Nepalese parents' knowledge and self-reported use of antimicrobial medicine in the children of 0-12 years

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Laurea University of Applied Sciences **Abstract**

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Antimicrobials treatment enables us to prevent and to treat ailments caused by bacteria, virus, fungi and parasites. Discovery of antimicrobials has played a major role in the increasing life span of human being. Along with the discovery of the antibiotic, antimicrobial resistance (AMR) has been inevitable phenomena ever since. Furthermore, inadequate knowledge about antimicrobial use and misuse is contributing in speeding up AMR. Therefore, the main objective of the survey is to find out any practice or knowledge that is potentially detrimental from the aspect of AMR. This study aimed to assess Nepalese parents' knowledge and self-reported use of antimicrobial medicine in the children from 0-12years.

A cross-sectional survey was carried out in Nepal among 101 respondents. For the data collection, a previously validated Lebanese instrument was used. It was further modified according to the cultural and contextual setting of the survey location. Data was collected by face to face method with the assistance of structured questionnaire. Questionnaire was pre-tested with 5 respondents for assessing readability and validity. Data was analyzed using SPSS version 23. Mean, standard deviation, percentage and frequency were used to analyze data. For the scale constructed by summated variables the reliability tests by Cronbach Alpha coefficient was used. In order to find out differences in knowledge and self-reported antibiotic use according to demographic characteristics, Kruskal Wallis H test, Mann Whitney U test and Chi square test were used. P value <0.05 is considered as statistically significant.

Among the respondents, 86.1% were young parents between 20-40 years, while female (69.3%) remained the highest respondents. Most of the respondents i.e. 71.3% had either secondary or university education. Almost all (97%) reported having 1-2 children under 12 years. Most of parents (92.1%) bought antibiotic according to doctor's prescription and 82.2% of parents followed instruction of health care personnel. On the other hand, 30% of parents would stop giving antibiotic when their children feel better. Only, 4% would share antibiotic with another sick children suffering from the same symptoms and 9% would keep antibiotic stock at home for later use. Fever was reported (47.5%) to be the most common reason for giving antibiotics and most parents (68%) thought that antibiotic reduce fever. More than half of the parents acknowledged that antibiotic kills bacteria. However, almost half (45.5%) reported that antibiotic also treats viral infection. Most of parents (74.3%) were unsure if Amoxicillin is an antibiotic. More than half (59%) knew that antibiotic overuse leads to antibiotic resistance and 73% of parents knew that antibiotic effectiveness is reduced if full course is not completed. Significant differences were found between "age of respondent" and purchasing antibiotics on doctors' prescription (p=0.009); and in between sharing antibiotics and "healthcare worker in the family" (p= 0.034). Also, significance differences in knowledge score were found with "education of parents" (p= 0.017) and "number of children" (p=0.031).

Although the parental knowledge regarding antibiotic was reported inadequate, the self-reported use of antibiotic was better. It was reported that most parents trust health care worker and follow their instruction. Therefore, recommendations should focus on training health care personnel on judicial antimicrobial use and educating parents in their doctor's visit. Further studies with adequate sample population are recommended to generalize results.

Keywords: antibiotic, antimicrobial medication, knowledge, practice, parents, children

Contents

1 Introduction

Antibiotics are antimicrobial drugs used to treat against bacterial infections in both human and animals (Centre for Disease and Control and Prevention (CDC) 2018). Antimicrobial drugs are chemicals that are biologically active against microorganisms. Mainly they act by inhibiting essential microbial functions for e.g., protein synthesis, DNA replication and cell-wall synthesis of infecting bacteria. (Gualerzi & Brandi 2013, 53.) Antibiotics are effective only against bacterial infection, they have no effect on the viral infection (CDC 2018). Along with the discovery of antibiotics in the human history, antibiotic resistance among pathogenic bacteria has been inevitable phenomena. Drug resistance is an intriguing aspect in molecular evolution, selecting fine mechanisms allowing survival under a hostile environment. In an evolution process, within the microbial population, such resistance genes are maintained and spread between the species of microbes. The main functions of such resistant genes are to counteract the toxic effects of antimicrobial drugs. (Gualerzi & Brandi 2013, 74.)

The problem of antibacterial resistance to the most standardly used antibacterial agents has announced anxiety that we may soon have to face a new post-antibiotic era (Gualerzi & Brandi 2013, 23). Antibacterial or antimicrobial resistance (AMR) threatens to increase the range of infections caused due to bacteria, parasites, viruses and fungi. The absence of effective antimicrobial leads to failure in major surgeries and cancer chemotherapies. Resistant infection leaves patients with higher costs, a longer duration of illness and the use of more expensive drugs. In the year 2016, the number of multi-drug resistant tuberculosis (TB) people alone has increased to 490 000. Drug resistance has started to complicate the fight against the human immunodeficiency virus (HIV) and malaria as well. (World Health Organization (WHO) 2018.)

