inclusion criteria

1. Patients with only a single diagnosis from the following list: common cold, pharyngitis, tonsillitis, pharyngitis, pharyngitis & tonsillities (pharyngeotonsillities), AOM and URTI.
2. Newly diagnosed acute infections. All diagnoses were considered acute unless specified as chronic.

Only prescriptions of patients diagnosed with an URTI were to be included in the study. In addition, the study also assessed the total number of medicines prescribed per prescription for patients seen at KHC. Hence, the following exclusion criteria were applied.

Exclusion criteria

1. Prescriptions with a chronic or recurrent diagnosis of the conditions under study.
2. Prescriptions having a diagnosis other than those under study.
3. Prescriptions from other facilities apart from Katutura Health Centre.

3.5 DATA COLLECTION TOOL

Data collection tools or instruments comprise of the actual physical devices employed to collect the information that is under investigation. (Boswell & Cannon, 2011)

The survey tool of the MoHSS of Namibia titled, “assessing impact of the comprehensive standard treatment guidelines on outpatients prescribing practices in public health facilities in Namibia”, was used as a guide to develop the data extraction form for this study. The data extraction form was developed to obtain the desired data elements from prescriptions.

The following was the process followed in developing the data extraction form:

1. Considering the objectives of the study, the researcher designed the tool into sections ensuring that the variables were relevant to the study.
2. Peer review: the tool was given to research supervisors and colleagues for review to ensure face validity. Face validity is the extent to which the tool appears to be addressing the variables or concepts of interest (Sim & Wright, 2000).
3. Piloting of the tool

The form had four sections. Section one comprised of patient demographic information such as date of birth, age and gender. The second section consisted of the diagnosis, the third section included the treatment of the diagnosed condition, i.e. antibiotics prescribed, dose, frequency, duration of treatment and quantity dispensed, compliance to the STG as well as the total number of antibiotics prescribed. In addition, data on other medicines prescribed and quantities dispensed was collected under the same section. Lastly, the fourth section gave an indication of the prescribers’ rank or position.

In this study, the term antibiotic meant antibiotics prescribed for all patients with URTIs by GPs or nurses during the study. The URTIs which were purposely selected for this study were non-specific URTIs, the common cold, pharyngitis, tonsillitis and AOM. The section on compliance focused on assessing the conformity of URTIs to the NSTGs (2011) and the WHO (2001) guidelines in respect to the choice of antibiotic (if recommended), dose, and frequency and treatment duration. Prescriptions that were in conformity to the guidelines in all the aspects were considered rational and vice versa. According to WHO (2013), rational treatment refers to patients receiving medications appropriate to their clinical needs (right drug), in doses that meet their own individual requirements, for an adequate period of time, and at the lowest cost to them and their community. In this study, rational prescribing meant the right choice of antibiotic, right dose, right frequency and right treatment duration as prescribed by both the NSTGs and WHO guidelines.

In all the mentioned sections of the data collection tool, data was collected on both categorical and numeric variables. The variables of interest were:

i. **Categorical dichotomous variables measured on a nominal scale**: Gender (female or male), age (adult and child), antibiotic prescribed, treatment compliance to guidelines and prescriber rank.

ii. **Categorical polychromous variable measured on a nominal scale**: Diagnosis (common cold, pharyngitis, tonsillitis, pharyngitis and tonsillitis, AOM and URTIs) and names of antibiotic prescribed.

iii. **Continuous variables**: Age in year and months.

iv. **Discrete Variables**: number of antibiotics prescribed and number of medicines prescribed

3.6 PILOT OF THE DATA EXTRACTION FORM

The instrument was piloted prior to the beginning of the actual data collection. A pilot study involves a few members of the population from which the study is to be drawn (Sim & Wright, 2000). Its purpose is to try out the research approach in order to identify potential problems that may affect the quality and validity of the results (Blessings & Chakrabarti, 2009). These potential problems with the tool could be ambiguity, poor wording, missing items, inappropriate response options and unclear instructions, ensuring content validity.

Data collection was conducted at KHC from the 6th of May 2013 to the 10th of May 2013.Using an inclusion criteria and a convenience sampling approach, the researcher collected data from 30 prescriptions (a sample size used in the collection of PMIS data for the indicator HF13). Data was collected on patient age and gender, diagnosis, treatment of the condition (whether antibiotic were prescribed or not), names of antibiotics prescribed, compliance with guidelines, the number of antibiotics prescribed, other medicines prescribed, total number of medicines prescribed, quantity dispensed of antibiotics and profession rank or position of prescribers. The prescriptions that were used for the pilot study were not included in the actual study, which commenced on the 18th of May 2013.

During the pilot study, it was noticed that some prescribers made two diagnoses of URTIs, for instance, diagnosis such as URTI & tonsillitis were observed , making it difficult to judge the basis upon which antibiotics were prescribed.This led to redefining the inclusion criteria so that only prescriptions of patients with only a single diagnosis from the following list: common cold, pharyngitis, tonsillitis, pharyngitis, pharyngitis & tonsillitis(pharyngotonsillitis) , AOM and URTI, were included in the study. Furthermore, the reference of judging whether a prescription was rational or not was revisited. Rationality of treatment was initially supposed to be based on the Namibian Treatment guidelines for all the conditions. Unfortunately, it was noticed during the pilot study that dosing for treatment of pharyngitis & tonsillitis is not given according to weight in children. Therefore, in order to obtain meaningful results on the rationality of treating pharyngitis or tonsillitis, the WHO guidelines were also used to access rationality of this condition. That is, the prescriptions that were found to be irrational according to NSTGs based on the dose and duration of treatment were further assessed for rationality with the WHO guideline. Rationality for treating the other conditions was assessed using the Namibian standard treatment guides.

Results from the study were used to finalize the tool, ensuring that only data that was relevant to the study was collected.

The research assistant was also trained and observed when collecting the data to ensure consistency in data collection based on the inclusion and exclusion criteria

3.7 DATA COLLECTION

Data collection is the process of gathering and measuring information on variables of interest, in an established systematic fashion that enables one to answer stated research questions, test hypotheses, and evaluate outcomes (Krishnamurthi, Cabrera, & Karlovsky, 2004).

The actual data collection only commenced after obtaining approval from the University of Namibia (UNAM) research review committee and MoHSS. In addition, the tool was piloted and the research assistant was trained before starting the collection of data.

For this study, a data extraction form (Annexure C) was used to collect the desired data from patients' prescriptions (Health passports). In order to ensure confidentiality and anonymity of both the prescribers and the patients, their names were not recorded on the extraction form. Instead, all data extraction forms were allocated an identification number from 1 to 385 and only the prescriber's profession was recorded.

Data was collected on patient age and gender, diagnosis, treatment of the condition (whether antibiotic were prescribed or not), names of antibiotics prescribed, compliance with guidelines, the number of antibiotics prescribed, other medicines prescribed, total number of medicines prescribed, quantity dispensed of antibiotics and profession rank or position of prescribers. The inclusion criteria were used to select prescriptions to include in the study. Based on the inclusion criteria, data was collected using a convenience sampling method until the sample size of 385 was reached. The data collection was done from KHC main pharmacy by the researcher and one assistant on every working day of the week from the 18th of May 2013 to the 24th of July 2013. At the end of each data collection day, the researcher checked all the filled forms for completeness and also assessed treatment appropriateness, after which the section on treatment appropriateness/ rationality was filled. All the filled forms were kept by the researcher and all the data elements on the extraction form were entered on Epi info version 7.1.1.14 for analysis. Entering of data on the analysis package was executed at the terminal of each data collection day.

3.8 STRATEGIES TO ENSURE VALIDITY AND RELIABILITY OF THE DATA EXTRACTION FORM.

Validity and reliability are important aspects of data collection methods and tools used in research. Having a valid and reliable tool affords credibility to the instrument and subsequent research (Moule & Goodman, 2009). Reliability is a part of validity in that an instrument that does not yield reliable results cannot be considered valid (Van der Walt & Van Rensburg, 2006).

3.8.1 Validity

Instrument Validity seeks to ascertain whether an instrument accurately measures what it is supposed to measure, given the context in which it is applied. (Van der Walt & Van Rensburg, 2006). Two types of validity were considered, that is, content validity and face validity. Content validity is an assessment of how well an instrument represents all the components of the variables to be measured (Van der Walt & Van Rensburg, 2006).This was ensured by having the tool reviewed by the research supervisors and statistician and by conducting a pilot study. After which the content of the instrument was refined to contain only variables of interest. Face validity refers to the extent to which the tool appears to be addressing the variables or concepts of interest (Sim & Wright, 2000). To ensure face validity, the tool was reviewed by peers, research supervisors a

3.8.2 Reliability

Reliability is the degree to which the instrument can be depended upon to yield consistent results if used over time on the same person or by two researchers (Van der Walt & Van Rensburg, 2006). This was ensured by conducting a pilot study that led to refining the inclusion and exclusion criterion. The research assistant was also trained on how to extract the data using the inclusion and exclusion criteria. Furthermore, the researcher ensured reliability of the data collected by observing the research assistant collect data during the pilot study so as to address any inconsistencies in the data collection.

To ensure data quality, the researcher checked all data forms for completeness at the end of each day during the data collection period**.**

3.9 DATA ANALYSIS

Data analysis is a process of categorising, ordering, manipulating, summarising data and describing them in meaningful terms (Van der Walt & Van Rensburg, 2006). Data was analysed with the help of a statistician using Epi info version 7.1.1.14 SPSS version 22.0.

Frequency distributions of all variables were generated to organise and identify errors of data entry like missing data. Descriptive and inferential statistics were used to summarise the findings of the study.

Descriptive statistics represent a set of methods and activities that permit description of a given body of data, without making inferences to the larger population. It enables researchers to represent vast amounts of data in ways that permit the reader or user of results to obtain relatively quickly an informative summary. This summary includes methods that accomplish (a) various graphical displays providing insights to the researcher and user, and (b) numerical data descriptions via summary indexes (Raykov & Marcoulides, 2013). In this study, descriptive statistics were then used to summarise the variables of interest. Percentages were used to summarise the variables: patient demographics, the rate of antibiotic prescribing, the proportions of the different diagnosis of URTIs, compliance to STG, the proportions of the choices of antibiotics prescribed, the proportions of other medicines prescribed (the different types) and the proportion of prescriptions by nurses and GPs as well as the cost of antibiotic prescribed.

In addition bar charts were also used to summarise and present patient demographics, the rate of antibiotic prescribing for the different diagnoses of URTIs, compliance to treatment guidelines and the names of antibiotics prescribed. Pie charts were used to present the rate of antibiotic prescribing and as well as to summarise and display the proportions of the different diagnoses of URTIs. Frequency distributions were also used to summarise antibiotic prescribing by profession and to summarise the quantities and cost of antibiotics. The presentation of results using bar and pie charts was done using Microsoft office excel 2010. The mean and its SD (Standard deviation) were used to summarise the average number of antibiotics per prescription and the average number of medicines per prescription. A SD is a mathematical tool which helps to assess how far the values are spread above and below the mean. A high standard deviation shows that the data is widely spread (less reliable) and a low standard deviation shows that the data are clustered closely around the mean (more reliable). In addition, SD can also be used to help decide whether the difference between two means is likely to be significant (does it support the hypothesis?), that is, if the 2 SD is smaller than the difference between the two means, then the hypothesis is supported (“standard deviation part II, n.d”).

Inferential statistics help investigators to understand the relationship between two or more variables. These statistics, called measures of association, allow the researcher to quantify the existence, strength and direction of association of the relationship (Healey, 2010). For this purpose, the chi-square test is used to determine whether or not two variables measured on a nominal scale or categorical scales are associated (Colman & Pulford, 2011). In this study, cross tabulations of antibiotics prescribing as a response variable, with variables such as age (grouped into an ordered category: children = ≤ 15 years and adults = > 15 years), diagnosis, profession and gender, as explanatory (exposure variable), were done to determine the existence and strength of association using the chi-square statistical test. The two tailed t-test was also used to determine if the difference of the two means (i.e. mean of total number of antibiotics per prescription and total numbers of medicines per prescription of GPS and nurses) was statistically significant. To determine the significance of these tests, the p values of the test were compared to a predetermined benchmark known as the significant level or alpha level, which is $\alpha = 0.05$. If the p – value is less than α ($p < \alpha$), then the result is considered statistically significant (Levine-Wissing & Thie, 2006). The confidence interval was also used to make inference to the population, for example to make inference about the rate of antibiotic prescribing. The confidence interval for a point estimate is the range of values that are consistent with that estimate. Confidence intervals are used to indicate the precision of descriptive results such as proportions or means, or analytic results such as risk ratios and risk differences. The wider the confidence interval, the less precise is the point estimate

(Browner, 2006). Schen –Chung & Jen Pei (2004) also describe confidence interval as the degree of certainty that the interval actually contains the unknown population parameter. It provides the assurance or confidence that the statement regarding the population parameter is correct.

