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Review Article

Finding Out Antibiotics Frequently Used in Pediatry case Study: Rwamagana Provincial Hospital

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ABSTRACT

Background: Antibiotics merge among the frequently prescribed medications for children in Rwanda and even worldwide. Recently, however, there was seen an uncontrolled rise in antimicrobial-resistant infections following that remarkable inappropriate use of antibiotic drugs, leading to increased morbidity, mortality, and healthcare costs.

Methodology: A retrospective study was conducted to determine the frequency of antibiotics use during the treatment of infections or diseases of pediatric patients who attended Rwamagana Provincial Hospital with involvement of antibiotics. Medical records or files of 300pediatric patients who attended the stated hospital between 1st January 2016 and 28th February 2017 were scientifically reviewed and analyzed using licensed software such as SPSS (version16.0) and captured using Microsoft excel and Microsoft Word 2007.

Results: The study included 300 pediatric patients. This population is made of more male patients gender 155 (51.7%) than females 145 (48.3%). The mean (average) age of this population was 3.0 years (±3.1). The most prevalent diseases was malaria (19.1%) followed by sepsis (7.6%), and the frequently prescribed single antibiotics were ampicillin (37.1%), followed by the third generation, Ceftriaxone (25.2%), whereas ampicillin and gentamycin (46.5%) are the mostly used antibiotics from the different groups or classes, followed by ampicillin and chloramphenicol. However, ampicillin and amoxicillin combination (16.6%) is the mostly used combination of two antibiotics from the same group.

Conclusion: There is a high frequency use of antibiotics as shown by the results of this study. Pediatric patients of age ranging between one and five were prescribed the higher percentage of antibiotics compared to patients of age groups below one year and those between six and twelve years, which requires big attention, focus and strategies to limit and control the use of antibiotics in this age group in pediatric patients. Penicillin group mainly, ampicillin was the most frequently prescribed followed by cephalosporin group mostly Ceftriaxone, then Cefotaxime as a single drug therapies and most preferred in combination with other antibiotics. Malaria was the most prevalent disease and the main cause of most of hospitalized patients, followed by pneumonia. Our study could add a contribution leading to improvement in antibiotic prescription pattern in pediatric department guidelines setting and implementation by the hospital.

Keywords: Probiotics; Immunity; Beneficial microorganism; Health; Gut microbiota;

INTRODUCTION

I.1. Background

For various medical conditions, antibiotics fall among the most common medications prescribed for children in Rwanda and even worldwide in general. In recent years, however, there was seen an uncontrolled rise in antimicrobial resistant infections following a high increase in the use of antibiotics, leading to a greatly increased morbidity, mortality, and medical care costs. The consequences of antimicrobial resistance are seen greatest on low-income countries, which face the problems of fewer antibiotic choices and higher levels of infectious disease. Therefore, proper and precise prescribing practices based on laboratory findings serve to combat this global public health challenge by preventing antibiotic overuse and misuse for rationality matters.

I.2. Problem Statement

From their discovery, antibiotics fall among the most commonly prescribed and dispensed drugs in pediatric population [1]. Due to an overall increase in medical care costs, non uniform drug prescribing practices and the high growth of antibiotic resistance, lack of monitoring and control of antibiotic use call for the

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concern and strict antibiotic policies to be taken into account [1]. In Rwanda , as for the entire world, infections and other diseases are common in children and their treatment include most of time the use of antibiotics, which are sometimes unnecessary, leading to an increased resistance of bacterial infections [2]. World Health Organization has long recognized antimicrobial resistance (AMR) as a growing worldly health problem, and through several resolutions, The World Health Assembly has called upon member States and the international community to take measures to prevent and control the emergence and spread of AMR [2]. Great medical achievements of the last century may suddenly be lost via the spread of antimicrobial resistance [2]. In next few years, curable infectious medical conditions may become untreatable and spread throughout the world, and this has already started to happen.

The inappropriate use of antibiotics is still a big, largely spread challenge which has become a barrier to public health in Rwanda and worldwide, as it has become one of the greatest reasons of the spread of antimicrobial resistance (due to the misuse of antibiotics) in addition to their high unwanted side effects, and these are the main reasons why this study will analyze the misuse of antibiotics in treating infections in pediatric.

I.3. Research Objectives

I.3.1. General Objective

The broad objective of this study is finding out antibiotics frequently used in pediatry of Rwamagana Provincial Hospital.

I.3.2. Specific objectives

- To determine the rate at which antibiotics are properly used or misused.
- To determine the rate of prescriptions of antibiotics for pediatric patients
- To determine recommended and non- recommended antibiotics for pediatric patients.

I.4. Research Question(s)

In order to find out the proper use of antibiotics in provincial hospitals based on the mostly used antibiotics in pediatry, the following research questions will be investigated:

- Are antibiotics used appropriately in treating infections?
- What are the most used antibiotics in treating infections?
- Does the use of antibiotics in treating infections lead to the microbial resistance?
- How do health care providers manage side effects caused by antibiotics?

1.5. Significance of the Study

This research study aims at finding out the level at which antibiotics are properly utilized in hospitals based on the commonly prescribed antibiotics in pediatry. The study will benefit Rwandans and health care providers as they will have a clear picture of the problem. It will also help in minimizing and managing the misuse, side effects and even resistance caused by the inadequate treatments with antibiotics.

II: LITERATURE REVIEW

II.1. Introduction

This chapter gives us the details about the frequency of antibiotic use in pediatric population from some documented writings. Different journals/articles, books and many other accepted scientific publications were used to explain more on this topic. It has 2 main parts: some definitions where some key words are explained for a clearer understanding and the background of this study where the literature of different authors on a worldwide scale is laid out.

II.2. Some Definitions

Antibiotics are referred to as substances that destroy the microbes (bacteria) with minor side effects to human beings. Etymologically, the word “anti” comes from anti- which means “against” and biotic- used for “life”[3]. According to the World Health Organization, an antibiotic is a chemical therapeutic agent that inhibits or abolishes the growth of micro-organisms called bacteria and the term originally referred to an agent sourced from biological organisms; however, “antibiotics are also now used for anti-parasitical activities [4]. Another research also defined antibiotics as chemotherapeutic agents which have transformed the treatment of infectious diseases by turning life threatening diseases into more manageable and treatable conditions [5].Antimicrobials: are group of substances that can destroy or inhibit the growth of harm full groups of microbes, including bacteria, viruses, fungi and parasites [6].

Empirical therapy is a term referring to the initiation of therapy prior to determination of a firm diagnosis [6].