Every year, death toll as a consequence of infection due to bacteria resistant to antibiotic reach up to 33000 that is comparable to the more than passenger of 100 medium size airplane (European Centre of Disease Prevention and Control (ECDC) 2020b). According to the Council on Foreign Relation reports, the global death toll from drug-resistant infection could be over 10 million by 2050 in case the AMR issue is ignored. That is more than the death toll caused due to cancer, auto accidents, diabetes and other disease combined (Chordas 2018).

Consumption of antibiotic is at an increasing pace. In between the year 2000 to 2010, antibiotic consumption has increased by 36% where India, China and the USA being the biggest consumers respectively. (Van Boeckel 2014.) ECDC (2017), reported that the average consumption of antimicrobials for the systemic use in EU/EEU countries was 23.4 defined daily doses (DDDs) per 1000 inhabitants per day) which ranged from 11 to 34.1 DDDs. The

profound use of antimicrobial agents is speeding up the evolutionary process of microbes. Ultimately, such resistance is acting as a seed to germinate microbes, which are resistant to all available antibiotics exposing threat to human civilization (Pattanayak 2017). From the year 2007 to 2015, the death toll due to infections with Kleibsiella pneumonia resistant to carbapenems (a group of last-line antibiotics) increased by six-fold. Such trend is worrisome because these bacteria spread easily in health care setting upon inadequate infection prevention measures. In addition, the death toll due to infection with third-generation cephalosporin-resistant E-coli increased by four-fold. (European Centre for Disease Control and Prevention (ECDC) 2020b.)

Colistin is a last-line antibiotic used to treat carbapenem-resistant Pneumoniae infections. One of the biggest concerns is that in 2013, for the first time, resistance to Colistin found in Europe. (ECDC 2014.) Therefore, it is extremely important to monitor the antibiotic usage in both humans and animals to prevent AMR in the future. Nonetheless, besides the consumption of antibiotics, some other factors such as the insufficiency of resources for bacterial diagnosis and resistance determinants also plays a major role in the rapid development of resistance. A study completed in developing countries such as Bangladesh, Nigeria, Sri Lanka and Vietnam showed that the consumption of antibiotics per habitants is less than a tenth of that in the industrialized world. However, the resistance situation in such countries is much worse. (Sköld 2011, 28.)

Antimicrobial resistance is exposing human health to the extreme threat. Therefore, in order to mitigate this problem, in May 2014, Global Action Plan has introduced five objectives:

1. To improve and understand antimicrobial resistance.
2. To strengthen knowledge using surveillance and research.
3. To minimize infection.
4. To improve usage of antimicrobial agents,
5. To secure sustainable investment against antimicrobial resistance. (WHO 2015.)

In response to the global action plan, the first antibiotic awareness week started in 2015 (WHO 2015). After this event, antibiotic awareness week is repeated every year for increasing awareness about global antibiotic resistance. Nonetheless, misconception about antibiotic use is still predominant among people. Especially children are one of the most vulnerable groups in the society in the context of antimicrobial misuse. Parents play a vital role in taking care of children. Therefore, the study intends to find out the Nepalese parent’s knowledge and practice of antimicrobials in children.

2 Common Childhood illnesses

There are many common infectious illnesses of childhood from birth to 18 years. Under upper and lower respiratory tract, illnesses such as bronchiolitis, bronchitis, common cold, ear infection, pneumonia, sinus infection, sore throat, cold sore, conjunctivitis, diphtheria, influenza, mononucleosis, mumps, Respiratory syncytial virus, strep throat, tuberculosis (TB) and pertussis are common illness. Most of the respiratory tract infections are caused by virus except some of the illnesses such as TB, Pertusis etc. Under gastrointestinal tract, common illnesses are gastroenteritis, giardia, hepatitis A, pinworms and Rotavirus. Gastroenteritis are caused by both virus and bacteria. Under Meningitis, common illnesses are Hemophilus influenzae type B, Neisseria meningitis, Streptococcus pneumonia and viral meningitis. Most of these diseases are bacterial origin except viral meningitis. Under skin diseases, most common illnesses are Chickenpox, Fifth diseases, German measles, Hand, foot and mouth diseases, head lice, Impetigo, Methicillin-resistant Staphylococcus Aureus, Molluscum, Ringworm on body and scalp, Roseola and Scabies. Most of these diseases are also caused by virus (Figure 1). (Georgia Department of Public Health 2019; Harcourt 2011, Chapter 2.)

Common infectious illnesses from birth to 18 years			
Eye,ear,nose, throat and chest Bronchiolitis, Bronchitis, Common cold, Ear infetion, Pneumonia, Sinus infection, Sore throat, Cold sore, Conjunctivitis, diptheria, influenza, monomucleosis, Mumps, Respiratory syncytial virus, Strepthroat, Tuberculosis(TB) and Pertusis	**Gastrointestinal** Gastroenteritis, Giardia, Hepatitis A, Pinworms and Rotavirus	**Meningitis** Haemophilus influenza type B, Nisseria meningitis, Streptococcus pnuemonia and Viral meningitis	**Skin and Rash** Chickenpox, Fifth diseases, German measles, Hand, foot and mouth diseases, Head lice, impetigo, Methicillin resisitant Staphylococcus Aureus, Molluscum, Ringworm on body and scalp, Rosela and Scabies