The rationality of prescriptions for patients with URTIs was assessed using the NSTG (2011) and the WHO recommendations. The illnesses that were assessed were the common cold, pharyngitis, tonsillitis and AOM. The rationality of prescriptions for patients with pharyngitis and tonsillitis was assessed using NSTG (2011) and due to some limitations in this guideline, WHO recommendations were also used in order to get meaningful results. Prescriptions that were compliant to the treatment guidelines in terms of the choice of antibiotic, the dose, the frequency and the duration of treatment were considered rational. Those that did not meet the one or more of the mentioned conditions were considered irrational.

The quantities of each antibiotic prescribed for all the URTIs were summed and stratified by compliance to STG. The quantities dispensed of each antibiotic stratified by rationality, were used to calculate the cost of both irrational and rational antibiotic prescribing using the prices from the Central Medical Stores (CMS) of Namibia. Quantities for each antibiotic were converted to a unit pack and the cost calculated by multiplying the cost per unit as per CMS pricing and the unit packs that was dispensed. The cost of rational and irrational antibiotic prescribing was summarised using counts and presented in a table.

3.10 SUMMARY

Chapter 3 presented the research methodology that was used to achieve the objectives of the study. The following were described: the population, sampling, the sample size, the development of the data extraction form, piloting of the data extraction form, the strategies to ensure validity and reliability of the data extraction form, the data collection process and data analysis. Chapter 4 will concentrate on the presentation and discussion of the research findings.

CHAPTER 4

PRESENTATION OF THE RESEARCH FINDINGS AND DISCUSSION

4.1 INTRODUCTION

Chapter 3 focussed on describing the research methodology that was used to meet the objectives of this study. Chapter 4 presents the study findings and discussion of these findings. Both descriptive statistics and statistical analyses for significance of association are used to present the findings. Descriptive statistics, that is, percentages, bar charts and pie charts will be used to summarize the study findings on the following variables: patient demographics, the rate of antibiotic prescribing in URTIs, the proportions of the types of URTIs, types of antibiotics and compliance to treatment guidelines. The mean will be used to summarize the total antibiotics prescribed and total medicines prescribed. Percentages are all rounded off to the nearest whole number except for percentages of other medicines prescribed which are rounded off to one decimal point. The Pearson chi-square test (X^2) will be used to present the significance of the association between antibiotics prescribing (response variable) with variables such as age (grouped into ordered category: children = ≤ 15 years and adults > 15 years), diagnosis, profession and gender, as explanatory (exposure variable). The two tailed t-test will also use to present the statistical significance of two means. That is the mean of total number of antibiotics per prescription and mean of total numbers of medicines per prescription of GPS and nurses. For both the chi-square and two tailed t-test, a p – value less than the predetermined α level (α =0. 05) was considered to be statistically significant. In addition, a confidence interval of 95% will be used to make statistical inferences of the sample to the population.

4.2 COVERAGE RATE

The coverage rate for this study was 100%. Only prescriptions that met the inclusion criteria and had the entire required variable indicated on the data collection tool were used to collect data and were analysed.

4.3 PATIENTS' DEMOGRAPHICS

4.3.1 Gender

Figure 4.1 Distribution of patients with URTIs according to gender (n=385)

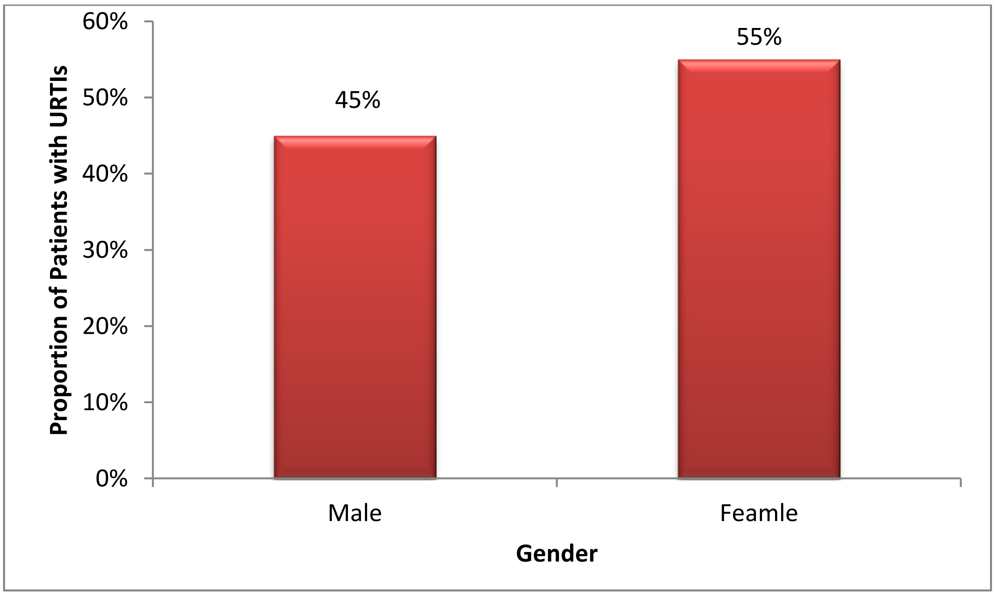


Figure 4.1 shows the distribution of patients' according to gender whose prescriptions were included in this study. 172 (45%) prescriptions were for male patients and 213 (55%) prescriptions were for female patients. This distribution shows that diagnosis of URTIs was made more in female than in male during the study period.

4.3.2 Age

Figure 4.2 Age distribution of patients with URTIs (n=385)

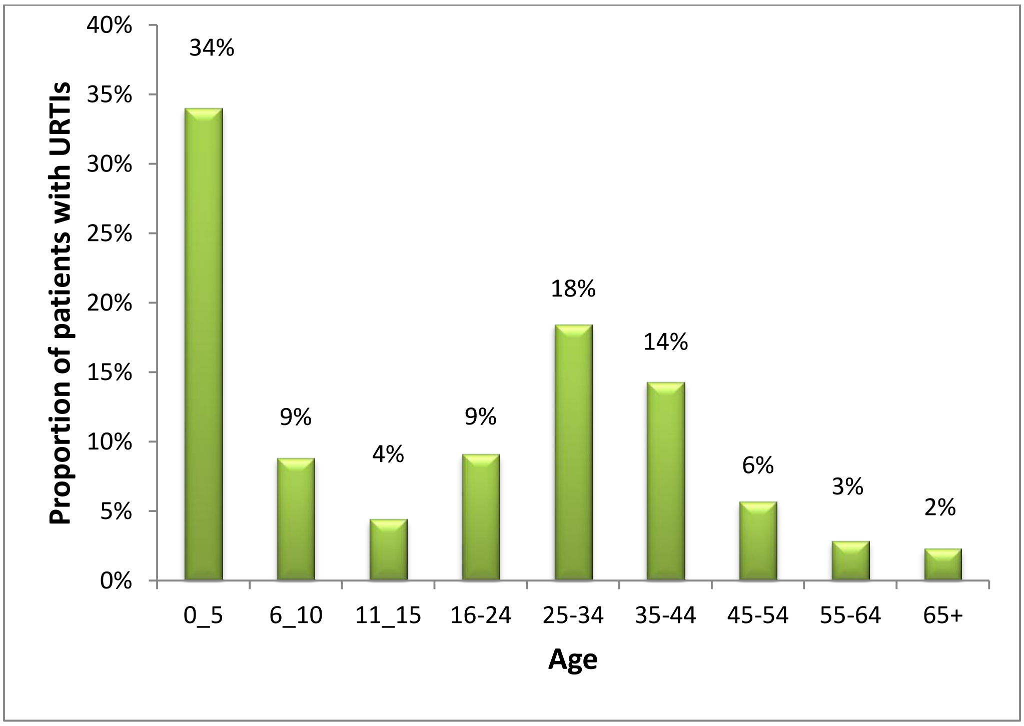


Figure 4.2 above shows the patients' age distribution. The sample was largely comprised of patients aged 5 and below, that is 131 (34%) patients. Patients aged 65 and above were only 9 (2%), making this age category the least of the sample. The

proportions of patients reduced with increasing age group, that is, from age group 25-34: 71 (18%) to the aged 65 and above: 9 (2%).

4.3.3 Sex and Age Group

Figure 4.3 Sex and Age group distributions of patients with URTIs (n=385)

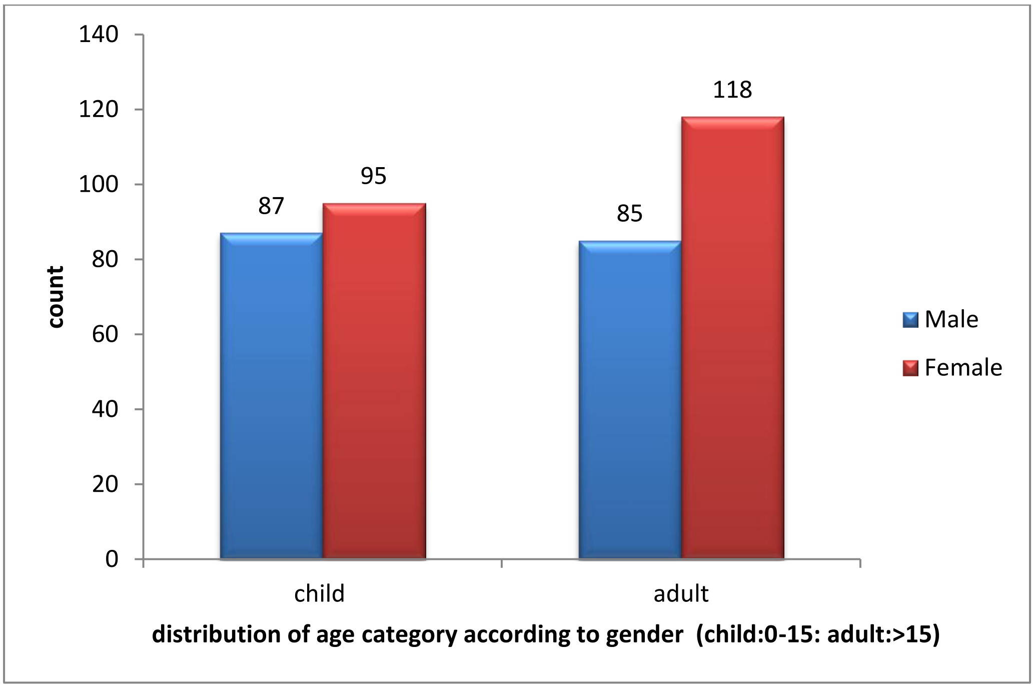


Figure 4.3 above shows that the study sample consisted of more adults than children. That is 203 (53%) adults and 182 (47%) children. It was also observed that in both age categories, there were more female than male. That is, the female adults were 188 (49%) while male adults were 95 (25%) female children were 95 (25%) while male children were 87 (23%).