II.3. Background of the study

Antibiotics and other antimicrobial medicines have brought back to life millions of lives and relieved patients suffering from different kinds of diseases caused by various bacterial microbes [7]. Antibiotics can be produced naturally by microorganisms or synthesized in laboratories [2]. They are considered clinically effective and useful in medicine if the destruction or growth inhibition of the microorganism is achieved in the respective concentrations of the antibiotic in the body [3].Although they have been dubbed “miracle drugs,” antibiotics are not always effective, reason being that over time, bacteria can develop resistance to existing drugs, making infections difficult if not impossible to treat [7]. Alexander Fleming is the scientist who discovered the first antibiotic compound in 1928, in great and meaning full breakthrough for medical sciences and this was the greatest achievement which marked the start of the era of antibiotic discovery from the start of life on earth [8]. Antibiotics fall among the most frequently used drugs in today’s medicines [6]. Some antibiotics are referred to as 'bactericidal', which means that they work by killing bacteria while others are 'bacteriostatic' which means, their activity is seen by stopping bacteria multiplication [9]. Each different type of antibiotic affects different bacteria in different ways, and this is to say that, an antibiotic might inhibit bacteria’s ability to convert glucose molecules into the needed form of energy, or even their capacity to make cell wall, which when it occurs, leads to the death of the bacteria instead of their reproduction. Antibiotic drugs used for the treatment of a wide range of bacterial infections are referred to as 'broad-spectrum' antibiotics; whereas those that act at narrow range of bacteria are called 'narrow-spectrum' antibiotic drugs [3]. The frequency and the duration of treatment depend on the nature and severity of the infectious disease and the response to therapy, but the treatment courses should not be unnecessarily prolonged, for this encourages resistance, and a long period therapy may also lead to unwished side-effects and unnecessary costs, but in certain diseases, like tuberculosis osteomyelitis or chronic diseases, it is beneficial and necessary to prolonged the duration of therapy

[10].

It is important and essential to recognize that, not necessarily all infections need to be treated with the use of antibiotics. For example the following infections do not require antibiotic treatment: common cold, flu due to influenza, most coughs and bronchitis, many ear infections, many skin rashes [11]. According to World Health Organization(WHO, 2015), in a study which intended to find out how antibiotics were used to fight resistance, young people(37%) tend to have used antibiotics more than older people of 65 years and above (24%)[12]. The survey also shows that, across the countries, about 81% of the population on which, the survey was conducted, say that antibiotics are given to them through prescriptions by the doctor or nurse, while, in another survey 93% were give the drugs from a pharmacy or medical store [12].

II.3.1. Public beliefs about antibiotic drugs and resistance

Pauline, et al, (2013) stated that, people still have little knowledge about of antibiotic resistance even though they seem to know the right ways of treating infections caused by bacteria but they think that antibiotics overuse is unwise for, it would decrease their activity and beneficial effectiveness in few year to come and others believe that strengthening their bodies would help them to resist infections than treatment means[13]. Studies found that other people tended to believe that antibiotics undermine immunity while others thought that their bodies might become used to them, making them ineffective [13].According to a WHO survey (WHO, 2015), mixed respondents from 12 countries in which the survey was conducted to find out the rate at which antibiotics are used properly, considering when and how they are used and the reason why they should be used, some people were thinking that it was acceptable to use antibiotic drugs from any other person or from their family members for the disease thought to be the same [12].43% of respondents thought that in case of the sickness it was acceptable to buy the same antibiotics which helped their friends or ask them from a doctor. However, 32% of respondents were thinking that they should stop taking antibiotics when they feel better, not when they have taken all of them as directed by the doctor.

II.3.2. Do children need antibiotics?

Children always need to be treated with antibiotics when their infections stay for long and lead too much pain as such infections are thought to be of bacterial origin, and require immediate antibiotic therapy [14]. It is always very important for children and more so for infants up to six months or even less, like babies from six months to 2 years, those with moderate to severe pain of ear, those with fever reaching 102.2 Fahrenheit or even beyond, those with any other disease which could make it more difficult to get healed, and children who have cleft palate, down syndrome, immune disorders and cochlear implant [14].The major reason why children need antibiotics is that bacterial infections often transmitted into more serious diseases, like head infections sometimes spread to the brain, causing meningitis and strep throat which mostly changes to rheumatic fever, and pneumonia which , when left untreated, frequently becomes a systemic infections, resulting into death [14].

II.3.3. No antibiotics against delayed prescribing

Children without pre-existing co-morbidities like liver, heart, lung diseases or immunosuppression, should not be prescribed antibiotics, which requires prescribers to first gain full knowledge about the disease and its description rather than hurrying to their prescription because delaying prescription of antibiotics seems to be more safe and protective to physicians in situations of disease complications [15]. Giving the first priority to the delayed prescription is very important for some disease conditions such asacute otitis media (a wait-and see period of about 2 to 3 days),sore throat (5 days estimations) and acute cough(between ten to fourteen days)[15].

II.3.4.Guidelines considered before starting antimicrobial (antibiotic) therapy for specific infectious illnesses

The following should be considered when making choices of an antibiotic agent for rational therapy:

Antibiotics should never be used to treated infections caused by viruses. Infections of the upper respiratory canal caused by viruses and diarrhea which is not complicated require no antibiotic therapy. Tests like sensitivity or susceptibility to antibiotics, culture as lab samples have to be considered, in case they are possible.

It is important to ensure that an antibiogram is obtained. For example, "blind" prescription of antibiotics for the fever whose cause is not known usually always results into difficulties in making diagnosis [10]. Information about the instant lab susceptibility or sensitivity tests of the microorganism which shows prevalence is very important in the selection of an antibiotic before the confirmatory finding of the responsible bacterium [10]. The antibacterial selection for a given infectious disease should be very targeted to reserve broads spectrum antibiotics for severely sick patients whether the microorganism(s) responsible for the infection is unknown or not [10].The antibiotic doses may vary with respect to different number of factors such as weight, age, renal function and hepatic activity and the level of severity of the disease [10]. The prescription of the "standard" dose in cases of serious infectious diseases may lead to the failure of the treatment; thus it is very crucial to prescribe a dose which meets the disease conditions, because an inappropriate dose may lead to the rise of the risk of bacterial resistance to the antibiotic used [10]. However for an antibiotic with narrow spectrum of activity whose doses fit between toxic and therapeutic doses like an aminoglycoside, it is equally essential to avoid high dose by adjusting its blood plasma concentration [10].The severity of the infectious disease determines by which administration route; the antibiotic has to be given. Life-threatening conditions always require intravenous (IV) route for accurate therapy, although, antibiotics which are well absorbed can be administered orally even for very severe infections [10]. Painful intramuscular administrations in children should not be granted when possible [10].

II.3.5. Antibiotic dosing formulary for children

WHO has designed model formulary which classifies pediatric population according to age range and doses of different medicines, mostly in terms of mg/kg [10]. The intention of the model is the use in children of up to 12 years old. The model placed age ranges in a way that neonates' age range from one to 28 days, infant ranging between one to twelve months and finally children range from one to twelve years of age. Through this model, the maximum dose is predetermined, providing an indication of the limit of the upper dose when dosing patient is per kilogram. Allowances must be made when using weight as a basis for dosing in edematous or obese children. In patients of this population the ideal weight for height and age has to be considered.