Figure 1: Common childhood illnesses (Georgia Department of Public Health 2019; Harcourt 2011, Chapter 2)

2.1 Antimicrobial medication in the children

The use of antibiotics for children is common in many parts of the world. A study completed in an urban community in Mongolia revealed that about 3/4 of children were given antibiotics. (Togoobaatar et al. 2010.) A next study completed in eight countries revealed that in the cities of Pakistan and Bangladesh, more than 98% of the children used antibiotics in their first 6 months of life. While in the other cities of Nepal, Tanzania, Peru, and India, more than half of the children received antibiotics by the age of six months. Furthermore, the difference in antimicrobial use is more than 11-fold in Pakistan than in Brazil. (Rogawski et al. 2017.) Another study, completed in the US, Korea, Italy, Germany, Spain and Norway revealed that south Korean children used the highest rate of antimicrobial in the first two years of life following by Italy, Spain, the US, Germany and lowest in Norway. The difference rate was significant i.e. 7.5-fold in Korea than in Norway. (Rogawski et al. 2017.) The rate of antibiotic use in children has vast regional differences. On the other hand, the regional differences in antibiotic prescription in the hospitalized neonates remains insignificant. (Versporten et al. 2016) Other different conditions are associated with the exposure to antibiotics during childhood such as the systemic antibiotic use in pregnancy, the antibiotic prophylaxis of vaginal group B-streptococcus and delivery, sepsis treatment, treatment of common pediatric infection and through the food supply chain and drinking water (Principi & Esposito 2016).

2.2 Common causes for antimicrobial use

The antibiotic usage in children is the highest in South Asia counting for 4.9 courses per child per year. Such repeated antibiotic usage in daily life in the treatment of diarrhea and non-specific respiratory illness does not follow international recommendations. (WHO 2017.) According to the Pediatric Antibiotic Policy (2016) antibiotics are not indicated for the treatment of diarrhea and vomiting unless there is a sign of septicemia, blood/mucus in stool or immune compromised children. Furthermore, common cold or non-specific upper respiratory tract infections should not be treated with antibiotics since they are caused by viruses (CDC 2018). Therefore, a program for rational antibiotic use in children might have the most fruitful impact in South Asia.

In Finland, respiratory tract infection was the most common cause for a primary care visit (74%), followed by skin/wound infections and urinary tract infections (Rautakorpi 2001). In outpatient care, the prescribing of antibiotics constitutes of 90% where primary health care counts for 60% (Public Health Agency of Sweden 2015). Respiratory conditions were predominant reason for using antibiotics in all age groups accounting for 43% of those using antibiotics. Lower respiratory tract infection and diarrhea are still one of the leading causes of the death in all age group in Nepal (Nepal Burden of Disease 2017). For the treatment of

diarrhea, in the 97% of cases, pharmacists unnecessarily recommended non-prescription antimicrobial while less than half (44%) recommended oral rehydration therapy. Only 3% suggested physician's consultation. (Wachter 1999.)

2.3 Antimicrobial prescription and influencing factors

The most common causes of prescribing antibiotics are the respiratory conditions (Mihani 2018; CDC 2018; Chem 2018). According to CDC (2019), at least 50 percent of antibiotic prescriptions for acute respiratory infections are unnecessary. Over-prescription of antibiotics for the respiratory tract infection was also notified in Sweden by the work of Strama (Public Health Agency of Sweden 2015). Although antimicrobial prescription should be dominated by presence of micro-organism infection, several other factors also influence in prescribing antimicrobial medication. According to Morley et al. (2020), those factors are divided into four categories which are 1. primary care provider (PCP); 2. patient factors; 3. clinical factors and 4. social and system factors. These factors are explained in the following paragraphs (Fig 2).

Under PCP, antibiotic prescription is affected by physician's time constraints, PCP's perception of patient's expectation for antibiotic and personal factors. Insufficient time and excessive patients in limited time are positively associated with higher prescription level (Kumar, Little & Britten 2003; O'Connor 2018). In addition, PCP's perception of patient's expectation for antibiotics, physician's educational level and work experiences have also direct effect on antibiotic prescription. (O'Connor 2018.) According to Morley et al. (2020), antibiotic prescription level decreases over the course of academic year. Physician with higher qualification such as post graduate qualification and physician with more than 20 years of experience are less likely to prescribe antibiotic. Also, PCPs who updates professional knowledge by journals, seminars etc. are less likely to prescribe antibiotics. However, physician practicing only in outpatient are more likely to prescribe antibiotics. (Bharathiraja 2005.) Also, General Practitioner aged 60 or more are most likely to prescribe antibiotic (Morley et al. 2020).

Another factor affecting antibiotic prescription is patients' factors that includes patient's expectation for antibiotic prescription and patient's socioeconomic background (O'Connor 2018; Morley et al. 2020). Patient's with private health insurance and parents with higher income do not expect antibiotic prescription (Salazar, English & Eiland 2012). The most common reason for expecting antibiotic is fever with upper respiratory tract infection (Zyoud et al. 2015). Also, younger parents and parents with higher education have lower expectation of antibiotics (Shlomo et al. 2003).