4.4 ANTIBIOTIC PRESCRIBING IN URTIs

4.4.1 Proportion of patients with URTIs

Figure 4.4 Distribution of types of URTIs diagnoses (n=385)

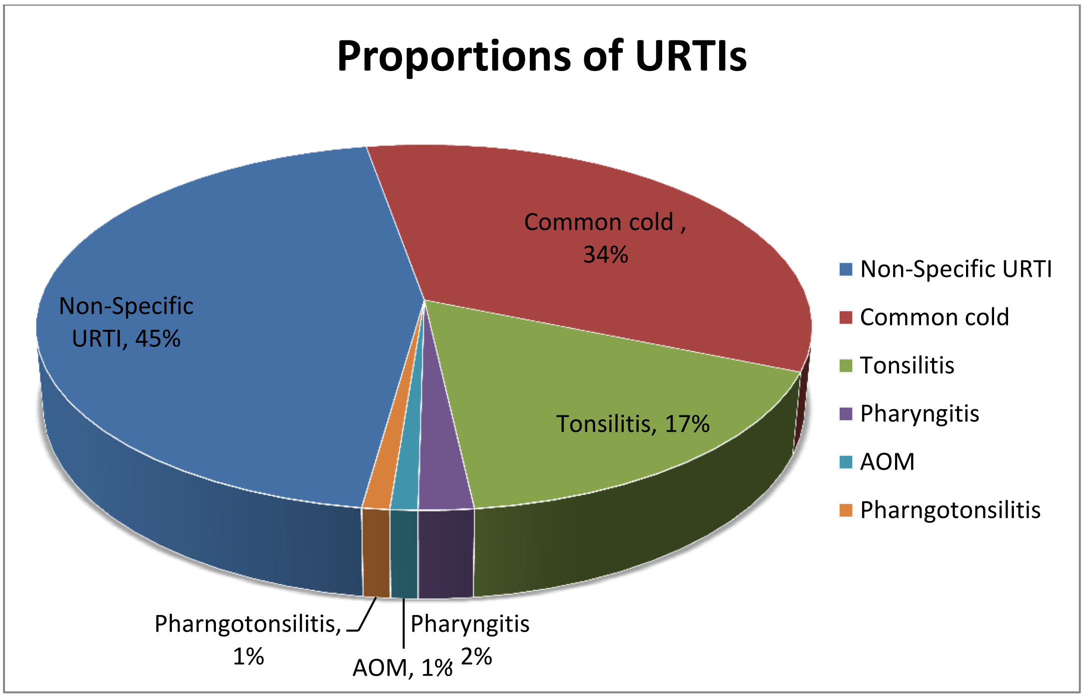
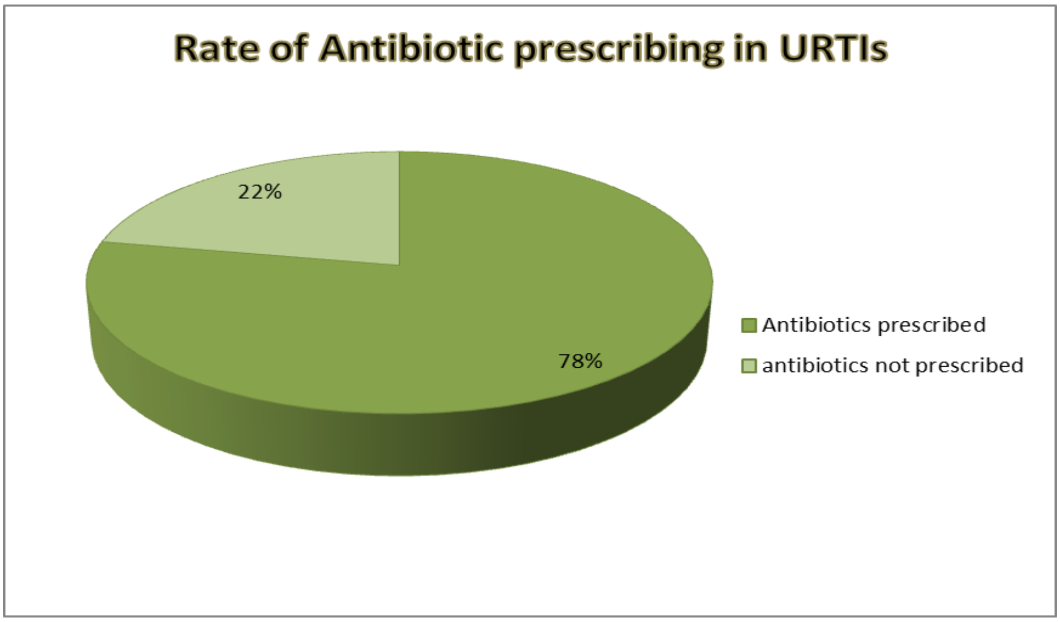


Figure 4.4 above shows the distribution of cases, according to illness. The most common diagnosis was non-specific URTI 174 (45%) followed by the common cold 130 (34%), then tonsillitis 67 (17%), pharyngitis 9 (2%), AOM 4 (1%) and pharyngitis & tonsillitis 4 (1%).

4.4. 2 Rate of antibiotic prescribing in URTIs

Figure 4.5 Antibiotic prescribing in URTIs (n=385)



Out of 385 prescriptions, 302 had an antibiotic/s which resulted in a 78% (95% CI 74%, 82%) rate of antibiotic prescribing in patients with URTIs in this study.

The rate of antibiotic prescribing in patients with URTIs at KHC is notably high. This is a matter of great concern because these infections are viral in 80% of the cases and do not respond to antibiotic therapy (Mazur 2010). The result of this study is similar to other research findings that showed that antibiotics are over prescribed for URTIs in many countries. For example, in Eritrea, it was confirmed that 75% of the adults and children diagnosed with URTI were prescribed antibiotics (WHO, 2004) and in Malaysia, the rate of antibiotic prescribing for URTIs was 64.8% (Kho, Ong, Tan and Wee, 2013). Antibiotic over prescribing has also been reported in some European countries were three times the amounts of antibiotics are used compared to other countries with similar disease profile. In developing and transitional countries, while only 70% of pneumonia cases receive an appropriate antibiotic, about half of all acute viral upper respiratory tract infections and viral diarrhea cases receive antibiotics inappropriately (WHO medicines report, 2011). This shows that antibiotic over prescribing is a global problem, of which Namibia is not an exception.

Antibiotic over prescribing entails an increase in cost, side effects and the emergence and spread of resistant bacteria. These bacteria become resistant to affordable and effective first line antibiotics, a situation that is worsened by the fact that, the development of new generations of antibiotics is not promising (Ivanovoska & Holloway, 2013). Gonzales et al. (2001), suggested that unnecessary adverse effects of antibiotics and the evolution of antimicrobial resistance can be reduced by judicious use of these drugs.

There are many reasons that lead to antibiotic over prescribing. For example, health care providers cite diagnostic uncertainty (uncertainty whether an illness is viral or bacterial), time pressure, patient demand and expectations as the primary reasons why antibiotics are over-prescribed (Hicks, 2010). Though patient expectations and demands are one of the reasons that antibiotics are over prescribed, Macfarlane et al. (2002) noted that, even though 75% of patients with URTIs who seek medical attention expect to receive antibiotics, patient satisfaction with an office visit is independent of a patient's initial belief about antibiotics and whether antibiotics were prescribed. Satisfaction is more closely related to whether health care providers addressed patients’ concerns (as cited in Mossad, 2010).

Some of the proven ways that help reduce antibiotic prescribing in PHC are patient education and the strategy of delayed antibiotic prescribing. Farquha (2002) reported that patient education through providing leaflets that describes the nature and expected course of their illness and discloses the uncertainty of benefit from treatment with antibiotics appears to reduce the rate of antibiotic use in primary practice without increasing the number of adverse outcomes. Delaying antibiotic use by giving the patient a prescription and instructing them only to have it filled if symptoms do not resolve is also an effective means of reducing antibiotic use for acute respiratory infections (Arroll, Keanely & Kerse, 2003).

4.4.3 Antibiotic prescribing by age group

Table 4.1 Antibiotic prescribing by age group

		Children			Adults		
		Frequency	Percent	95% CI	Frequency	Percent	95% CI
Antibiotic prescribed	Yes	163	90%	84%-94%	139	68%	62% -75%
	No	19	10%	6% -16%	64	32%	25-38%
Total		182	100%		203	100%	

According to table 4.1 above, the rate of antibiotic prescribing in children was 90% (95% CI 84, 94%) while antibiotic prescribing in adults was 68% (95% CI 62%, 75%). Further statistical analysis using the chi-square test of antibiotics prescribing (response variable) and age group (exposure variable) showed that children were more likely to receive an antibiotic prescription than adults, X^2=27. 073, p =0. 000. In other words, young age (children) influenced antibiotic prescribing.

Other studies have shown similar prescribing patterns by age. For example, a study by Kho, Ong, Tan and Wee (2013) also showed that prescribers are significantly influenced by age when prescribing antibiotics for URTIs and this is, more in children than adults. A study by Stone, Gonzales, Maselli & Lowenstein (2000) also demonstrated that patients younger than 18 years were less probable to receive antibiotics than adults. Contrary to the findings of this study which showed an increase in the rate of antibiotic prescribing with increasing age among children (< 5 years =70%, 6-10 years = 20% and 11-15 = 10%), a study in the United States showed antibiotics were more often prescribed to children aged 5- 11 years than those below the age of 5 (Nyquist, Gonzalez, Stelner & Sande, 1998). Though there are varying rates of antibiotic prescribing by age, prescribers most frequently prescribe antibiotics for children than adults.

4.4.4 Antibiotic prescribing by patient gender

Table 4.2 Antibiotic prescribing in URTIs stratified by gender

		Male			Female		
		Frequency	Percent	95% CI	Frequency	Percent	95% CI
Antibiotic prescribed	YES	134	78%	71%-84%	168	79%	73%-84%
	NO	22	22%	16% -29%	45	21%	16% -27%
Total		156	100%		213	100%	

Table 4.2 above shows that the rate of antibiotic prescribing in male patients was 78 % (95% CI 71, 84%) and that for female patients was 79% (95% CI 73, 84%). Further statistical analysis using the chi-square test, of antibiotics prescribing

(response variable) and gender (exposure variable) showed that there was no significant relationship between gender and antibiotic prescribing, X^2=0. 53 and p=0. 819. This implies that the prescription of antibiotics was independent of whether the patient is male or female or that gender did not influence antibiotic prescribing. This result is similar to the findings by Teng et al. (2004) which showed that, antibiotic prescribing did not differ by gender (males 70.4%, females 66.2%, X^2=1. 902, p=0. 168)

4.4.5 Antibiotic prescribing in the different types of URTIs

Figure 4.6 Distribution of antibiotic prescribing according to types of URTIs

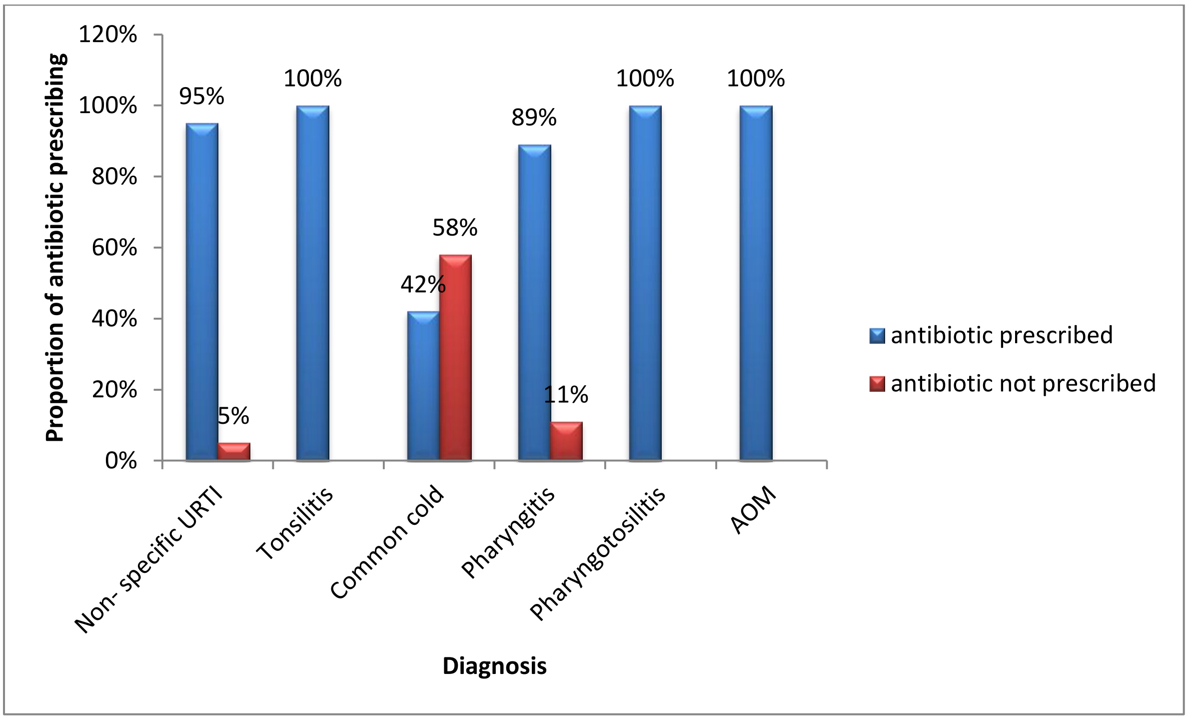


Figure 4.6 above shows that, for each specific diagnosis the rate of antibiotic prescribing was: 169 (95% CI 90%, 98%) for non-specific URTIs, 67 (100%; CI 100%, 100%) for tonsillitis, 55 (42% CI 34%, 51%) for the common cold,

8 (89%; CI 52%, 100%) for pharyngitis, 4 (100%; CI 100% -, 100%) for pharyngotonsillitis and 4 (100%; CI 100%, 100%) for AOM.

This study also showed a significant relationship (X^2=143. 790, p =0. 000) between illness and antibiotic prescribing.