II.3.6. Impact of antibiotic resistance and its awareness in pediatry

In a multi-country public awareness survey on antibiotic resistance by WHO (WHO, 2015), the occurrence of antibiotic resistance was

everywhere in the world, compromising the treatment of infectious diseases and undermining many other advances in healthcare and medicine, which was found to represent one of the biggest threats to global health today, and can affect any one, of any age, in any country [12]. Antibiotic resistance leads to longer hospital stays, higher medical costs and increased mortality [12]. Antibiotic resistance occurs naturally, but misuse of antibiotics in pediatric humans is accelerating the process. Findings by WHO (2015) show that antibiotic use is widespread, and it is higher in the lower income countries included in the survey, where 42% of people say they used antibiotics within the past month compared with 29% of people surveyed in higher income countries [12].

II.3.7. Allergy to antibiotic

Some patients using antibiotics for the treatment of various infections meet situations where they develop allergic reactions of different kinds, which makes allergy to be a common problem to patients, as they can even become allergic to any kind of medication, but some are more likely to lead to a highlighted allergic event for antibiotics [16]. The two common antibiotics which cause allergy are penicillin and sulfa. However allergies to penicillins are more common than for salfa although severe allergic reactions to penicillin drugs [16] .Lengel (2009) stated that around 90% of patients on which the study was conducted report that the suspected allergies to penicillin were either not allergic or that they diminished or even vanished away over time [16]. Sulfa is the second common antibiotic which causes allergy. Common antibiotic drugs which contain sulfa are Bactrim, Septra and Pediazole. In Lengel's study (2009), three percent of the population had allergic reactions to sulfa antibacterials, and their harmful effects were the same as those of the immune system diseases like HIV/AIDS [16].

Common sulfa allergic reactions include Stevens - Johnson syndrome, rash, phato-sensivity, hives, liver problems, kidney problems, breathing difficulty, worsening asthma and reduced blood cells [16]. Individuals with allergic reactions to sulfa antibiotics are often allergic to many other drugs than those already mentioned and the following drugs can also cause problems in those that are allergic to sulfa: Sulfasalasine, Sulfacetamide eye drops, silver sulfadiazine cream and some diuretics such as hydrochlorothiazide and diabetic medications like sulfonylurea medications [16]. Allergic reactions due to antibiotics always need treatments but the treatment must be done by a qualified and experienced medical practitioner [16]. Mild allergic reactions may include mild rash or photosensitivity and patients would be watched and given treatment to deal with the allergy. For example if the allergic reaction was an itchy rash, anti-histamines such as Benadryl would be used to deal with symptoms [16]. The selection of an antibacterial agent (antibiotic) relies on the nature of the suspected pathogen and its antibiotic sensitivity. Other factors which are related to the patients are also considered. These include for example, the patient's history of allergic reaction, renal and hepatic state of activity, immune status, and severity of the infection, age and ethnic origin [10]. Guidelines and policies regarding the proper use of antibiotics at a local level are the key thing to reduce the availability of antibiotics to attain reasonable consistence of the economy with enough anti-bacterial cover and to reduce the development of resistant bacteria microorganisms [10].

II.3.8. Classification of antibiotics

I. Beta-lactams: This group or class of antibacterials includes penicillins, cephalosporins and carbapenems and monobactams (aztreonam) [17]. Monobactams have got similar structure to other beta-lactams except that they have only one ring whereas other beta-lactams have two rings. Monobactams have very low cross allergy with other beta-lactams [17]. Agents of this group contain a 3-carbon and 1-nitrogen ring that is strongly reactive, and interfere with protein components necessary for synthesis of the cell wall of bacteria, and in the process either inhibits the growth of or kills bacteria [18] (Table 1).

Table1 : Penicillins

Antibiotic class and its members	Spectrum of action
Beta-lactams (Penicillins) *Penicillins(pen G) Penicillinase-stable* **penicillins** *(pen M)* *Oxacillin Methicillin* *Aminopenicillins (pen A).* *Ampicillin Amoxicillin*	1. Penicillin G is one of the natural penicillins: it acts against gram negative microorganisms which not are not able to produce beta lactamase enzymes such as Neisseria and other anaerobic bacteria 2. Penicillinase resistant penicillins: these include Penicillin M, which has the activity against penicillinase producing Staphylococci. 3. Extended spectrum penicillins: they are aminopenicillins antibiotics with Slightly less activity compared to penicillin G on Pneumococci, Streptococci and Meningococci; but they show activity against many strains of Salmonella, Shigella, and P.mirabilis, H.influenzae
Carboxypenicillins (pen C) Ticarcillin Ureidopenicillins* (pen U) : Piperacillin	Carboxypenicillins have got more stability compared to Aminopenicillins for hydrolysis by the ß-lactamases of most Enterobacteriaceae and Pseudomonas aeruginosa and Ureidopenicillins which are more active than carboxypenicillins in fighting infections caused by Gram positive, enteric and P.aeruginosa bacteria

β-lactam / β-lactamase inhibitor combinations *Amoxicillin + clavulanic acid Ampicillin + sulbactam Ticarcillin + clavulanic acid* *Piperacillin + tazobactam Amidinopenicillins Mecillinam*	4. Co-Drugs like Beta-lactam combined with beta-lactamase inhibitor: ß-lactamase inhibitors (BLI) combinations produce greater activity against beta-lactamase producing microorganisms, including Staphylococcus species, some enterics, H.influenzae and Bacterioides species 5. Amidinopenicillins: these include Mecillinam which was restricted for use against urinary infections caused by E.coli but is active against Penicillinase and low level cephalosporinase producing bacteria.

Cephalosporins (Cephems): they are similar to penicillin in structure and mode of action [17]. They take a big part of the most commonly prescribed and administered antibiotics worldwide and they account for one-third of all antibiotics prescribed and administered [18] (Table 2).

Table 2: Cephalosporins (Cephems)