Under clinical factors, there are two factors affecting antibiotic prescription i.e., diagnostic uncertanty and perceived severity of illness (O'Connor 2018; Morley et al. 2020). Antibiotic

prescription is most likely when there is a diagnostic uncertainty, abnormal finding of rales, rhonchi, percussion abnormality and external anterior cervical lymphadenopathy. Under perceived severity of illness, patients having four or more sign and/or symptoms are more likely to be prescribed antibiotics. This means patients with more sign and symptoms are more likely to be prescribed antibiotic. (Morley et al.2020.) Influence of day care provider and self-medication are also affecting antimicrobial prescribtion. Day care providers practices and policies may encourage guardians to consult GP and ask for antibiotic prescription which act as a driving force for expecting antibiotic prescription. (O'Connor 2018; Rooshenas 2014.)

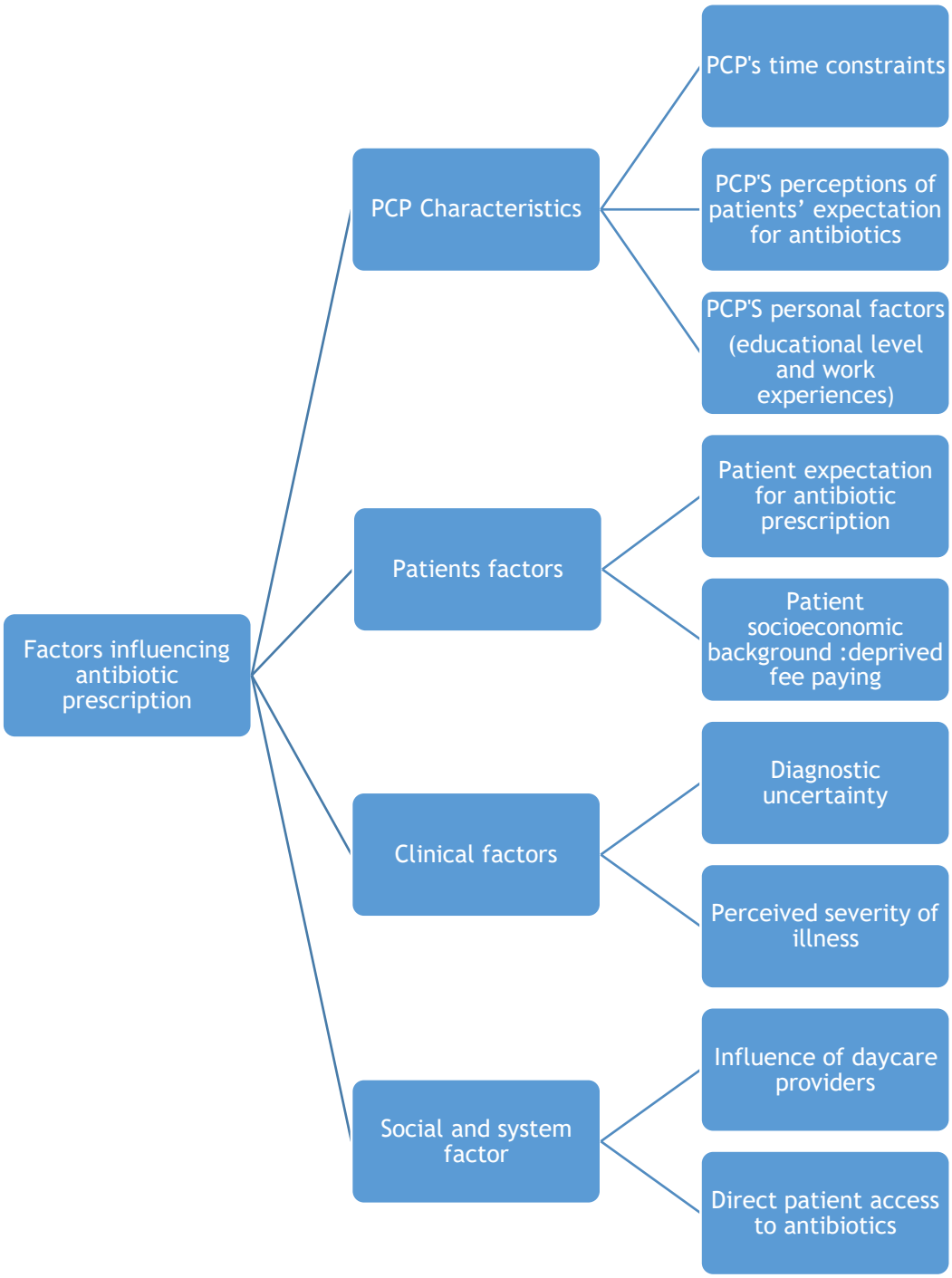

Figure 2: Factors influencing antibiotic prescription (Morley et al. 2020)

2.4 Consequences of antimicrobial use

Antimicrobial use in children differs from the antimicrobial use in adults. Early-life antibiotic exposure have a broader effect on health altering gut microbiome, exposing them with long-term consequences such as diabetes mellitus and obesity (Yallapragada 2015; Reist 2016). Antimicrobial use in children is positively related to a long-term distortion in the intestinal microbiota that may hinder the development of a healthy immune system and metabolism (Korpela et al. 2016). If the immature immune system is exposed to the altered bacterial environment, the possibility for abnormal immunity development increases later in life. Such alteration in the flora is a possible explanation for childhood obesity, asthma, allergies and other autoimmune diseases. (Perna 2016; Principi & Esposito 2016.) Therefore, it is essential to consider the intestinal microbiota while prescribing antibiotics for the children (Yallapragada 2015).