These results are similar to the study by Kho, Ong, Tan and wee (2013) that revealed that prescribers are more likely to prescribe antibiotics for patients diagnosed with tonsillitis and pharyngitis (97% and 95 % respectively). In addition, they also reported a 61.3% rate of antibiotic prescribing in patients with URTIs.

The results of this study also showed that 374 (97%) patients received one antibiotic and 11 (3.5%) had two antibiotics prescribed. All the patients that received two antibiotics were diagnosed with tonsillitis. That is, 7 (64%) received benzathine penicillin injection and phenoxymethylpenicillin, 2 (18%) received ceftriaxone injection and phenoxymethylpenicillin, 1 (9%) received azithromycin and benzathine injection and 1 (9%) patient received ceftriaxone injection and azithromycin.

4.4.5.1 Antibiotic prescribing for the common cold

About 42% (95% CI 34%, 51%) of patients with the common cold were prescribed an antibiotic. This rate is a cause for concern because antibiotics have no role in the treatment of the common cold. The result of this study is higher than that of Paraidathathu, Li & Siang (2012) in Malaysia, where the rate of antibiotic prescribing for common cold was 18.5%. Kho, Ong, Tan and wee (2013), also reported a much lower rate of 3.9%. This suggests that compared to the mentioned studies, the results of this study suggest that the problem of antibiotic prescribing for the common cold could be worse in Namibia.

It is well known that the common cold is caused by viruses and studies have also shown that prescribing antibiotics for common cold does not benefit patients (adults and children) in any way but could increase the risk of developing side effects, especially in adults. In addition, antibiotics do not warrant better outcome in terms of cure or persistence of symptoms in patients that receive antibiotics compared to those that do not (Arrol & Keanely, 2013). Unfortunately, the practice of antibiotic prescribing for common cold has continued and is often an attempt to meet patient's expectations (Fischer, Fisher, and Kocher & Hummers-Pradier, 2005). Some of the other reasons that fuels this irrational use of antibiotics are: health care providers' unfounded beliefs in the effectiveness of antibiotics and believe that antibiotics could prevent complications of common cold even though they know that the common cold is a viral infection that is self-limiting (Cho , Hong & Park, 2004), physicians perceived parental expectations (Ciofi et al., 2006), unrealistic patient expectations, patient pressure to prescribe antibiotics and insufficient time to educate patients about the effectiveness of antibiotics (Macfarlane, Holmes, Macfarlane & Britten, 1997).

4.4.5.2 Antibiotic prescribing for non- specific URTI

URTI was a common diagnosis 174 (45%). URTI is a nonspecific term used to describe acute infections involving the nose, paranasal sinuses, pharynx, larynx, trachea, and bronchi. The prototype is the illness known as the common cold (Mossad, 2010) with symptoms that last up to 10-14 days (CDC, 2012). Non-specific URTI is typically an acute viral infection and as already mentioned, it can also involve lower airway symptoms, which are frequently present, but are not prominent (Gonzales et al., 2001). In this study, 95% (95% CI 90%, 98%) of the patients with a diagnosis of a non- specific URTI had an antibiotic prescribed, that is, 60% adults and 50% children. A study by Teng et al (2004) showed a result comparable to the one of this study, that is, antibiotics were prescribed for 68.4% (95 %CI 65.4%, 71.4%) diagnosed to be URTI whereas Gill, et al. (2006), reported a lower rate of 33%. Teng et al. (2004) also noted that antibiotics were more commonly prescribed in patients with a URTI diagnosis than those without URTI (68.4% versus 20.5%, c2=707. 36, $p<0.001$). All these results show that, although viruses cause most URTIs, antibiotics continue to be widely and inappropriately prescribed in many places. In Namibia, this problem could be fuelled by the lack of specifications in the treatment guidelines on how to manage nonspecific URTIs and whether antibiotics should be prescribed in non-specific URTIs. This gap in the guidelines could have attributed to the high rate of antibiotic prescribing, especially in adults (60%). Other guidelines like the CDC do not recommend antibiotic prescribing in non-specific URTIs because antibiotics neither enhance illness resolution nor prevent complications (CDC, 2012).

4.4.5.3 Antibiotic prescribing for AOM

All patients (2 children aged < 5 years and 2 adults) that were diagnosed with AOM received antibiotics. The proportion of patients diagnosed with AOM was too small (1%) to make a meaningful conclusion about antibiotic prescribing in AOM among patients with URTIs at KHC. However, the result shows that all patients 4 (100%; CI 100%, 00%) with AOM were treated with an antibiotic in conformity with NSTG that recommend antibiotic therapy in the management of AOM. The recommended antibiotics are amoxicillin in adults and children and phenoxymethylpenicillin in children. However, the guideline does not give an alternative choice of antibiotic in patients allergic to penicillin. WHO (2001) also recommends amoxicillin, cotrimoxazole and cefuroxime as in penicillin allergic patients. AOM can be caused by viral or bacterial infection. Bacterial infection with the common respiratory pathogens (*Streptococcus pneumoniae*, *Haemophilus influenza*, and *Moraxella catarrhalis*) is often preceded by a viral infection. Viruses (especially respiratory syncytial virus and influenza) can cause AOM without confection with bacteria (Morris & Leach, 2009). This means that since the NSTGs only gives antibiotic therapy as first line, this could be promoting irrational antibiotic prescribing in some of the cases that are viral. According to the CDC guidelines (2012) AOM does not always require antibiotic therapy, but observation is an acceptable option in, for example, cases of healthy children with mild symptoms. This option is appropriate only when follow-up can be ensured and antibacterial agents started if symptoms persist or worsen. Symptoms of mild illness include mild otalgia and fever < 39°C in the past 24 hours. Severe illness is moderate to severe otalgia or fever > 39°C. Antibiotics are recommended in all children younger than six months, in those between six months and two years if the diagnosis is certain, and in children with severe infection. A certain diagnosis of AOM meets the following 3 criteria: rapid onset, signs of middle ear effusion and signs and symptoms of middle-ear inflammation.

4.4.5.4 Acute pharyngitis or tonsillitis (sore throat)

About 8 (89%; CI 52%, 100%) of patients with pharyngitis, 67 (100%; CI, 100%-100%) with tonsillitis and 4 (100%; CI, 100%-100%) with pharyngotonsillitis had an antibiotic/s prescribed. The Namibia standard treatment guidelines (2011), recommend antibiotic therapy and analgesics for patients with tonsillitis/ pharyngitis or both. This could explain the high rate of antibiotic prescribing in these conditions. The other explanation being that, even though a definition and cause (viral or bacterial) of these infections is given in the guideline, there is no clear guideline of identifying and managing the infections that could be viral.

This study also showed that only 1 (11 %) patient with pharyngitis did not receive antibiotics. This result could mean that, since pharyngitis can also be a viral infection, a bacterial pharyngitis could have been unlikely.

Acute pharyngitis is caused GABHS in only 5-15% of adults. The large majority of adults have a self-limiting illness which can be managed supportively (CDC, 2012). In this study, antibiotics were prescribed in 96% of adults with pharyngitis/ tonsillitis (27 out of 28 adults with pharyngitis / tonsillitis). This indicates that prescribers assume bacterial infections in the majority of adults, which is contrary to the fact that most adults with acute pharyngitis or tonsillitis have a viral infection which is self-limiting. In addition, only 15% of pharyngitis is caused by GABHS and most of them are viral in children. Furthermore, this result shows a practice of antibiotic over prescribing in these illnesses, is a problem that needs to be addressed through prescriber and patient education on the epidemiology of bacterial pharyngitis or tonsillitis as well as the risks associated with antibiotic over prescribing.

In order to promote rational antibiotic prescribing in adult patients, the CDC (2012) recommends that antibiotic prescribing be limited to those patients with the highest likelihood of GABHS using clinical decision criteria: screening of all adults with pharyngitis for the presence of 4 centor criteria. That is, history of fever, tonsillar exudates, no cough and tender anterior cervical lymphadenopathy. Then only testing and treating of patients with two or more of the criteria. These patients should be tested using a rapid antigen test and antibiotic therapy limited to patients with a positive test. Treating of patients with none or only one of these criteria is not recommended because these patients are unlikely to have a bacterial infection. The WHO (2001) also states that the presence of the three major signs: fever >38^{o}C, intense pharyngeal pain and absence of rhinitis and cough has a high positive-predictive value of streptococcal pharyngitis. When these three signs are not all present, streptococcal etiology is unlikely. In the Namibia standard treatment guidelines, the stepwise recommendations by CDC help prescribers reduce on the prescribing of antibiotic prescribing in patients with acute tonsillitis or pharyngitis are not clearly documented. Though antigen test and cultures are important in deciding whether to treat acute pharyngitis infections with antibiotics, routine laboratory tests are expensive in places that are resource constrained in terms of finances and human resource. In addition, the streptococcal antigen test is known to be expensive and have relatively high specificity and low sensitivity rates, which makes it unlikely to be used in most countries (WHO 1995). Therefore, since treatment of streptococcal pharyngitis is known to prevent the development of acute rheumatic fever and rheumatic carditis especially in low and middle income countries where rheumatic heart disease is still a major public health problem and is the leading cause of cardiovascular morbidity and mortality in children and young adults (Rimoin, et al., 2005). Therefore, clinical decision rules using selected signs and symptoms have been recommended to help prescribers to suspect GABHS and treat with antibiotics in the absence of microbiological data, thereby reducing routine antibiotic therapy for all pharyngitis. The selected clinical signs and symptoms are exudative pharyngitis or tonsillitis and tender anterior cervical lymph nodes (WHO, 1995). Even though this clinical decision rule helps in reducing routine antibiotic prescribing in pharyngitis and tonsillitis, studies have shown that this decision rule has a high specificity but low sensitivity and misses most children (91.5-100%) with streptococcal sore throat. Therefore, this clinical decision rule should probably not be used to guide individual treatment or policy in countries with a relatively high incidence of rheumatic diseases after streptococcal infection (Rimoin, et al., 2005). In children, treatment with antibiotics is recommended only if an antigen test with rapid Strep kits or culture is positive, confirming negative antigen tests with culture. Treatment with antibiotics pending culture results is not recommended and if started, antibiotics should be stopped when culture is negative.

Further analysis of the relationship between illness and rate of antibiotic prescribing showed a significant association (X^2 =143. 790, p = 0.000). In other words, illness had a significant influence on the prescriber's decision to prescribe an antibiotic.

4.4.6 The rate of antibiotic prescribing according to profession or rank

Table 4.3 Distribution of the rate of antibiotic prescribing according to profession or rank

		Antibiotics prescribed				Total
		No	Percent	Yes	Percent	
Profession	GP	55	66%	185	61%	240
	Nurse	28	34%	117	39%	145
Total		83	100%	302	100%	385

Table 4.3 above, shows that 185 (61 %) antibiotic prescriptions were by GPs and 117 (39 %) by nurses. Although GPs prescribed antibiotics for a greater number of patients than nurses, analysis with the chi –square test of, antibiotic prescribing (response variable) and profession rank (exposure variable), showed that the difference was not statistically significant (X^2=0.695, p =0.404). However, since the knowledge and skills that GPs have acquired is more advanced than that of nurses, it is expected that GPs prescribe more rationally than nurses, especially that there are hardly any in service training or trainings on rational use of antibiotics in URTIs that could help improve the knowledge and skills for nurses as well. This logic is evident in a study by Kho, Ong, Tan and Wee (2013) which showed that medical assistants (MAs) were more likely to prescribe antibiotics compared to Medical Officers (MOs).

4.4.7 Number of antibiotics per prescription

Table 4.4 Antibiotics per prescription (n=385)

Total number of prescriptions with an antibiotic/s	Total number of antibiotics	Average number of antibiotics per prescription	Standard Deviation	Minimum number of antibiotics per prescription	Maximum number of antibiotics per prescription
302	312	0.81	0.460	0	2

Table 4.4 above, shows that the total number of antibiotics for the entire sample (n=385) was 312 and on average each prescription contained 0.81 antibiotics

(SD = ±0.460).

Table 4.5 Distribution of prescriptions containing an antibiotic/s by prescriber rank/ position

Position/ rank	Total number of prescriptions with an antibiotic/s	Total number of antibiotics	Average number of antibiotics per prescription	Standard Deviation	Minimum number of antibiotics per prescription	Maximum number of antibiotics per prescription
GP	185	190	0.79	0.463	1	2
Nurse	117	122	0.84	0.455	1	2

According to table 4.5 above, prescriptions by both GPs and nurses had 1 to 2 antibiotics. The average number of antibiotics per prescription for GPs was 0.79 (SD = ± 0.463). The average for nurses was 0. 84 (SD = ± 0.455). The assumption was that GPs prescribe fewer antibiotics than nurses since they have acquired more knowledge and skills. This assumption was not supported because the difference between the means is 0.05 (0.84-0.79). In addition, the two t- test analysis, showed no statistical significance (t = - 1.028, p=0.305) of the difference between the two means. Therefore, there was no difference in the number of antibiotics prescribed by GPs and nurses.