Beta-lactams (Cephems) **1stGeneration** **Cephalosporins (C1G)** Cephalothin Cefazolin **2ndGeneration** **Cephalosporins (C2G)** Cefuroxime Cefamandole Cephamycin (new C2G) Cefoxitin Cefotetan – removed **3rdGeneration** **Cephalosporins(C3G)** Cefotaxime Ceftazidime Ceftriaxone **4th Generation** **Cephalosporins (C4G)** Cefepime Oral C3G Cefixime Cefpodoxime **Next Generation** **Cephalosporins** Ceftobiprole Ceftaroline	The first generation of cephalosporin antibiotics (C1G): they have narrow spectrum of action; relatively modest Gram-negative activity and good Gram-positive activity, but they are relatively inactivated by gram-negative bacteria with beta-lactamase enzymes. The second generation of cephalosporin antibiotics (C2G): members of this generation have got a better activity against Gram-negative bacteria, but have minimal activity against Staphylococci. Cephamycins remain susceptible in presence of broad Spectrum ß-lactamase (ESBL) as they are not substrates for the enzyme. They are used as an indicator for extended spectrum ß-lactamase derived from Streptomyces lactamdurans bacteria The third generation cephalosporin antibiotics (C3G): they have got wider spectrum of activity compared to C1G and C2G, although they show less activity when compared to narrow spectrum agents against Gram-positive cocci. However they are highly active against Enterobacteriaceae and Pseudomonas aeruginosa, with a better Stability to betalactamase (Jumaa & Karaman, 2015). The fourth generation cephalosporin antibiotics (C4G): members of this generation have the highest (broadest) spectrum of Activity, especially, against high level cephalosporinase of Enterobacteriaceae and Pseudomonas aeruginosa. They are not always used with ESBL producing organisms, and they all do not have activity to MRSA or Enterococcus species . Next generation of cephalosporin antibiotics: they have broad spectrum of activity against Gram-negative bacteria which are common but also have some Gram-positive activity. Next generation cephalosporins are bactericidal, except that they are not approved by FDA and the time approved, FDA can no longer say if Staphylococcus is resistant to Oxacillin, and report all beta-lactams as Resistant.

Monobactams : These antibiotics are considered to be members of beta-lactams exception that, their beta-lactam ring stands alone with no other ring fused to like other cephalosporins. Aztreonam remains the only monobactam antibiotic commercially available[18] (Table 3).

Table 3: Monobactams:

Monobactams Aztreonam	Aztreonam has a narrow spectrum of activity and works only against Gram-negatives such as Enterobacteriaceae and Pseudomonas. It does not get hydrolyzed by most commonly occurring plasmid and chromosomally mediated ß-lactamases, and the production these enzymes is not induced.

Penems: Carbapenems are broad spectrum β-lactam antibiotics. They are stable to almost all β-lactamases and differ from other β-lactam antibiotics in their nuclear structure, in which the sulfur is replaced by a carbon group and there is an unsaturated bond between carbon 1 and 3 in the thiazolidine moiety (Table 4,5).

Table 4: Penems:

Penems Carbapenems Imipenem Meropenem Ertapenem Doripenem **Penem**(Faropenem)	Imipenem and Meropenem are both administered via I.V injection. Meropenem is more active against gram negative bacteria than Imipenem, while the latter is more active against gram positive bacteria. Both are active against lower respiratory tract infections, but Meropenem is the only carbapenem that was evaluated in children and is FDA approved to be used in paediatric meningitis. Slightly different structure than the other ß-lactams, make the Penems much more resistant to beta-lactamase hydrolysis Penems: they are administered orally and are primarily chosen for respiratory tract infections. They show poor activity against Serratia, Pseudomonas, Stenotrophomonas, though Faropenem not yet FDA approved.

Table 5: Glycopeptides

Glycopeptides: Vancomycin&Glycopeptid e **Lipoglycopeptide(new)** Dalbavancin Oritavancin TelavancinTeicoplanin	Vancomycin: this antibiotic has the activity against Methicillin Resistant Staphylococcus aureus, Clostridium difficile and Streptococci including Strep pneumoniae, and it is alternative to Penicillin G in serious infections, has good diffusion in all tissues (except cerebral spinal fluid), but it is associated with High toxic effects of ears and kidneys. An antibiotic called Vicuron is a second generation Lipoglycopeptide having bactericidal effects against Methicillin Resistant Staphylococcus Aureus and MRSE per week for intravenous dosing. It has long activity but not approved by FDA. Oritavancin is also a member of the 2nd generation glycopeptide and Lipoglycopeptide, given through IV route of administration once daily and is indicated in casesof skin and soft skin structure Infections. It has activity similar to Vancomycin on Staphylococcus and Enterococcus but not yet FDA approve, Telavancin (Theravance) is bactericidal for all Gram-positive, where it inhibits bacterial cell wall synthesis and inhibits bacterial phospholipid membrane synthesis.

Aminoglycosides: These antibiotics have broad spectrum of activity and rapid bactericidal effect [18].They work by binding to 30S ribosome and inhibit bacterial protein synthesis and are used for the treatment of aerobic gram negative bacilli, staphylococci and certain mycobacteria [17] (Table 6).

Table 6: Aminoglycosides

Aminoglycosides (Bactericidal) Gentamicin Amikacin Tobramycin Streptomycin Kanamycin Netilmicin	Streptomycin is used for tuberculosis. Gentamicin, amikacin and netilmicin are used for pneumonia, sepsis and meningitis Neomycin is used for burns, and wounds; ulcers and dermatitis. Aminoglycosides are only available for parenteral, intramuscular and intravenous administrations because they are polar compounds They are excreted unchanged in the urine. Aminoglycosides accumulate in the renal tubules which causes nephrotoxicity Another common side effect is ototoxicity that can be acute, reversible, or chronic and irreversible hearing loss which can be caused by cochlear hair cells degeneration .Monitoring Aminoglycosides is mandatory. It is important to control its serum level for peak and trough blood concentration to ensure the Bactericidal effect and avoid side effects.

Tetracyclines: Are four rings hydrocarbon containing antibiotics [17]. These antimicrobial agents were originally derived from Streptomyces bacteria, but the newer derivatives are semi-synthetic. Some promising examples of this group are oxytetra cycline and Doxycycline[16] (Table 7).

Table 7: Tetracyclines

Tetracyclines **(bacteriostatic)**Tetracycline Doxycycline Minocycline oxytetracycline Tigecycline	Tetracyclines have broad spectrum of activity; but their resistance is common which limits their use. Tetracyclines are primarily used for the treatment of genital infections (chlamydiae) and atypicals (Rickettsiae, Mycoplasma), but is not recommended for pregnant women and children (less than 2 years old) due to its toxicity on bones and teeth of the fetus.Tetracycline is short acting, whereas, Minocycline and Doxycycline are long acting (have broad spectrum of activity) and is more active than Tetracycline. Like tetracycline it may have activity against multi-drug resistant organisms

Phenocols

Chloramphenicol was the first broad spectrum antibiotic, has extremely bitter taste but modified forms are available for oral and parenteral administration. Chloramphenicol palmitate is available as suspension and capsules for oral administration and chloramphenicol sodium succinate are available for intravenous administration. The bacteriostatic effect of chloramphenicol is a result of protein synthesis inhibition by binding to 50S ribosomal subunit (Table 8).

Table 8: Phenocols

Phenocols **(Bacteriostatic)** Chloramphenicol	Chloramphenicol is very active against many Gram-positive and Gram-negative bacteria, such as, Chlamydia, Mycoplasma and Rickettsiae. It is used for extra-intestinal severe salmonella infection When Chloramphenicol is considered for the empiric treatment of meningitis, it crosses blood/brain barrier well Toxicity is high in Phenocols, causes bone marrow aphasia and other hematological abnormalities

Macrolides

They work on micro-organisms like S.pneumoniae and Staphylococcus pyogenes, Mycoplasma, Legionella and less serious Staphylococcal infections . Macrolides are widely used for the treatment of gram positive bacterial infections such as Staphylococcus aureus and Staphylococcus pneumonia (Table 9).