3 Factors affecting Antimicrobial Resistance

There are several factors contributing to the development of the Antimicrobial Resistance. In the following paragraphs, some of the important contributing factors are elaborated to further understand AMR.

3.1 Off-label prescription

One of the unseen factors affecting antibiotic resistance is the use of off-label medicine. The off-label use of medicine means use of licensed medicine outside their recommended age, dose, indication and route (Mukattash 2016). In other word, the use of off-label replaces the treatment option by the clinicians when the approved medication either failed or are related to undesirable adverse event (Tansarli 2012). The off-label antibiotic use is very common in many parts of the world (Mukattash 2016; Porta 2010; Hafeez 2020). The use of off-label medicine was prescribed according to the vulnerability of ill patient where no alternative antibiotic might be available and mainly prescribed in sepsis, lower respiratory tract infection and as a surgical prophylaxis (Porta 2010). The frequency of off-label prescription of antibiotic in children varied from 1%-94% (Mukattash 2016; Porta 2010; Hafeez 2020; Tansarli 2012; Palčevski 2012). Although using off-label antibiotic outweighs the risk, the issue cannot be ignored in the shed of development of AMR.

3.2 Self-medication

In many countries of the world, including Nepal, many groups of antibiotics are available without doctors' prescriptions. The free availability of antibiotics means the power of making decision about antibiotic use shifts from the health care worker to the general public. Such

free availability predisposes incorrect use of antibiotics against insusceptible pathogens and in inadequate doses (Sköld 2011, 28). Such behaviors imply that the general public is contributing in the development of AMR.

Self-medication with antibiotics in children is one of the issues of concerns in many parts of the world. Caregiver have misconception about self-medication. Most of them believed that antibiotic is needed for flu or cold. (Togoobaatar et al. 2010.) Self-medication with antibiotics for the treatment of common cold was predominant in Kuwait counting for 54.5% of the respondents (Awad 2015). Self-medicating with antimicrobial varies in a significant level according to different parts of the world. In Mongolia, 42% of parents had used antibiotics without prescription. (Togoobaatar et al. 2010.) In rural and urban China, 62% and 48 % of parents respectively, practiced self-medication with antibiotics in children (Yu 2014; Chang 2018). In Cameroon, 51% had practiced self-medication with antibiotics in children (Grace-Ange 2019). Also, in Yemen, Lebanon and Saudi Arabia, 60%, 35% and 68.6% respectively, had used antibiotics without medical prescription. (Mohanna 2010; Mouhieddine 2015; Mohammad 2019). While on the other hand, in Cyprus and Greece, self-medicating with antibiotics was 6% and 10% respectively for the similar symptoms if doctors had prescribed antibiotics earlier (Rouusounides 2011; Panagakou 2011).

Pharmacist (86%) were reported as the main source for non-prescription medication (Togoobaatar et al. 2010). It has been reported for upto 97% cases of diarrhea, pharmacists recommended antimicrobials. When patients are treated inappropriately with antibiotic, patients are exposed to the risk of antimicrobial resistance without any benefit. (Morgan 2011.) Other factors such as inappropriate duration of treatment, increasing or decreasing doses also expose patient for the development of AMR (Le 2011; Morgan 2011). Self-medication with antimicrobials also predisposes patients with potential and proven adverse events. There has been shown upto 90% risk for masked diagnosis in self-medication (Morgan 2011). There are many factors contributing self-medication such as perception of illness, assuming similarity to the previous illness, drug seller's advice and previous prescription (Le 2011). Poverty was also reported as the major socioeconomic driving force for self-medication. Furthermore, using of left-over antibiotics and incompliance of the full course are also major behavioural factors affecting self-medication. (Johansson 2010.) In addition, incompliance of full course is often predominant in using non-prescribed medicine (Mate 2019).

3.3 Environmental factor

There is complex relationship between environmental and human health in the contribution of antimicrobial resistance. Various factors contaminate environment that is interlinked with each other that enhancing transfer of antibiotic resistance genes in pathogenic organism.

Such inter-relation of various factor perpetuates the cycle of antimicrobial resistance (Figure 3) (Fletcher 2015).