4.4.8 Names of Antibiotics prescribed

Figure 4.7 Distribution of antibiotics prescribed

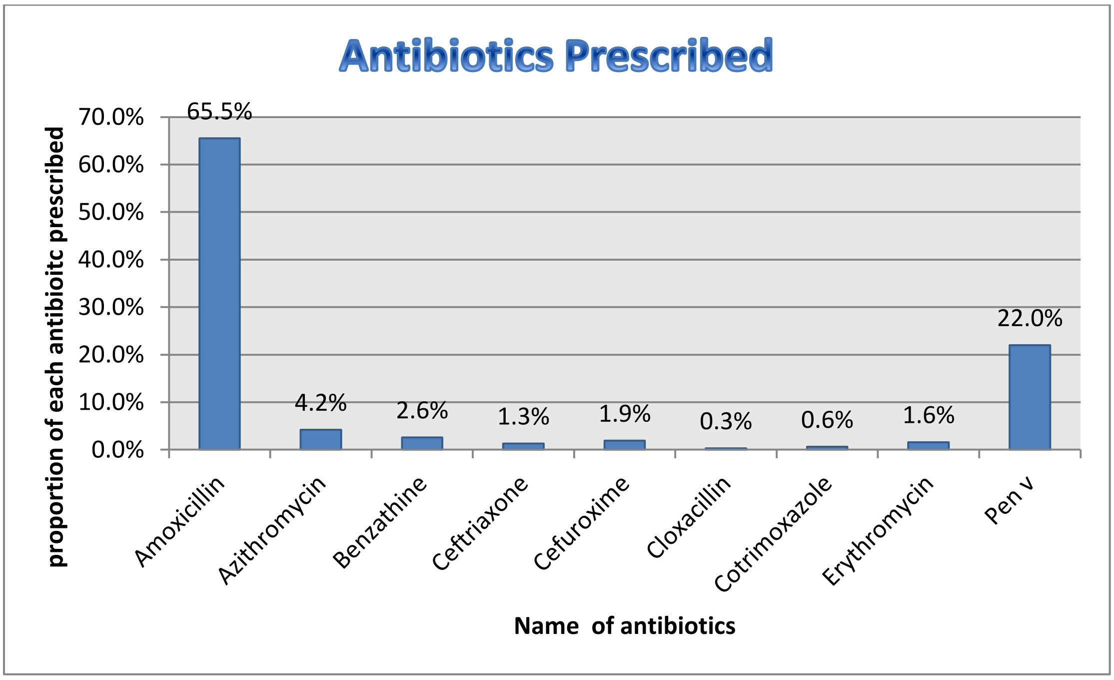


Figure 4.7 above, presents the types of antibiotics that were prescribed in all cases of URTIs. The most prescribed were beta lactam antibiotics, amoxicillin (65.5%) being the most prescribed, followed by phenoxymethylpenicillin (22.0%), benzathine penicillin (2.6%) and cloxacillin (0.3%). Macrolides were also prescribed. That is, azithromycin (4.2%) and erythromycin (1.6%). This result shows that penicillins

were mostly prescribed which are the recommended first line antibiotics of choice in the treatment of bacterial URTIs (NSTG, 2011). The macrolides, azithromycin and erythromycin are recommended in penicillin allergic patients. Unfortunately, the nature of this study could not determine whether these macrolides were really prescribed for patients allergic to penicillins. Broad spectrum, second line antibiotics were also prescribed. These are cephalosporins (3.2%); cefuroxime (1.9%) which is a second generation cephalosporin and ceftriaxone (1.6%) which is a third generation cephalosporin. The use of first line antibiotics in the treatment of URTIs at KHC is a commendable practice because the use of broad-spectrum antibiotics instead of the narrow spectrum antibiotics, further contributes to wastage of resources because broad-spectrum antibiotics are generally more expensive than narrow spectrum antibiotics. Furthermore, studies have shown that using broad spectrum antibiotics in the treatment of URTIs, for example, acute uncomplicated sinusitis does not have better clinical outcomes, but the cost is higher in those treated with second line antibiotics (Piccirillo, Mager, Frisse, Brophy & Goggin, 2001). On the other hand, the prescribing of cephalosporins in these infections is worrisome because of the risk of developing antibiotic resistance of these antibiotics that are important in treating serious bacterial infections that may not respond to first line antibiotics, besides the obvious wastage of resources. Cotrimoxazole, a combination of a sulphonamide, sulfamethoxazloe and trimethoprim was also prescribed in 0.6% of the patients.

4.4.9 Other medicines prescribed

Table 4.6 Distribution of other medicines prescribed

Other medicines prescribed		
	Frequency	**Percentage**
Paracetamol	320	39.50%
Multivitamins	146	18.00%
Chlorphenamine	135	16.60%
Ascorbic Acid	94	11.60%
Ibuprofen	29	3.60%
Paracetamol+ codeine	23	2.80%
Normal saline drops	21	2.60%
Methyl salicylate ointment	21	2.60%
Promethazine	8	1.00%
Indomethacin	3	0.40%
ORS	3	0.40%
Oxymetazoline eye drops	3	0.40%
Folic +ferrous sulphate	1	0.10%
Calcium gluconate	1	0.10%
Thiamine	1	0.10%
Diclofenac injection	1	0.10%
Chlorhexidine mouth wash	1	0.10%
Total	811	100.00%

Table 4.6 above, shows the distribution of medicines, other than antibiotics, that were prescribed in this study. The most frequently prescribed medicine was paracetamol (39.5 %), followed by multivitamins (18.0%), chlorphenamine (16.6%),

ascorbic acid (11.60%), ibuprofen (3.6%), paracetamol+ codeine (2.8%), nasal decongestants, that is normal saline drops (2.6%) and methyl salicylate ointment (2.6%). Other medicines were: promethazine (1.0%), indomethacin (0.6%), oral rehydration salts (0.4%), oxymetazoline eye drops (0.4%), calcium gluconate (0.1%), ferrous + folic acid (0.1%), thiamine (0.1%), diclofenac injection (0.1%) and chlorhexidine mouth wash (0.1%).

The most prescribed analgesic was paracetamol (39.5% %) followed by ibuprofen (3.6%), and diclofenac injection (0.1%). The antihistamines that were prescribed were chlorphenamine (16.6%) and promethazine (1%). Vitamins were commonly prescribed with multivitamins being the most frequently prescribed vitamins (18%) followed by ascorbic acid (11.6 %) and thiamine (0.1%).

The main emphasis on the management of URTIs is symptomatic relief of fever, headache, malaise, nasal congestion and cough. The medicines that are used for this purpose are: antipyretics (paracetamol), first generation antihistamines, nasal decongestants (normal saline drops, pseudoephedrine) and nonsteroidal anti-inflammatory drugs (NSAIDs) like ibuprofen (Cotton, Innes, Jaspan, Madide & Rabie, 2008). Cough and cold preparations include antitussives and expectorants but their role in the treatment of URTIs remains controversial

(Mossad, 2010).Common constituents of these medications include first generation antihistamines, antipyretics or anti-inflammatory agents cough suppressants such as dextromethorphan, expectorants (guaifenesin) and decongestants such as pseudoephedrine and phenylpropanolamine (Cotton, et al. ,2008). In Namibia, these cough and cold preparations are not available in the state but in private. However, for symptomatic relief, analgesics such as paracetamol, antihistamines, saline drops, and adrenergic agonists such as oxymetazoline nasal spray, chlorhexidine and ascorbic acid are recommended and available in state facilities (NSTG, 2011). It is worth noting that, the role of vitamin C for the treatment of URTIs remains controversial after many decades and numerous studies. Large doses of vitamin C are necessary to achieve its beneficial effect as an antioxidant in activated leukocytes. However, doses in excess of 4 g per day have been associated with diarrhea. The average benefit in studies using 2 to 4 g per day of vitamin C has been a decrement of about half a day (15%) in the duration of illness (Douglas & Hemilä, 2005).

4.4.10 Number of medicines per prescription

Table 4.7 Number of Medicines Per prescription (n = 385)

Total number of prescriptions	Total number of medicines prescribed	Average number of medicines per prescription	Standard Deviation	Minimum number of medicines per prescription	Maximum number of medicines per prescription
385	1114	2.89	0.69	1	5

Table 4.7 above shows the number of medicines prescribed in this study. A total of 1114 medicines were prescribed and on average, each prescription contained 2.89 medicines (SD=0.69). Similar studies showed an average number of medicines per prescription of 2.15 (Ahuja & Nandimath, 2012) and 3.0 (Khairnar & Patil, 2013).

Table 4.8 Distribution of the number of medicines per prescription by prescriber's profession

Profession	Total number of prescriptions	Proportion of prescriptions (%)	Total number of medicines	Proportions of the number of medicines (%)	Average number of medicines/ prescription	SD	Min number of medicines/ prescription	Max number of medicines/ prescription
GP	239	62%	713	64%	2.98	0.67	1	5
Nurse	146	38%	401	36%	2.75	0.68	2	5
Total	385	100%	1114	100%	-	-	-	-

Table 4.8 above, shows the distribution of the number of medicines per prescription according to the profession of the prescribers. The total number of medicines prescribed were 1114, of which 713 (64%) were by GPs and 401 (36%) by nurses. This difference could be attributed to the difference in the number of prescriptions of GPs and nurses. The results show that 239 (62%) of prescriptions were by GPs and 146 (38%) by nurses. There were more prescriptions by GPS in the study because all prescriptions by GPs are dispensed at the pharmacy, while those by nurses are dispensed by nurses at the nurses' dispensary and screening rooms. For the purpose of this study, nurses were asked to send all patients diagnosed with URTIs to the pharmacy. As the results show, it is possible that not all these patients were sent to the pharmacy. As shown in table 4.7 the average number of medicines per prescription for GPs was 2.98 (SD = ± 0.67) and that for nurses was 2.75 (SD = ± 0.68). Further analysis using the statistical two tailed t- test for the analysis of the significance of the difference of two means showed a statistical significance

(t =3.35, p = 0.001). Therefore, according to this test of significance, GPs prescribed more medicines per prescriptions than nurses.

According to the results presented in Table 4.6 (mean = 2.89) and Table 4.7 (means: GP = 2.98 & nurses 2.75), the number of medicines per prescription in this study did not meet the WHO recommendation of 2.0 medicines per prescription. These results show a practice of polypharmacy in patients with URTIs. Polypharmacy is the use of multiple medications to treat a patient (Kramer, 2000), which indicates irrational prescribing practices which may lead to drug related problems such as adverse drug reactions and unnecessary drug expenses (Saurav, Sushil, Sushil & Nepal, 2009).

4.5 Rational prescribing in URTIs

Figure 4.8 Proportions of rational treatment of URTIs according to STGs (n=214)

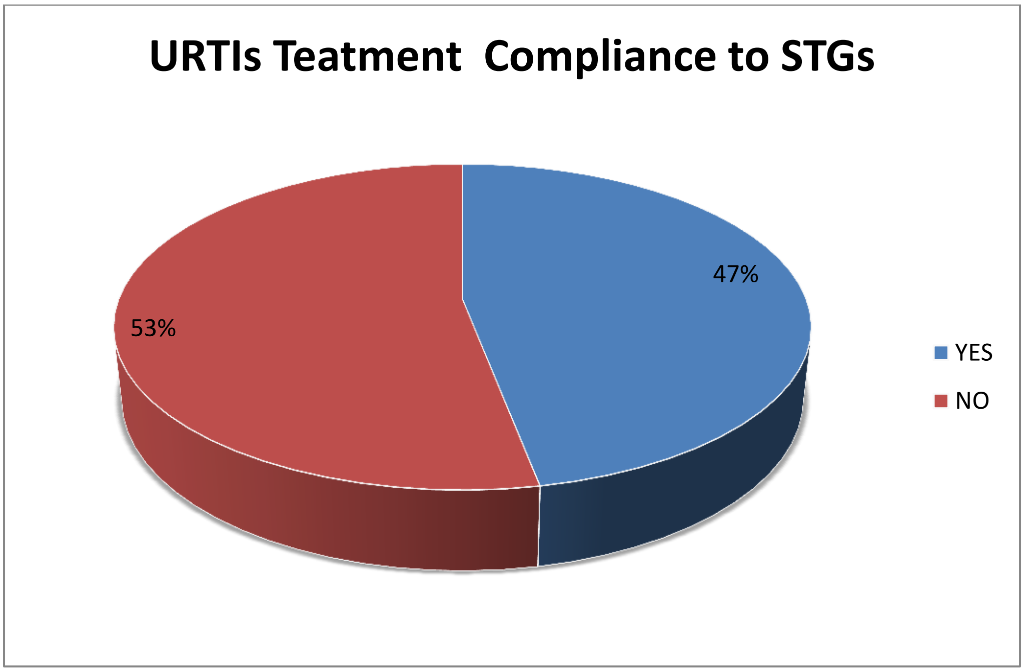


Figure 4. 8 above, shows the proportions of antibiotic prescriptions that were compliant to STGs or rational and those that were not compliant to STGs or

irrational. 101(47%) of the prescriptions were compliant to the STGs and therefore were considered rational and 113 (53%) were irrational.