Table 9: Macrolides

Macrolides Erythromycin, Azithromycin, Clarithromycin, Dirithromycin, Troleandomycin	Erythromycin is used for Mycobacterium pneumonia and Legionella pneumonia infections, diphtheria, pertussis, conjunctivitis and bacillary angiomatosis Clarithromycin is used for the treatment of upper and lower respiratory tract infections, and is widely used for H. pylori infections. Azithromycin has a better antibacterial activity against gram negative than erythromycin, and it is the most active macrolides against H. Influenza and Legionella species. It is used as single dose therapy for sexually transmitted diseases (STDs). Azithromycin has a short duration of therapy of 3-5 days for skin, soft tissue and some respiratory tract infections due to its concentration that remains high in these tissues for extended period of time.

Quinolones

Fluoroquinolones are very active against enteric gram negative bacilli and cocci, gram negative bacteria, gastrointestinal tract and urinary tract bacterial pathogens. Ofloxacin and ciprofloxacin are preferred for gram positive bacterial infections (Table 10).

Table 10: Quinolones

(Furanes) 1 st Generation, narrow spectrum Nalidixic acid Cinoxacin *Fluoroquinolones* Ciprofloxacin Norfloxacin Ofloxacin Levofloxacin Enoxacin Garenoxacin Lomefloxacin Sparfloxacin Gatifloxacin Moxifloxacin Trovafloxacin	Nalidixic Acid and Cinoxacin are the only 1st Generation Quinolones used for Gram-negative bacteria and in the treatment of urinary tract infection due to their high concentrations that reach in the site of infections easily. Garenoxacin has both Gram-negative and Gram- positive antibacterial coverage including Anaerobes, Atypicals, S.pneumoniae and Pseudomonas. Fluoroquinolones: ciprofloxacin, levofloxacin, norfloxacin, ofloxacin are more effective at lower Minimal inhibitory concentrations (MIC) values and have extended spectrum of activity against Staphylococci, Streptococci and Pneumococci (sparfloxacin). They are more widespread tissues and reach the intestines and the lungs. Ciprofloxacin and Ofloxacin are used for systemic infections . Trovafloxacin was removed from market very quickly after release due to their cardiac arrhythmias, liver destruction, and phototoxicity. Gatifloxacin (Tequin®) removed from market due to its harmful side effects . Quinolones have no problem crossing the outer membrane but with rapid bactericidal activity.

Nitrofurantoin

This antimicrobial is effective in the treatment of lower UTI and achieves therapeutically active concentrations only in the urinary tract, which makes it a target selective drug and does not change the normal flora growth (Table 11).

Table 11: Nitrofurantoin

Inhibitors of nucleic acid synthesis Nitrofurantoin	Nitrofurantoin acts on urinary tract infections caused by Gram-negative and Gram-positive organisms. It has abroad spectrum and is bactericidal. It works by damaging bacterial DNA and gets reduced by flavoproteins (nitrofuran reductase) in the bacterial cell. These reduced products are highly active and attack ribosomal proteins, DNA, respiration, pyruvate metabolism and other macromolecules within the cell. It is not known which of the actions of nitrofurantoin is primarily responsible for its bactericidal acitivity. Pseudomonas and most Proteus spp. are naturally resistant to nitrofurantoin.

H. Sulfonamides

Sulfonamides are broad spectrum antibiotics that are active against both gram negative and positive bacteria and inhibit the synthesis of folic acid leading to their bacteriostatic effect (Table 12).

Table 12: Sulfonamides

Sulfonamides (F o l a t e p a t h w a y inhibitors) *Trimethoprim/ Sulfamethoxaz o* *lecombination (Bactrim or co- trimoxazole)*	Trimethoprim/Sulfamethoxazole combination (known as Bactrim or co-trimoxazole) is prescribed for treatment of certain diseases such as UTIs and otitis media in children, chronic bronchitis in adults, enteritis and Travelers' diarrhea. Trimethoprim/Sulfamethoxazole combination resembles a microbial substrate and competes with that substrate for the limited microbial enzyme by tying up the enzyme and blocking one of steps in bacterial metabolism. Sulfonamides such as Sulfamethoxazole tie up the enzyme pteridine synthetase while trimethoprim ties up the enzyme dihydrofolic acid reductase preventing produced of tetrahydrofolic acid essential for the synthesis of bacterium's nucleic acids. Sulfonamides, trimethoprim each alone or in combination block(s) folic acid essential for the synthesis of adenine and thymidine that make up the DNA, RNA. Therefore, folate pathway inhibitors do not have direct antibiotic activity but the end result is that the bacteria are unable to multiply. The combination SXT (thrimethoprim-sulfamethoxazol) is synergistic and the association provides a bactericidal effect.

II.1.1. Previous research findings about the usage of antibiotics in pediatric hospitals

In a research carried out in United States of America, Pradeepkumar et al(2017), found that, throughout different classes of antibiotics, the group of Cephalosporins (46.33%) was the most prescribed, followed by Penicillins (25.3%), Macrolides (12.77%), Fluoroquinolones (10.63%) [19].

Tetracyclines (6.62%), Aminoglycosides (9.7%), Metronidazole (1.65%), and Sulfonamides (1.2%) and lastly [19]. The common route for drug administration was parental (71.8%). The age wise distribution of antibiotics were (37.9%) in patients 1-5 years old, (36.6%) in patients less than 1 years old and 25.5% in patients of age more than 5 years old [19]. The most commonly prescribed single antibiotics were Ampicillin 25.4% in patients less than 1 years of age, Ceftriaxone 16.8% in patients between one to five years of age and Ceftriaxone (37.5%) in patients of age greater than 5 years [19].

At the hospital in Chitwan district in Nepal, most of the hospitalized pediatric patients belonged to age group of less than a year as an indicator of susceptibility of infant below one year towards various infective diseases [9]. Palikhe (2004) stated that infants less than one year of age received antibiotics more frequently than older children and stated that this could be due to a higher susceptibility of infections at a younger age and needs a greater concern for infant's health relatively [1]. Mezgebe, et al, (2015) stated that the age distribution of antibiotics were higher in patients 1-5 years old (36.6%) [5].

II.3.9. Previous research findings about the usage of antibiotics in pediatric hospitals

In a research carried out in United States of America, Pradeepkumar et al(2017), found that, throughout different classes of antibiotics, the group of Cephalosporins (46.33%) was the most prescribed, followed by Penicillins (25.3%), Macrolides (12.77%), Fluoroquinolones (10.63%) [19].

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CHAPTER III. METHODOLOGY

This chapter shows how the study was done from the targeted population to the analysis of the results. It shows the way through which this research study was conducted. It has different parts including: methods and data source, study area, study population, participants' inclusion criteria, sampling method and sample size, tool for data analysis and ethical considerations.