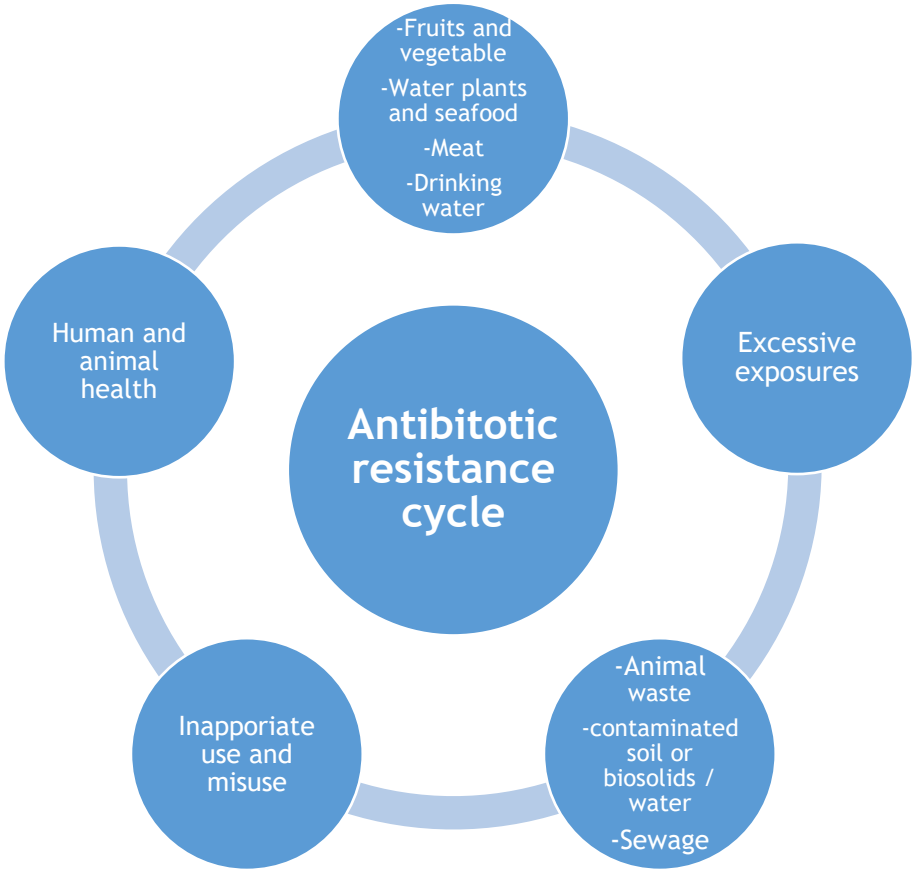

Figure 3: Relationship of antibiotic resistance cycle with various environmental factor (Fletcher 201)

Antibiotics used in animals enters in the environment through various ways. Animal waste or fecal excretion ends into the manure tank or waste which further ends into the vegetable fields. From vegetable fields, antibiotics further disposed to ground water and aquatic environment. Such disposition has direct effect on the aquatic organisms as well as terrestrial organism (Sarmah 2006; Fletcher 2015.) Significant amount of antibiotic residue is excreted in the faeces and urine of animals that can exceed up to 90 % of the main compound (Fletcher 2015; Alcock 1999). Such animal excreta are further used to the field for vegetables as an organic supplement of fertilizer. Bacteria from animal gut exposed to the antibiotics were five times more likely to be resistant which is further intensified in animal manure sharing extrachromosal antibiotic resistance plasmids with non-resistant microbes. (Sarmah 2006.)

3.4 COVID-19

Corona virus disease 2019 (COVID-19) is one of the highly pathogenic infectious diseases into the human population in twenty-first century after severe acute respiratory syndrome (SARS) and middle east respiratory syndrome (MERS) epidemic. It is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) emerged in Wuhan, China in December 2019 which is rapidly spread all over the world. (WHO 2020; ECDC 2020b; CDC 2020; Wang 2020.) From 31st December to 11 October, 37 287 908 laboratory confirmed COVID-19 cases were reported all around the world including 1 073 675 deaths (ECDC 2020c). Affected person suffer from mild to moderate respiratory illness in 80 % of diagnosed cases that recovers without any specific treatment. People with underlying medical problems for e.g. Cardiovascular diseases, diabetes, chronic respiratory disease, cancer and older age groups tends to develop serious illness that count for around 20 % of the cases. (WHO 2020; Getahun 2020.)

While treating the patients in such pandemic, antimicrobials plays vital role. Firstly, antimicrobial agents such as Azithromycin® and antivirals are used empirically in clinical trials as a potential therapy to treat severe acute respiratory syndrome of COVID-19 despite of the lack of the evidence to improve clinical outcomes. Secondly, antimicrobials are frequently used for the treatment of either perceptive or confirmed bacterial co-infection related to COVID-19. Also, antimicrobials are used for health care associated infection related to prolonged admission in critical care. (Rawson 2020b; Zhou 2020.) Sen (2020) stated that 50 % deceased COVID-19 cases reported secondary infection. Critically ill COVID-19 patients often require prolonged hospitalization associated with hospital acquired bacterial infection that needs antibiotic treatments (Yam 2020). When bacterial infections are confirmed, rational antibiotic use relieve symptoms and lower the leucocyte count. For the treatment of SARS, there was no evidence to prove any effect in clinical outcome. The use of broad-spectrum antibiotics increases the risk of dysbacteriosis that can cause hospital acquired infection. (Wang 2020.)