Compliance to STGs was 47% (95% CI 40%, 54%). This result is similar to those of other studies, for example, a study in the United States showed a 57% overall adherence to guidelines for pharyngitis, URI, and acute sinusitis (Crocker, et al., 2013).

Standard treatment guidelines are systematically developed statements to help practitioners or prescribers to make decisions about appropriate treatments for specific clinical conditions. (Managing drug supplies as cited in Walley & Wright, 2010). Failure to prescribe according to clinical guidelines is one of the problems associated with the irrational use of medicines. Low adherence to clinical guidelines is a worldwide problem, for example, the proportion of patients treated according to clinical guidelines in developing countries for common diseases in primary care is less than 40% in the public sector and 30% in the private sector. Furthermore, only 50 to 70% of people with pneumonia are treated with appropriate antibiotics, yet up to 60% of people with viral upper respiratory tract infection receive antibiotics inappropriately (WHO, 2010).

Figure 4.9 Proportions of rational treatment of URTIs according to STGs by illness or condition

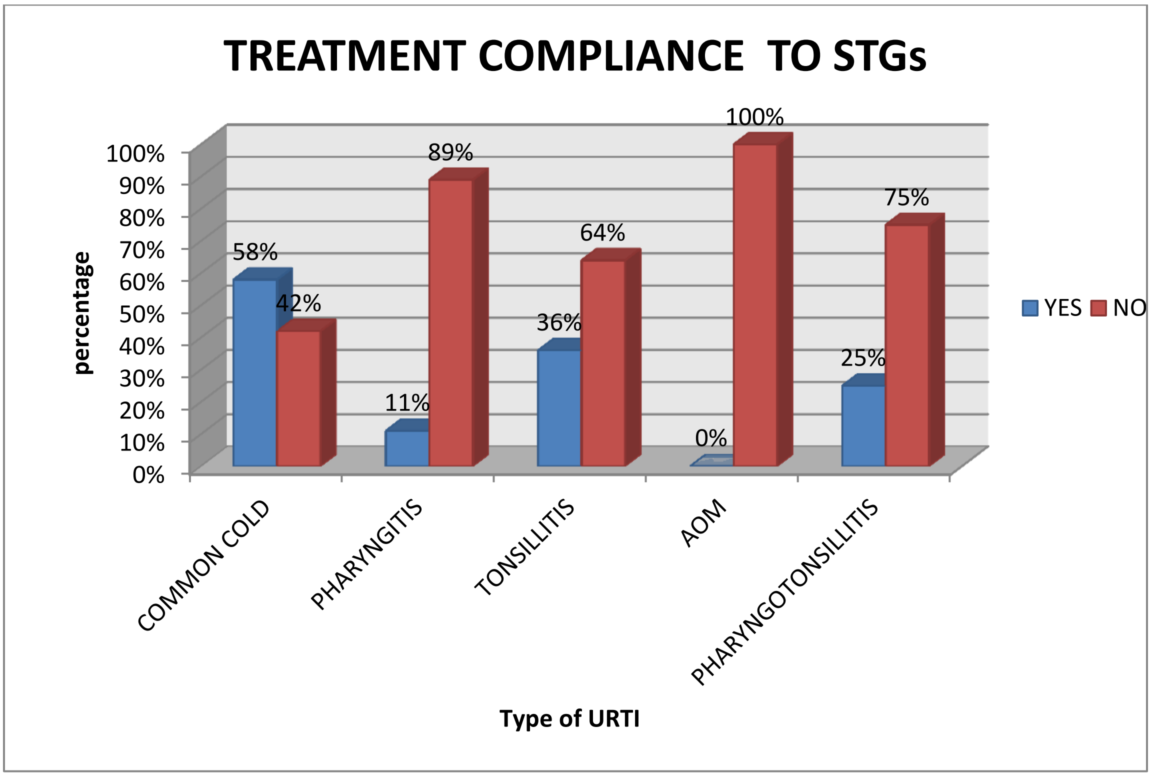


Figure 4.9 above, shows that 55 (42%) of patients diagnosed with common cold had an antibiotic prescribed and 75 (58%) did not receive an antibiotic. Antibiotic prescribing for the common cold is not recommended according to the NSTG and other international guidelines. As for the illness for which antibiotics could be prescribed, only 1 patient (11%) of patients with pharyngitis had antibiotics prescribed in accordance with the guidelines while antibiotic prescriptions of 8 (89%) did not comply with the guidelines. Among the antibiotic prescriptions for tonsillitis 24 (36%) complied with the guidelines while 43 (64%). Only 1 (25%) antibiotic prescription for patients with pharyngotonsillitis was in accordance to the guidelines and these prescriptions were considered rational while 3 (75%) were not.

The low adherence to guideline for individual conditions (common cold = 58%, pharyngitis =11%, tonsillitis =36% , AOM = 0% & pharyngotonsillitis = 25%), indicates a high prevalence of irrational prescribing which has consequences of the development of bacterial resistance, wastage of resources, side effects and poor therapeutic outcomes. If antibiotic treatment is indicated for AOM and pharyngitis or tonsillitis, compliance to guidelines is also very important to avoid the risk of complications, treatment failure and the development of antibiotic resistance. This can occur if the doses, duration of treatment and frequency are lower than the recommended.

All choices of antibiotics for treating pharyngitis or tonsillitis were in line with the NSTG. These were, phenoxymethylpenicillin, benzathine penicillin and azithromycin. A number of antibiotics are effective in treating these illnesses. These include penicillins (such as ampicillin amoxicillin and phenoxymethylpenicillin), as well as numerous cephalosporins and macrolides and clindamycin. However, phenoxymethylpenicillin remains the treatment of choice because of its proven efficacy, safety, its narrow spectrum and low cost. Amoxicillin is often used in place of penicillin V as an oral therapy for young children; the efficacy appears to be equal. Erythromycin is a suitable alternative for patients allergic to penicillin (Bisno, Gerber, Gwaltney Jr, Kaplan & Schwartz, 2002). In Namibia, azithromycin is recommended as an alternative in patients with penicillin allergy. Azithromycin has an advantage over erythromycin because it has fewer gastrointestinal side effects and the shorter duration of treatment and once daily dosing guarantees better adherence.

(“Macrolide Antibiotics Comparison”, 2007). First-generation cephalosporins are also acceptable for patients allergic to penicillin who do not manifest immediate-type hypersensitivity to β-lactam antibiotics. For the rare patient infected with an erythromycin-resistant strain of GABHS who is unable to tolerate β-lactam antibiotics, clindamycin is an appropriate alternative (Bisno, et al., 2002).
This study also revealed that though the NSTG do not specify doses by weight in children for the treatment of pharyngitis or tonsillitis with benzathine benzyl penicillin or phenoxymethylpenicillin. However, some prescribers prescribe according to the weight of a child, which is a commendable practice. These doses were found to be in accordance with the WHO recommendations. In addition, the prescribed duration of treatment in this study was 5 or 7 days for pharyngitis or tonsillitis with oral phenoxymethylpenicillin and amoxicillin. Five day treatment with phenoxymethylpenicillin is the recommendation of the NSTG and not seven days. Both of these durations of treatment are not sufficient enough to completely treat pharyngitis/ and tonsillitis. A 10 day course of oral penicillin is needed to achieve maximal rates of pharyngeal eradication of *group A streptococci* (Bisno, et al., 2002). WHO (2001) recommends it and it is a standard duration in many settings (Altamimi, et al., 2012).

The choice of antibiotic for AOM was only compliant to the NSTG in 25% of the patients. That is, one patient for whom the dosage prescribed was less than the recommended. Cloxacillin was prescribed in 25 % of the patients and cefuroxime in 50% (2 patients). This result reveals a practice of irrational prescribing, inadequate management and a very low compliance to the STGs in the treatment of AOM. In most cases, the choice of antibiotic was not the recommended. Use of cephalosporins in illness that can respond to penicillins not only wastes resources but also promotes the development of bacterial resistance to this vital group of antibiotics. Antibiotic use in AOM is beneficial and whenever indicated, it is important that patients are treated according to the recommendations because inadequate management of AOM can lead to complications which include CSOM, mastoiditis, labyrinthitis, facial palsy, meningitis, intracranial abscess, and lateral sinus thrombosis (Morris & Leach 2009) which can that can lead to death or severe disability (WHO, 2012).

There are several factors that could have influenced this low adherence rate to treatment guidelines in this study. Some of these factors are providers may not be familiar with or may not agree with the guidelines, too much workload; it often takes longer to explain to patients that antibiotics are not always needed for URTIs than to actually generate a prescription (Crocker, et al., 2013). In most cases, providers are aware of standards but may hold beliefs or attitudes that inhibit them from adhering to them, they may doubt the efficacy of or disagree with specific standards or reject the idea of explicit standards in general, believing that practice guidelines restrict provider autonomy or compromise the “art” of medicine, Even when health workers recognize the appropriateness of standards, they may not believe in them and thus are unable to carry them out or may not do so out of habit or lack of motivation to change their behaviour (USAID ,n. d.). This study did not focus on exploring the influence of these factors on antibiotic prescribing in URTIs. Therefore, future research should be conducted to determine if these factors, among others, could be associated with antibiotic prescribing for URTIs in Namibia.

4.6 The cost of rational and irrational antibiotic prescribing

Table 4.9 Comparison of the cost of rational and irrational antibiotic prescribing

Name of Antibiotic	Dosage form	Quantity: Rational	Rational Cost (N$)	Quantity: irrational	Irrational Cost(N$)
Amoxicillin	Suspension	0	0	32	172.48
	Capsules	0	0	980	156.47
Phenoxymethylpenicillin	Suspension	12	86.04	32	229.44
	Tablets	456	90.76	284	56.53
Erythromycin	Tablets	0	0	120	49.51
Cloxacillin	Capsules	0	0	40	9.19
Azithromycin	Tablets	3	27.66	9	82.98
	Suspension	0	0	2	108.56
Cefuroxime	Tablets	0	0	48	67.12
	suspension	0	0	1	56.42
Cotrimoxazole	Tablets	0	0	20	2.74
	suspension	0	0	0	0
Benzathine penicillin inj	Injection	0	0	8	52.02
ceftriaxone inj	Injection	0	0	3	8.61
Total	-	-	**204.46**	-	**1052.07**

Table 4.9 shows a comparison of the cost of antibiotics prescribed rationally and irrationally for the conditions, AOM, pharyngitis, tonsillitis and pharyngotonsillitis. All quantities of amoxicillin that were dispensed were irrationally prescribed, that is 32 (100 ml) bottles of amoxicillin suspension and 980 capsules. The total cost for the suspension was N$ 172.48 and the cost for the capsules was N$ 156.47. 12 (twelve) suspension bottles of phenoxymethylpenicillin that were dispensed were rationally prescribed while 32 suspension bottles that were dispensed were irrationally prescribed. A comparison of the cost of prescribing for phenoxymethylpenicillin suspension shows that irrational prescribing was costing more than rational prescribing (N$ 229.44 and N$ 86.04 respectively). As for quantities of

phenoxymethylpenicillin tablets, the quantities dispensed that were rationally prescribed were more than those that were irrationally prescribed (456 tablets and 284 tablets respectively). As a result, the cost of rationally prescribed phenoxymethylpenicillin tablets was more than that of those that were irrationally prescribed (N$ 90.76 and N$ 56.53 respectively). These results suggest a higher rate of rational prescribing when tablets are prescribed than suspension is prescribed. Since suspensions are usually given to children, this could mean that most phenoxymethylpenicillin prescriptions for children were irrational compared to those of adults who usually receive tablets.

All quantities of erythromycin tablets (120 tablets) that were dispensed were irrationally prescribed and the cost was N$ 49.51. The quantities of cloxacillin capsules (40 capsules) that were dispensed were also irrationally prescribed and the cost was N$ 9.19.