III. 1.Type of the study design

This is a retrospective and quantitative method to investigate the antibiotics used to treat pediatric patients who attended Rwamagana

Provincial Hospital with antibiotic involvement for different medical conditions. Medical records of all pediatric patients who attended the stated hospital between 1st January 2016 and 28th February 2017 are scientifically reviewed and analyzed.

III.2. Study population

The study population is all pediatric patients who attended Rwamagana Provincial Hospital between 1st January 2016 and 28th February 2017.

III.3. Sampling and sample size

The population of this study is composed by pediatric patients who attended Rwamagana Provincial Hospital between the 1st January 2019 and 28th February 2017. The sample 385 patients but only, 300 patients were selected from this population due the problem of acquiring medical files which was very hard. The size of this sample was determined using the following

Where n is the sample size from a given population proportion (p) at a z level of confidence (which is 95% in this study) and w (= 0.05) being the margin of error.

III.4. Study area

This study was conducted in Rwamagana Provincial Hospital which is located in the Eastern Province of Rwanda, Rwamagana district, Kigabiro sector. It is a provincial hospital which serves all the health centers located in Eastern Province. Rwamagana Provincial Hospital's activities consist mostly of administrative and clinical activities, and the first mission is the service to the community.

III.5. Inclusion criteria

All pediatric patients' files diagnosed of diseases which are considered to be of antibiotic requiring at Rwamagana Provincial Hospital.

Pediatric patients with well documented and clear medical files.

III.6. Exclusion criteria

All patients' files diagnosed of other diseases which are not antibiotic requiring and in which antibiotics were not used at Rwamagana Provincial Hospital.

Pediatric patients with unclear and incomplete medical files. Patients with other associated misleading pathologies Non-pediatric patients.

III.7. Limitations of the study

Since this study is retrospective, it totally depends on hospital information's data and if recordings were not taken properly, this can lead to wrong final results.

III.8. Content scope

Through this study, knowledge and practices related to rational use of antibiotic drugs in pediatry and management of side effects caused by the frequently used antibiotics were explored.

III.9. Time scope

The study was conducted between the 1st December 2017 and the 25th.June2018.

III.10. Data analysis

Data collection process and their entry took a period of 5 weeks, where data were collected on designed sheets filled by the researcher, then analyzed using licensed software such as SPSS (version16.0) and captured using Microsoft Word 2007. Main statistical analyses performed include, the calculation of means, standard deviation and correlation coefficient. The differences between proportions are determined using chi-squared tests, while differences between means will be assessed using Student-t test or ANOVA. A p value of <0.05 is considered statistically significant.

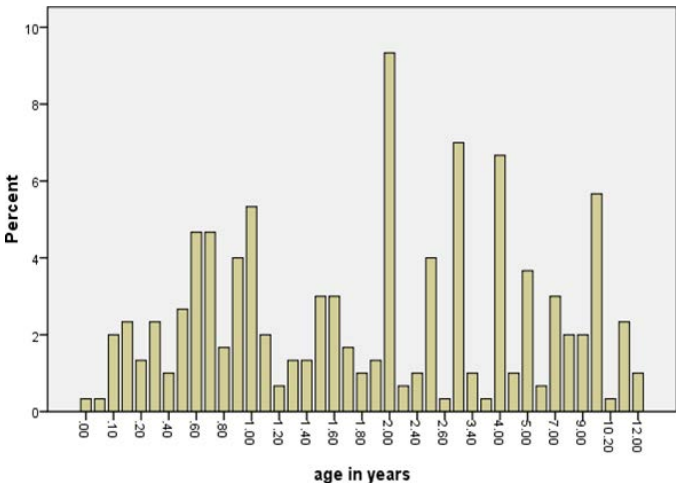
II. 12. Ethical considerations.

The study protocol was examined and approved by the supervisor and the Department of Pharmacy, School of Medicine and Pharmacy at University of Rwanda. The research was organized and implemented in scientific way with respect , honesty and proper communication, respect of promises and fulfillment of the agreement where a written letter requesting the authorization to conduct our research was submitted, accepted and approved by the authority of the Rwamagana Provincial hospital prior to data collection process. Confidential information was respected and protected where no patient's names or addresses information appeared on the data collection sheets.

CHAPTER IV: RESULTS AND DISCUSSION

This study included 300 pediatric patients. This population was made of more male patients' gender (51.7%) than females (48.3%). The mean (average) age of this population was 3.0 years (±3.1), where the lowest and the highest age were 2days and 12 years respectively and the predominant age being 2years. The population was grouped into neonates (0–28 days) (0.6%) as the lowest age range, followed by infants (1–12months) (27.7%) and Children (1–12 years) (71.7%) Figure-1.

Figure1: Age distribution



IV.1. Patients demographic parameters

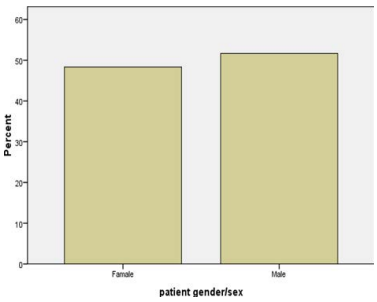
Most of the pediatric population of Rwamagana Provincial hospital on which the research study was done belonged to the class of children (1–12 years) as 67.3 % patients, and when they were classified according to age range , the most (50.7%)of this population was between1-5 years old.

This indicate that children of age range from 0ne to twelve are mostly exposed to infectious diseases and consumed more antibiotics in relation to this situation. However a research study conducted by Palikhe (2004)in Kathmandu, Nepal, revealed that infants under 1 year of age received antibiotics more frequently than older children

and suggested that this could be due to a higher susceptibility of infections at a younger age [1]. The same was stated by Thapaliya in 2015, in a research done in Chitwan district, Nepal [5].

From the population of 300 pediatric patients male patients were the dominant gender with 51.7%, whereas females were 48.3%. Similar findings were shown in the research study done by Thapaliya in 2015, in Chitwan district, Nepal [5]. Muenchhoff and Gaulder, in 2014, put it that gender has a great and major outcome impact on a range of infectious diseases beginning from the origin of life and quoted that the rates of morbidity and mortality are higher in males than in females throughout life, where, the accountability was attributed to less stronger humoral and cellular immune response to infection or antigenic stimulation in males than in females [20] Figure 2.

Figure 2: Gender distribution



IV.2. Disease or diagnosis pattern.

Among the patients included in this study, the most prevalent disease was malaria (19.1%) followed by sepsis and bronchopneumonia (7.6% each). Then follows febrile gastroenteritis (7.3%) and lastly come tonsillitis, viral pneumonia with urinary tract infections, virginal trauma and others with 1% each. This was probably due to the pre-lab diagnostic reasons where symptoms and signs which are considered in order to start treatment suggest that the patients suffer from malaria, which makes malaria to be the most thought of first among other several diseases.