Despite the lack of etiological evidence, significant number of COVID-19 cases were treated with antibiotic (Wang 2020). Although COVID-19 recovers without any specific treatment, studies reported that up to 100 % of diagnosed cases received antibacterial therapy (Wang 2020; Chibabhai 2020; Yam 2020; Cornelius & M Hong 2020; Rawson 2020a). In children with COVID-19 cases, antibiotic use ranged from 19 % to 100 % (Wang 2020). In those cases, only 1%-27% had reported to have coinfected with fungus or bacteria. (Yam 2020; Cornelius & M Hong 2020; Rawson 2020a; Wang 2020.) Such abundant use of antimicrobials agent in this pandemic further exacerbate the global threat of antimicrobial resistance bacteria that could ultimately lead to more death and morbidity (Hsu 2020; Getahun 2020; ECDC 2020b; CDC 2020; Yam 2020)

4 Parental knowledge and practice about antimicrobial medication

Knowledge about antibiotics varies worldwide (Cantarero-Arévalo et al. 2017). The majority of participants have an inadequate knowledge about antibiotics (Elong et al. 2017; Abu et al. 2019). People are uncertain about weather colds and flu are caused by bacteria or virus. A majority of people agreed that cold and flu were caused by both virus and bacteria. Also, they thought that antibiotics are usually or sometimes necessary to treat viral infections. (Larson 2009.) Fever was believed to be the most common cause for antibiotic prescription (Agarwal 2015). Almost 2 out of five parents believed that fever demands antibiotic use (Alsuhaibani 2019). And majority of parents believed that in order to treat fever and cough, antibiotics are necessary (Chan 2006).

In Macedonia, although majority were aware that antibiotics treats bacterial infection, almost 1/4 also thought that antibiotics also treats viral infection (Alili-Idrizi 2014). Also, in India, parents did not know if antibiotics are used against virus or bacteria. More than 1/4 of parents knew that antibiotics are used to treat bacterial infection and almost same number of parents also believed that antibiotics are used against viral infection (Agarwal 2015.) Also, In Lima and China, majority of the respondents, believed that antibiotics also treats viral infection (Paredes 2019; Yu 2014). Futhermore, most (41.3%) of the viral infections were also treated by antimalaria agents. Almost (44.8%) of the children were also treated by antibiotics without doctors' prescriptions. (Ocan 2017.)

Insufficient knowledge about antibiotics is the major issue of concern (Awad 2015). In Kuala Lumpur, Malaysia, although most of parents (65%) acknowledged the difference between antibiotic and pain relievers (Alili-Idrizi 2014), only around 1 out of 5 parents could identify the most common antibiotics (i.e., Amoxacillin® and Penicillin®) used in children (Teck 2016). While in Macedonia, most people could recognize Penicillin® as an antibiotic. (Alili-Idrizi 2014). In Saudi Arabia, many acknowledged that Amoxacillin® is an antibiotic (Al-Ayed 2019). In Palestine, more than half parents acknowledged that Amoxacillin® is an antibiotic while only less than 10% could acknowledge Amoxacillin Clavulanic acid® was an antibiotic (Zyoud 2015).

When assessing knowledge about antibiotic resistance, most parents (53% to 79%), responded that inappropriate usage of antibiotics reduces efficacy and promote bacterial resistance (Teck 2016; Alsuhaibani 2019; Yu 2014; Chang 2018; Fatokun 2014). Also, most people were aware that antibiotic may cause harm (Shlomo 2003). On the other hand, majority of parents were unaware of the term antibiotic resistance (Agarwal 2015) and believed that flu-like symptoms resolved faster when antibiotics are given (Zeru 2020). Antibiotic use in children is directly related to the misconception and lack of knowledge leading to the expectation for an antibiotic prescription. Such expectation leads to an unnecessary use of antimicrobials for

upper respiratory tract infection, ear infection and pneumonia. (Salazar et al. 2012.) Most people used the antibiotics for treating the common cold in Lebanon (Mouhieddine 2015). Only about 1/3 of the parents believed that upper respiratory tract infection (URTI) is caused by virus and cannot be treated by antibiotics. Significant number of parents also believes that antibiotic prevent complication from URTI. (Zeru 2020.)

Parents have inadequate knowledge about the consequences of antibiotic use i.e., adverse effect, recurrent infection and emergence of antibiotic resistance. Many believed that the presence of fever demands antibiotic administration. (Zahreddine, Hallit, Shakaroun, Al-Hajje, Awada, Lahoud 2018; Agarwal 2015.) and antibiotics can be discontinued when symptom is relieved (Barker et al. 2017). Only half of the participants complete the full course of antibiotics and most discontinued when symptoms disappear which is driven by inadequate knowledge about the function of antibiotics and AMR. (Fatokun 2014). Most parents also believed that antimicrobials shorten the duration of illness (Coxeter et al. 2017).