The quantity dispensed of the azithromycin that was irrationally prescribed was more than that which was rationally prescribed (9 tablets and 3 tablets, respectively) and consequently, the irrational cost was more than the rational cost. That is N$ 82.98 and N$ 27.66 respectively. Furthermore, all the azithromycin suspension that was dispensed was irrationally prescribed (Quantity =2; cost =N$ 108.56).

Other quantities of medicines dispensed that were irrationally prescribed were cefuroxime tablets (quantity = 48 tablets; cost = N$ 67.12), cefuroxime suspension (quantity = 1, 100 ml suspension bottle; cost =N$ 56.42), cotrimoxazole tablets (quantity = 20; cost =N$ 2.74), benzathine penicillin injection (quantity = 8; cost N$ 52.02), ceftriaxone injection (quantity: =8; cost =N$ 8.61).

The total cost of antibiotic for these conditions was N$ 1,256.53. The rationally prescribed antibiotics cost N$ 204.46 while the irrationally prescribed ones cost N$ 1052.07. According to this, 84% of the total cost of antibiotic treatment of the common cold, pharyngitis, AOM, pharyngotonsillitis & tonsillitis) was irrational. This result is much higher than that of the United States of America (USA), where Mainous & Hueston (1998) found that 23% of the total cost of antibiotic use to treat URTIs in outpatient setups was unnecessary.

Table 4.10 Cost of antibiotic prescribing in non-specific URTIs

Name of Antibiotic	**Dosage form**	**Quantity dispensed**	**Cost ($N)**
Amoxicillin	Capsules	2520	402.34
	Suspension	57	307.23
Phenoxymethylpenicillin	Tablets	128	22.50
	Suspension	4	28.68
Erythromycin	Tablets	80	32.80
Azithromycin	Tablets	18	165.96
	Suspension	1	58.28
Cefuroxime	Tablets	48	67.12
	suspension	1	56.42
Cotrimoxazole	Suspension	1	9.12
Total cost	-	-	**1150.45**

Table 4.10 shows the cost of antibiotics prescribed in patients with nonspecific URTIs (N$ 1150.45). This cost could have been less, because in most cases, non-specific URTI is a viral infection and antibiotics have no benefit.

The total cost of antibiotic prescribing in URTIs was N$ 2406. 98, of which antibiotics in non-specific URTIs accounted for 48% total cost. These results (table 4.9 & table 4.10) suggest that the cost of antibiotic use in URTIs could be of a significant proportion in comparison to the total cost of all medicines dispensed during the study. Unfortunately, this study did not determine the total cost of all medicines (of other conditions inclusive). According Mainous & Hueston (1998), URTIs are one of the low- cost, high volume conditions that have significant implications for the cost of health care. Pestotnik, Classen, Evans, & Burke (1996) reported that antimicrobial agents are one of the costliest drug categories in hospital expenditures, accounting for approximately 20% to 50% of the total spending on drugs in the USA.

Wastage of resource is one of the consequences of irrational antibiotic prescribing. The WHO (2010) reports that, 10–40% of national health budgets are spent on medicines and if medicines are not prescribed and used properly, billions of dollars of public and personal funds are wasted. This problem occurs in many countries, for example USA where $1.1 billion is spent annually on unnecessary adult upper respiratory infection antibiotic prescriptions (CDC, 2012). The results of this study suggest that this could also be a problem that requires attention in Namibia.

4.7 SUMMARY

Chapter 4 presented the findings of the study and discussion.

The rate of antibiotic prescribing for patients with URTIs at KHC was 78% (95% CI 74%, 82%). The rate was higher in children 90% (95% CI 84%, 94%) than in adults, 68% (95% CI, 62%, 75%). In male patients, the rate was 78 % (95% CI, 71, 84%) and in female patients it was 79% (95% CI, 73, 84%). Further analysis with the chi-square test of, antibiotic prescribing (response variable) and illness, age, gender and profession (exposure variables) showed that age and illness were significantly associated with antibiotic prescribing ($p < 0.05$) while gender and profession rank were not.

On average, each prescription (n=385) contained 2.89 medicines (SD=0.69) 0.81 antibiotics (SD = ±0.460). There was no difference in the average number of antibiotics prescribed by GPs and nurses ($p=0.305$) but GPs prescribed more medicines than nurses ($p= 0.001$).

Compliance to treatment guidelines was 47% (95% CI 40%, 54%). The total cost of antibiotic prescribing in this study was to N$ 2406.98 of which non-specific URTIs accounted for 48% (N$ 1150.45; irrationally prescribed antibiotics, 44 % (N$ 1052.07) and those that were rationally prescribed accounted for only 8% (N$ 204.46). The total cost of antibiotic treatment of illnesses assessed for rationally was N$ 1256.5 of which, N$ 1052.07 (84%) was the cost of irrationally prescribed antibiotics N$ 204.46 (16%) for the rationally prescribed antibiotics. This showed that the cost of irrational prescribing was cost five times more than that of rational prescribing.

CHAPTER 5

CONCLUSIONS, RECOMMENDATIONS AND LIMITATIONS OF THE STUDY

5.1 INTRODUCTION

Chapter 4 presented the results of the study and discussions making comparisons to other research studies. Chapter 5 will present the conclusions and recommendations that based on these conclusions. In addition, the limitations of the study are also highlighted.

5.2 CONCLUSIONS FROM THE STUDY

The purpose of this study was to explore antibiotic prescribing in patients with URTIs at KHC. In order to achieve this, the following objectives were formulated: the first was to determine the rate of antibiotic prescribing in patients with URTIs, the second was to assess the rationality of antibiotic treatment of URTIs and the last was to compare the cost of rational and irrational antibiotic use in URTIs. The following conclusions were drawn based on these objectives.

5.2.1 Objective 1: To determine the rate of antibiotic prescribing in patients with URTIs

The rate of antibiotic prescribing was 78%. In addition, the rate of prescribing was higher among children < 15 years of age than among adults (90% and 68%, respectively). Furthermore, for each specific diagnosis, the rate of antibiotic prescribing was: nonspecific URTIs =95%, tonsillitis =100%, common cold =42%, pharyngitis = 89%, pharyngotonsillitis=100% and AOM = 100%.

The overall rate of antibiotic prescribing in this study (78%) is a cause for serious concern because these infections are viral in 80% of the cases and antibiotics have no role in the treatment of most URTIs .Age and diagnosis were found to be significantly associated with frequency of antibiotic prescribing ($p < 0.05$).Therefore, future research should focus on conclusively establishing such associations because determining factors associated with antibiotic prescribing was not explored in this study.

5.2.2 Objective 2: To assess the rationality of antibiotic treatment of URTIs

Assessment of the rationality of treatment was done using the NSTG and the WHO recommendations. Compliance to STGs of antibiotic prescriptions for the treatment of URTIs was 47%.

5.2.3 Objective 3: To compare the cost of rational and irrational antibiotic use in URTIs

The total cost of antibiotic prescribing in this study was N$ 2406.98 of which non-specific URTIs accounted for 48% (N$ 1150.45); irrationally prescribed antibiotics, 44 % (N$ 1052.07) and those that were rationally prescribed accounted for only 8% (N$ 204.46). The total cost of antibiotic treatment of illnesses assessed for rationally was N$ 1256.5. N$ 1052.07 (84%) was the cost of irrationally prescribed antibiotics N$ 204.46 (16%), showing that the cost of irrational prescribing was costing five times more than that of rational prescribing.

5.2 RECOMMENDATIONS

5.2.1 Introduction

There are several recommendations that originated from this study. These recommendations for the Ministry of Health and Social Services are based on ways to reduce the irrational use of antibiotic prescribing in URTIs and recommendations for future research.

5.2.2 Recommendations to promote rational use of antibiotics at health facility and community level.

Health facility level

- MoHSS should consider purchasing cough syrups (antitussives and expectorants). Though they have doubtful efficacy, these could help reduce antibiotics prescribing by giving a placebo effect to patients. Cough syrups can be the first line choice in patients with URTIs especially in cases where bacterial infection is unlikely or has been excluded, for example the common cold and non-specific URTIs. In addition, these cough syrups also contain antihistamines, analgesics, etc. that help alleviate symptoms of URTIs. Having these in state facilities will also prevent prescribers from rushing into prescribing antibiotics for even conditions like common cold that do not require antibiotics. Even though the cost of these cough syrups could raise concerns, the cost of antibiotic resistance is even higher.

- Health worker continued education through workshops focused on rational use of antibiotics and short problem based training courses in pharmacotherapy.
- Periodic antibiotic use audits should be introduced which can provide feedback to prescribers in clinics and hospital wards on antibiotic use expenditure and resistance patterns (McKenzie, Rawlins & Del Mar, 2013).
- MoHSS should consider adopting a strategy of delayed antibiotic use, which has shown effectiveness in reducing antibiotic usage for URTIs. This strategy involves giving the patient a prescription and instructing them only to have it filled if symptoms do not resolve (Arroll, Kenealy & Kerse, 2003).
- Additions to the Namibia treatment guidelines on treatment of URTIs
    1. The dosing for phenoxymethylpenicillin in children should be revised so as to give doses by weight.
    2. The duration of treatment of tonsillitis should be changed to 10 days because a 10 day course of oral penicillin is needed to achieve maximal rates of pharyngeal eradication of GABHS (Bisno, et al., 2002). This duration of treatment is also recommended by WHO.

3. Include a section on the management of non-specific URTIs in both adults and children.

- In order to limit antibiotic prescribing in acute pharyngitis or tonsillitis, MoHSS should consider adopting the CDC clinical decision criteria for prescribing antibiotics. That is, screening of all patients with pharyngitis for the presence of 4 centor criteria: (1) history of fever, (2) tonsillar exudates, (3) no cough and (4) tender anterior cervical lymphadenopathy. The presence of two or more of these symptoms gives an indication of a high likelihood of a bacterial infection. Furthermore, in order to confirm the diagnosis of a bacterial infection, a rapid streptococcal antigen test is recommended in patients with two or more criteria and antibiotic therapy limited to patients with a positive test.
- MoHSS should make available streptococcal antigen test kits in all health facilities which should only be used to confirm the diagnosis of bacterial pharyngitis.

At community level

- Patient education: increase awareness among patients about antibiotics, uses and dangers of irrational use among patient and the community. Strategies can include: providing patients with leaflets with information on the course of illness, benefits and risks of antibiotics, media campaigns through radio and television on rational use of antibiotics. Patient education has been seen to be effective in reducing antibiotic use (Farquha, 2002).

5.2.3 Recommendations for future research

- Further research is needed to identify factors that contribute to antibiotic over prescribing in URTIs in Namibia
- Identify barriers of compliance to standard treatment guidelines.

5.3 STUDY LIMITATIONS

The following were the limitations pertaining to this study:

- The study was conducted at one health facility. This prevented generalisation of the results to the larger population of Windhoek or Namibia.
- In this study, the NSTGs of 2011 were intended to be used to assess compliance to guidelines, in order to access compliance to these new comprehensive guidelines. Unfortunately, the guidelines could not be used in isolation to assess compliance to the recommended treatment for pharyngitis or tonsillitis in children. This is because the NSTG do not specify dosing in children by weight. Hence, the WHO recommendations of 2001 were also used to access rationality of prescriptions with doses by weight for children.
- This study did not confirm the accuracy of diagnosis in terms of correlating symptoms, diagnosis and treatment. To remedy this shortcoming, further research is needed to identify which subsets of respiratory tract infection and correlating symptoms and signs are more likely to result in the prescription of an antibiotic.

5.4 SUMMARY

Chapter 5 presented the conclusions of this study, described the recommendations for MoHSS and presented the limitations of this study. All the objectives of this study were met.

5.5 CONCLUSION OF THE STUDY

Antibiotic prescribing in patients with URTIs at KHC is an area of concern. This is reflected by the high rate of antibiotic prescribing in URTIs, the low compliance to STGs in treating these illnesses as well as the higher cost of irrationally prescribed antibiotics. Therefore, implementing strategies that promote rational use of antibiotics in URTIs is of uttermost importance in order to preserve the efficacy of these vital drugs and avoid wastage of scarce resources.

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ANNEXURES

ANNEXURE A: UNIVERSITY Of NAMIBIA POST GRADUATE COMMITTEE APPROVAL LETTER

UNIVERSITY OF NAMIBIA

EDUCATION · SERVICE · DEVELOPMENT

☎ (+264 61) 206 3111
Website: www.unam.na

340 Mandume Ndemufayo Avenue
Private bag 13301
Windhoek
NAMIBIA

Inspiring minds & shaping the future

Enquiries: Dr. H. J. Amukugo
Private Bag 13301
Mandume Ndemufayo
Windhoek

Tel. No.: 061- 2064617
Fax No.: 061-
e-mail: hamukugo@unam.na

All correspondence must be addressed to the Office of the Associate Dean

LETTER OF PERMISSION:
POST GRADUATE STUDENTS

Date: 08 January 2013

Dear Student: Mr Mwape Kunda
Student number: 201047080

The post graduate studies committee has approved your research proposal.