However, in research done by Thapaliya (2015)in Chitwan district, Nepal, pneumonia was the most prevalent disease (22.5%) followed by acute gastroenteritis (16.3%), then lower respiratory tract infections (9.4%)[5]. Thapaliya (2015) continued and stated that pneumonia was still the leading killer disease of young children despite the simple, safe, effective, and inexpensive interventions to minimize its risks[5]. Thapaliya (2015) went on to emphasize that the reason may be poverty and inadequate access to healthcare in most of all developing countries [5] (Table 13).

Table 13: Disease pattern of pediatric patients at Rwamagana Provincial hospital

Diagnoses/ Diseases	Frequency	Percentages (%)
Cerebral Malaria	60	19.1
Sepsis	23	7.6
Bronchiolitis And Pneumonia	23	7.6
Febrile Gastroenteritis	22	7.3
Severe Malaria Anemic Form	14	4.6
Malaria With Gasto-entestinal Symptoms	13	4.3
Severe Malaria	13	4.3
UTI & Sepsis	13	4.3
Severe Pneumonia	13	4.3
Simple Pneumonia	12	4
Gastroenteritis	11	3.6
Severe Cerebral Malaria	11	3.6
Urinary Tract Infections	10	3.3
UTI& Cerebral Malaria	8	2.66
Bronchiolitis	6	2
Sepsis With Anemia	6	2
Meningitis	5	1.6
Others	63	21

IV.3. Antibiotics prescribed

As the average number of drug is an important indicator for assessing rationality of prescription, in this study the average number of antibiotics per patient was 2.4.

It is recommended to keep the mean number of drugs per prescription as low as possible to avoid the effects of polypharmacy like increased risks of drug interactions, costs of therapy, non- compliance and incidence of resistance following the use of antibiotics. The WHO recommends that the average number of drugs per prescription should be less than 2 (two) (Table 14).

Names Of Antibiotics	Number of patients	Percentage (%)
Ampicillin	59	37.1
Ceftriaxone	40	25.1
Amoxicillin	27	16.9
Cefotaxime	22	13.8
Metronidazole (Flagyl)	3	1.8
Chloramphenicol	3	1.8
Cloxacillin	2	1.2
Meropenem	2	1.2
Ciprofloxacin	1	0.6

This study found penicillins (29%) to be the leading class of antibiotics prescribed, followed by Cephalosporin (22%) as widely prescribed antibiotics. But as individual drugs ampicillin (37.1%), followed by the third generation, Ceftriaxone (25.2%) was the second antibiotic highly prescribed followed by Cefotaxime (22%) and other antibiotics. The least prescribed antibiotic was Meropenem which constituted 0.6% (Table 15).

Table15: Classes of antibiotics prescribed

Antibiotic Classes	Frequency	Percent (%)
Penicillins	88	29.3
Cephalosporins	66	22
Carbapenems	2	0.6
Fluoroquinolones (Quinolones)	1	0.3
Nitro-Imidazoles (METRONIDAZOLEs)	5	1.6
Chloramphenicols (Phenocols)	3	1
Penicillin & Cephalosporins	18	6
Cephalosporins & Aminoglycosides	3	1
Penicillins, Cephalosporins & Nitro-Imidazole	1	0.3
2 Penicillins	5	1.6
Penicillin & Aminoglycosides	65	21.6
Penicillin & Chloramphenicols	27	9
Cephalosporins, Aminoglycosides	2	0.6
Cephalosporins, Nitro-Imidazoles & Fluoroquinolones	6	2
Penicillins, Cephalosporins & Aminoglycosides	2	0.6
Cephalosporins & Nitro-Imidazoles	2	0.6
Cephalosporins &Chloramphenicols	1	0.3
Penicillins & Nitro-Imidazoles	2	0.6
Cephalosporins &Fluoroquinolones & Tetracyclines	1	0.3

In this study, the high increase in beta-lactams (penicillins and cephalosporins) prescription was related to their tolerance in terms of toxicity, in addition to their broad spectrum of activity. Carbapenems and fluoroquinolones were the least prescribed classes of antibiotics due to their side effects and toxicities which are not tolerable in pediatric population. Antibiotics were found used to treat viral infections which increases treatment costs and leads to prolonged hospital delay as this was not meant to be the appropriate treatment choice and that instead anti-viral could have been the best selection. In a research conducted by Schibler in 2015

in Tanzania, it was stated that patients who attended outpatient clinics with fever were tested negative for malaria and prescribed antibiotics [21]. The author found that this was appropriate in less than 20% of the case and explained that such procedures lead to poor health outcomes, huge wastage of medicines and rapid spread of bacterial resistance (Table 16).

Table 16: Combinations antibiotics

Names of antibiotics combinations	Number of times then combination was used	Percentage (%)
Ampicillin & Gentamicin	67	46.5
Ampicillin & Chloramphenicol	24	16.6
Ampicillin & Cefotaxime	7	4.8
Cefotaxime, Flagyl & Ciprofloxacin	6	4.10
Ampicillin & Amoxicillin	5	3.4
Cefotaxime & Gentamicin	4	2.7
Ceftriaxone & Chloramphenicol	4	2.7
Metronidazole (Flagyl) & Amoxicillin	3	2.0
Ampicillin, Gentamicin, Cloxacillin & Cefotaxime	1	0.6
Ampicillin & Ceftriaxone	2	1.3
Ampicillin & Gentamicin & Ceftriaxone	3	2.0
Ceftriaxone & Metronidazole	2	1.3
Ampicillin, Gentamicin & Metronidazole	1	0.6
Cefotaxime, Gentamicin & Ceftriaxone	1	0.6
Ceftriaxone & Amoxicillin	1	0.6
Cefotaxime & Cloxacillin	3	2.0
Cefotaxime + Ciprofloxacin & Doxycycline	1	0.6
Ceftriaxone & Cloxacillin	2	1.3
Ampicillin & Metronidazole	1	0.6
Cefotaxime & Amoxicillin	1	0.6
Ampicillin ,Gentamicin& Amoxicillin	1	0.6
Cefotaxime & Then, Ceftriaxone	1	0.6

However, in this research malaria (19.1%) was the most prevalent disease treated with antibiotics ahead of all other diseases. Although Rwamagana is in eastern province which is the endemic area for malaria as it applies to Rwanda and the whole of east Africa, and could be due to excessive and inaccurate pre-diagnostic treatments which increases the risks of antibiotic resistance, increased and un necessary costs as well as unwanted drug effects.

Among 300 patients in this research, 143 patients received combination antibiotics, that is to say 47.7% of the population. As combinations ampicillin and Gentamicin (46.5) are the mostly used antibiotics from the different groups followed by Ampicillin and chloramphenicol1((6.6). However, ampicillin and amoxicillin are the mostly used from two different groups.

In a study done by Thapaliya (2015), the usage of combination of antibiotics was found to be 60%, which is quite upper than that of our study (44%) [5]. In comparison to our study, it could be seen that there is a lower severity of disease or failure of treatment with monotherapy.