INVESTIGATION ON ANTIBIOTIC PRESCRIBING IN PATIENTS WITH UPPER RESPIRATORY TRACT INFECTIONS AT KATUTURA HEALTH CENTRE

It may be required that you need to apply for additional permission to utilize your target population. If so, please submit this letter to the relevant organizations involved. It is stressed that you should not proceed with data collection and fieldwork before you have received this letter and got permission from the other institutions to conduct the study. It may also be expected that these organizations may require additional information from you.

Please contact your supervisors on a regular basis

Ms. L. van der Westhuizen
Deputy Associate Dean (SoNPH)

ANNEXURE B: MINISTRY OF HEALTH AND SOCIAL SERVICES APPROVAL LETTER

9-0/0001

UNITY LIBERTY JUSTICE

REPUBLIC OF NAMIBIA

Ministry of Health and Social Services

Private Bag 13198	**Ministerial Building**	**Tel: (061) 2032560**
Windhoek	**Harvey Street**	**Fax: (061) 222558**
Namibia	**Windhoek**	**E-mail:** tkakili@yahoo.com
Enquiries: Ms. T. Kakili	**Ref:** 17/3/3	**Date:** 15 April 2013

OFFICE OF THE PERMANENT SECRETARY

Ms M. Kunda
P.O. Box 62599
Soweto
Windhoek

Dear Ms Kunda

Re: Investigation on Antibiotics prescribing in patients with upper respiratory tract infection.

1. Reference is made to your application to conduct the above-mentioned study.

2. The proposal has been evaluated and found to have merit.

3. **Kindly be informed that permission to conduct the study has been granted under the following conditions:**

3.1 The data to be collected must only be used for completion of your Master's Degree in Public Health;
3.2 No other data should be collected other than the data stated in the proposal;
3.3 A quarterly report to be submitted to the Ministry's Research Unit;
3.4 Preliminary findings to be submitted upon completion of study;
3.5 Final report to be submitted upon completion of the study;
3.6 Separate permission should be sought from the Ministry for the publication of the findings.

Yours sincerely,

MR. ANDREW NDISHISHI
PERMANENT SECRETARY

" Health for All "

ANNEXURE C: DATA COLLECTION TOOL

1) ID #______	2)Date of data collection: __/__/___	3) Data Collector Initials:

SECTION A : Patient's Demographics

4) Gender : Male (1) ☐ Female (2) ☐	5) Date of birth (dd/mm/yy) ____/____/____	6)Age ____ (1)☐ Adult (2) ☐ Child	7) Weight (Kg)_______

SECTION B: 8) Diagnosis (tick from the list given)

1) ☐ Common cold
2) ☐ Pharyngitis
3) ☐ Tonsillitis
4) ☐ Pharyngitis and Tonsillitis
5) ☐ Acute otitis media
6) ☐ URTI

SECTION C: 9) Treatment of the condition: Antibiotics prescribed	(1) ☐ Yes (2) ☐ No

(1) Name/s of antibiotics prescribed	(2)Dose	(3)Frequency	(4)Duration	(5)Quantity Dispensed	10)Treatment complies with STG. (if NO indicate which aspect is not compliant with STG					
					(1) ☐ Yes	(2) ☐ No				
						1	2	3	4	All
1)										
2)										
3)										

11) Total number of antibiotics prescribed ----------------------

12) Other medicines prescribed

(1) Name	(2) Quantity dispensed
1)	
2)	
3)	

13) Total number of medicines prescribed (including antibiotics)--------------------------------

SECTION D: 14) Prescriber's rank/position (1) ☐ Medical Doctor (2) ☐ Nurse

ANNEXURE D: AN EXTRACT OF THE NAMIBIA STANDARD TREATMENT GUIDELINES

6.1 Ear Disorders

6.1.2 Otitis Media

Otitis media (OM) or middle ear infection is of two types:

- *Acute*—of sudden onset in the middle ear. It is usually found in children younger than 5 years and usually comes after a cold or flu.
- *Chronic*—an infection that does not clear for over one month. It can be suppurative (pus discharge with perforated eardrum) or serous (eustachian tube blockage due to allergy or infection).

Causes

- Viral infections of upper respiratory tract (e.g., rhinitis, common cold)
- Bacterial infections (e.g., streptococcus, haemophilus influenza)
- Chronic allergy
- Chronic enlargement of tonsils, adenoids
- OM not adequately treated (chronic)
- Bottle feeding in infants

Symptoms and signs (acute)

- In adults—
  - Fever
  - Pain in the ear
  - Headache
  - Malaise, weakness
- In children—
  - High fever
  - Acutely painful ear
  - Irritable, crying
  - Poor sleeping patterns
  - Itching ears
  - Poor feeding
  - Pain upon drinking and chewing
  - Nausea and vomiting
  - Diarrhoea
  - Sometimes purulent discharge from the ears
  - Otoscopy: eardrum is red and dull, instead of white or grey and shining

History and symptoms and signs (chronic)

- Previous treatment for acute OM
- Previous history of perforated eardrum
- Discharge from the ear for more than one month
- Painless
- Hearing loss
- Deafness in children with speech impairment, poor school performance
- Fluid level behind eardrum.

Management for acute OM

In clinic, health centre, or hospital–

1. Give paracetamol for pain and fever.
2. Prescribe an antibiotic.
    - Adults: amoxicillin[1] 500 mg every 8 hours for 5 days
    - Children: phenoxymethylpenicillin[1] 25–50 mg/kg per day in four divided doses. Amoxicillin[1]: less than 20 kg, 40 mg/kg per day divided in 3 doses, every 8 hours for 5 to 10 days; more than 20 kg, 250 to 500 mg every 8 hours for 5 to 10 days
3. Follow up after 1 to 2 days (especially small children).
4. Refer if–
    - No improvement after acute OM treatment
    - Severe fever, vomiting, and drowsiness in children
    - Swelling over mastoid area

History and symptoms and signs (chronic)

- Previous treatment for acute OM
- Previous history of perforated eardrum
- Discharge from the ear for more than one month
- Painless
- Hearing loss
- Deafness in children with speech impairment, poor school performance
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3. Follow up after 1 to 2 days (especially small children).
4. Refer if–
   - No improvement after acute OM treatment
   - Severe fever, vomiting, and drowsiness in children
   - Swelling over mastoid area

6.3 Throat Disorders

6.3 Throat Disorders

6.3.1 Acute Tonsillitis and Pharyngitis (Sore Throat)

Infection and inflammation of the throat and tonsils are usually due to viral or bacterial causes. If the tonsils are still *in situ,* the sore throat is usually due to tonsillitis. Lack of tonsils does not exclude acute pharyngitis.

Causes

- Streptococcal bacterial infection is the major cause and needs to be treated to prevent complications.
- Many different virus infections (often those associated with common cold, influenza, and nasal infections)
- Infectious mononucleosis
- Diphtheria
- Herpangina

Symptoms and signs

- Sore throat
- Dysphagia (difficulty in swallowing)
- Malaise
- Headache
- Earache
- Fever
- Vomiting (sometimes in children)
- Red and inflamed tonsils, pharynx
- Pus collections and follicles on tonsils
- Enlarged lymph glands of the neck (cervical)
- Halitosis
- Sometimes diffuse red rash
- *Danger:* development of rheumatic fever if not treated properly

Management

- Patients <15 years with sore throat, dysphagia, fever, red and inflamed tonsils, follicles on the tonsils, or enlarged lymph glands need active treatment.

6.3 Throat Disorders

- Follow this procedure—
  1. Provide pain relief (e.g., paracetamol)
  2. Recommend gargling with salt water or diluted chlorhexidine.
  3. If available, provide local antibiotic spray.
  4. Prescribe antibiotics:
     - Phenoxymethylpenicillin[1]
       - Adults: 500 mg PO four times daily for 5 days
       - Children: 250 mg/5 mL PO four times daily for 5 days

     —— OR ——

     - Benzathine penicillin[1]
       - Adults: 1.2 million units stat
       - Children: 0.6 million units stat

     —— OR ——

     - Azithromycin
       - Adults: 1 g PO daily for 3 days
       - Children: 10 mg/kg per day PO for 3 days

- Specific—from syphilis, TB, leprosy, fungal infection
- Acute sinusitis—cause: pneumococcus, streptococcus, staphylococcus, *H. influenza, Escherichia coli.*
  - Acute sinusitis may follow acute rhinitis.
  - Swimming and diving cause direct spread of nasal infection.
  - Dental infection or extraction cause spread of infection from tooth root to maxillary antrum.
  - Predisposing factors include the following—
    - Local factors such as nasal and sinus ostia obstruction due to allergy, polyps; neighbouring infections; previous infection in same sinus
    - General factors such as chilling, fatigue, poor diet, atmospheric irritants, or pollution
- Chronic sinusitis—cause: mixed, streptococcus, anaerobes, *E. coli,* pneumococcus, proteus
  - Nonspecific—follows single or repeated acute sinusitis attacks
  - Specific—TB, syphilis, fungal (actinomycosis)
  - Chronic

Note: Infection may be restricted to a single sinus, affect several sinuses (multi-sinusitis), or all the sinuses (pansinusitis—unilateral or bilateral).

Symptoms and signs

- Infections of the external nose
  - Pain; red, swollen, tender nasal tip
  - Headache and fever
  - Evacuation of pus usually spontaneously in 4 to 5 days
- Common cold (coryza)
  - Ischaemic stage: incubation (1 to 3 days)—sneezing, shiver, malaise
  - Hyperaemic stage: profuse watery rhinorrhoea, nasal obstruction, pyrexia

6.2 Nose and Paranasal Sinus Disorders

- Secondary infection stage: thicker yellow or green discharge
- Resolution stage: in 5 to 10 days

- Chronic rhinitis
  - Nasal obstruction: marked, usually alternates from side to side
  - Postnasal drip: clear, viscid becoming mucopurulent
  - Blocked or heavy feeling in nose; mild headache and mental apathy common
  - Transient hypo/anosmia (i.e., inability to smell)
- Specific chronic rhinitis—syphilis
  - Congenital
  - Acquired
- Acute sinusitis
  - Pain over infected sinus (stabbing or aching, worse on bending or coughing); sometimes referred pain to other sites
  - Discharge in nose or nasopharynx if open sinusitis
  - Nasal obstruction due to mucosal swelling
  - Tenderness can often be elicited over maxillary and frontal sinuses
  - Constitutional symptoms: pyrexia, malaise, mental depression, halitosis
- Chronic sinusitis
  - Nasal, postnasal discharge
  - Anosmia, hyposmia, cacosmia (i.e., the perception of a bad smell due to some intrinsic cause)
  - Constitutional (usually mild): malaise, anorexia, mental apathy, sore throat, cough

Management

- Infections of the external nose—
  - Early: Local antibiotic ointment tetracycline
  - Later: Systemic wide-spectrum antibiotic
- Common cold (coryza)—
  - Prophylactic—avoiding contact with known cases

6.2 Nose and Paranasal Sinus Disorders

- Therapeutic—general symptomatic management
  - Rest and warmth (ideally, stay in bed)
  - Analgesics
  - Antihistamines, ascorbic acid (vitamin C): of doubtful value
  - Antibiotics: reserve for secondary infections
- Local—
  - Steam inhalations
  - Saline drops
  - Vasoconstrictors: oxymetazoline nasal spray or drops give quick, temporary relief, but advise the patient not to abuse them.

- Chronic rhinitis—
  - General (i.e., predisposing factors)—Advise the patient to correct some general factors such as tobacco or alcohol use and to avoid others such as contact with anyone who has a cold.
  - Local—Treat any sinusitis or adjacent infection with mild vasoconstrictors and saline nasal drops.
- Acute sinusitis—
  - Treat the infection using antibiotics PO for 10 to 14 days: amoxicillin[1] or azithromycin.
  - Treat the pain using—
    - Analgesics (e.g., paracetamol or NSAIDs)
    - Local heat (e.g., hot water bottle or steam)
  - Establish drainage using—
    - Decongestant solutions (oxymetazoline drops)
    - Irrigation
- Chronic sinusitis—
  - Prescribe systemic antibiotics. [1]
  - Provide drainage using—
    - Decongestants
    - Irrigation

If the patient shows no improvement, refer to an ENT specialist. Patients with chronic or recurrent sinusitis

[1] Refer to appendix 5 for treating patients with a history of penicillin allergy