In another study done by Palikhe (2004) in Nepal, it was showed that 79% of patients received multiple antibiotics and 21% of patients received a single antibiotic [1].

Thapaliya (2015) also showed that IV beta-lactam or a combination of beta lactamase inhibitor and beta-lactam antibiotic with a macrolide added may be given to children having severe pneumonia[5]. Thapaliya (2015) proceeded and said that young infants having risks of acquiring a gram negative infection should be given a betalactam antibiotic and aminoglycoside [5]. The same author also quoted that there cannot be a single recommendation for the antibiotics regimen of neonatal sepsis for all settings. The author again mentioned that the choice of antibiotics depends on the prevailing flora in a given unit and their antimicrobial sensitivity. The superiority of therapy with a combination of antibiotics is that antibiotic combination treatment acts at 2 different locations or sites in the cell wall of bacteria by beta-lactams and the inhibition of protein synthesis by Macrolides. However in our study, antibiotic combinations were high in that, there are cases where three or four drugs were prescribed which could not be easily explained scientifically. And there are cases were some antibiotics were stated and shortly replaced by others, which indicates inappropriate use of antibiotics, which is costly and tends to lead to antibiotic resistance.

CONCLUSION

There is a high frequency use of antibiotics as shown by the results of this study. Pediatric patients of age ranging between one and

5 were prescribed the higher percentage of antibiotics compared to any other age group, which requires a big attention, focus and strategies to limit and control the use of antibiotic in this age group in pediatric patients. Penicillin group, mostly Ampicillin, was the most frequently prescribed, followed by cephalosporin group mostly Ceftriaxone, then Cefotaxime as single drug therapies. Cefotaxime was also the most preferred in combination with other antibiotics.

In our study, malaria was the most prevalent disease in the most of hospitalized patients, followed by pneumonia in Rwamagana provincial hospital. The most frequently used antibiotics were ampicillin, Ceftriaxone and Cefotaxime, Gentamicin, and amoxicillin. Moreover, there is high inappropriate use of antibiotics caused by the prescription of many antibiotics per patient (polypharmacy), their use in non-bacterial diseases such as malaria and viruses, and shifting from some antibiotic therapies to others.

Therefore, this might lead to resistance and increased overall cost related to treatment of the patients, which may be reduced by prescribing antibiotics based on sample cultures and antibiogram results. Our study will greatly add a vital contribution in the improvement of antibiotic prescription pattern, in pediatric department, guidelines setting and implementation by the hospital.

RECOMMENDATIONS

In view of the above findings and discussion, following recommendations are made:

Intensive and continuous trainings should be given to healthcare practitioners who are involved in prescribing and dispensing practices about the appropriate use of antibiotics to meet pediatric patient's needs and prevent cases of polypharmacy and irrational use of antibiotics.

The hospital has to ensure that prescribers are equipped with updated guidelines for diagnosis. They should also be equipped with knowledge about disease signs and symptoms in order to enable them to prescribe exact antibiotics in relation to patients' conditions so as to combat and eradicate resistance as well as reduce the net medical treatment costs.

SUGGESTION FOR FURTHER RESEARCH.

This study didn't put much emphasis on the determination of the real cost paid by the patients for all medical services given during the whole period of stay at the hospital. Therefore, a further research is needed for that reason so that all unnecessary costs incurred during the hospital admission are avoided.

But also another research is needed to determine whether lab antibiotic susceptibility tests are normally conducted which will enable hospitals to reduce the incidence of polypharmacy and antibiotic resistance at large.

REFERENCES:

1. Palikhe N.Prescribing Pattern of Antibiotics in Pediatric Hospital of Kathmandu Valley. J Nep Heal Res Cou. 2004;2(2):31–36.
2. WHO.Antimicrobial resistance. Global Report on Surveillance.2014;1:12–256.
3. Kourkouta L, Kotsiftopoulos C, Papageorgiou M, Iliadis C, Monios A.The Rational Use of Antibiotics Medicine. J Healthc Communs.2017; 2(4):1–4.
4. WHO. Step-by-step approach for development and implementation of hospital antibiotic policy and standard treatment guidelines.2011;1:2–38.
5. Mezgebe HB, Tadesse B, Legesse B.Antibiotics prescribing pattern in pediatric unit of Ayder referral hospital , Tigray region , Northern. J of Sci. Inno. Res.2015;4(2):57–60.
6. Pathak A. Lessons from diagnosis-prescribing and antibiotic resistance surveillance in Ujjain , India : The lull before the storm, J Antimicrob Chemother.2012; 65(10):2247-52.
7. Infectious Diseases Society of America IDSA.Bad bugs, no drugs.2014; 1(7):9–31.
8. Bayarski Y .Antibiotics and their types, uses and side effects .2006;1–6.
9. Thapaliya K, Shrestha S, Bhattarai S, Basnet D, Chaudhary RK.Prescribing pattern of antibiotics in pediatric hospital in Chitwan District in Nepal. Int J Pharm Pharm Sci.2015;4(11):1631–1641.
10. WHO.WHO Model Formulary for Children.2010;12–28.
11. Hildreth CJ, Burke AE, Glass RM.Inappropriate use of antibiotics. JAMA.2009; 302(7):816.
12. WHO. Antibiotic resistance: multi-country public awareness survey.2015;1–45.
13. Pauline N, Kerry C, Kevin D, Jonathan G, Darrin H, et al. A Qualitative Study: Infection and Resistance: Public Beliefs about antibiotics. Antibiotics.2013;2:465-476.
14. Consumer Reports Health. Antibiotics for ear infections in children: Choosing Wisely. American Academy of Family Physicians.2013;
15. Kutty N. Treating Children without Antibiotics in Primary HealthCare. Oman Medical Journal.2011;26:303-305.
16. Lengel R.Guide to Understanding Antibiotics Prescribed in Your Doctor's Office (1st Edition).North Ridgeville: Mini-Medical School.2009
17. Gallagher JC, MacDougal.Antibiotics simplified: Anti-Bacterial Agents Handbooks (2nd Ed.). Jones & Bartlett Learning, LLC.2012.
18. Etebu E, Arikekpar I.Antibiotics: Classification and mechanisms of action with emphasis on molecular perspectives. J Appl Microbiol Res Bio.2016; 4:90-101.
19. Pradeepkumar B, Alameri T, Narayana G, Reddy YP, Ramaiah JD. Assessment of antibiotic prescribing pattern in pediatric patients: A Cross-sectional Hospitalbased Survey. Journal of Health and Research. CHRISMED J Health Res.2017;4:235-7.
20. Muenchhoff M, Gaulder PJR. Sex difference in Pediatric Infectious Diseases. J Infect Disease.2014; 209(S3): S120-6.
21. Schibler J.Rational use of medicines: safety, challenges and potentials of electronic mobile devices for implementing a new algorithm for management of childhood illness (ALMANACH) in low and middle income countries.2015;1:453-460