4.1 Association between knowledge, attitude and practice (KAP) about antibiotic use and demographic features

A significant positive association found between the parental educational level and the knowledge about antibiotics (Zahreddine et al. 2018; Yu 2014; Samar 2020; Cantarero-Arévalo et al. 2017). Also, social determinants such as the income level and accessibility of medical services were associated with the antibiotic misuse (Agarwal 2015; Parimi 2004; Alili-Idrizi 2014). Knowledge about use of antibiotic is associated with educational level (Alili-Idrizi 2014; Khoury 2018; Mate 2019; Agarwal 2015; Parimi 2004), monthly income (Khoury 2018; Mate 2019) and access to media source of information on the topic (Kuzujanakis 2003). Participants with higher educational background had better knowledge regarding prevention and treatment of upper respiratory tract infection. On the other hand, participants with less education tends to believe that antibiotics are needed to treat cold and influenza. (Larson 2009.) Lower parental knowledge about antibiotic is associated with lower parental education, fewer children and less exposure to information in media regarding AMR (Kuzujanakis 2003). There was negative relationship between age of the respondents and knowledge about antibiotic (Mate 2019).

Non-prescribed antibiotic use was associated with lack of instruction on antibiotic use, incompletion of the course and poor knowledge about antibiotics. Use of non-prescribed antibiotics was higher in for self-user than for the children. Non-prescribed antibiotic is mostly obtained from pharmacy. The main reason for using non-prescribed medicine was reported as the perception of unnecessity to visit health care facility. (Mate 2019.) In addition, parents prefer to buy antibiotics without doctors' prescription because it takes

considerably less time than in hospitals (Chan 2006). Such malpractice is due to lack of knowledge about undesirable effect and bacterial resistance (Chan 2006;Ocan 2017).

When assessing KAP about antibiotic use; education, gender and previous use of antibiotics were predisposing factors (Agrawal 2015). Gender was associated with incompliance of antibiotic course (Fatokun 2014). Caregivers with high antibiotic knowledge use more antibiotic than caregivers with low knowledge score. Demanding for antibiotic prescription and keeping antibiotic stock at home is higher in caregiver with low knowledge score. All caregiver with high and low knowledge score believed that antibiotic do not have side-effect and also cure all infections. (Parimi 2004.) All caregivers in general donot expect for the antibiotic prescription. But, caregiver with higher income, with private insurance and hispanic donot expect antibiotic prescription. (Salazar 2012.)

People with low-income were unaware of the risk of prematurely stopping the treatment. Therefore, for them, it's a logical and an economical decision to stop the antibiotics once the symptoms alleviate. (Barker et al. 2017.) Parental lower socio-economic status is more associated with antibiotic misuse and malpractice (Moro 2009) that flourish AMR. Malpractices include poor adherence to the prescribed dose, the storage of antibiotics at home for future use and the self-reported practice of the antibiotic use without doctors' consultation. (Khoury 2018.) Such practices imply that the general public are contributing for the development of AMR. Another leading cause behind AMR might be misconception whether antibiotics can be used in viral infection or not. In fact, such misconception is likely to do more harm than good (Salama 2018).

5 Guidelines for antibiotic use

Many authorities are working continuously for the prevention of AMR by providing key messages for general public, doctors, nurses, veterinarians, pharmacists and other health workers (WHO 2015; ECDC 2020a; CDC 2020). It is recommended that any prescription or dispensing of the antibiotic should be proceeded by all the efforts to test and confirm the necessity of the antibiotics for human or animals. To prevent antimicrobial resistance, infection prevention is a valuable measure. For the prevention of infection, different measures should be applied such as handwashing, using clean/disinfected or sterile instruments according to the defined need, safeguarding the environment and providing vaccination whenever it is appropriate. (WHO 2015; ECDC 2020a; CDC 2020.)

World Health Organization regional office for Europe (2011) developed strategic plans on AMR. For the prevention and control of antimicrobial resistance, WHO (2018) developed guidelines intended for the individual is as follows: 1. Using antibiotics only under the

prescription of certified health professional. 2. Not demanding antibiotics. 3. Following the instruction of the health care worker. 4. No sharing of leftover antibiotics. 5. Using infection prevention measures e.g. regular hand washing, hygienic food preparation, safe sex, vaccination and avoiding close contact with infected people.

About hygienic food preparation, WHO has provided with five salient concepts which are: 1. keeping clean; 2. storing raw and cooked food separately; 3. cooking thoroughly; 4. storing food in a safe temperature; 5. using safe water and safe raw material which means choosing food which is produced without using antibiotics for the growth promotion or prevention of diseases in healthy animals. (WHO 2018.)

In ECDC (2020a) guidelines, the key messages for the general public are as follows: 1. Antibiotics are only prescribed by medical doctor. 2. Antibiotics is not painkiller and do not treat every illness. 3. Taking antibiotics against colds and flu will not help get better any faster and also may have side effects. 4. It takes time to get better. 5. Pharmacist are key person for seeking advice. There are other medicines that relieves symptoms.

In addition to these key messages, general public is also recommended to act responsibly to save antibiotics (ECDC 2020a). According to CDC (2020) guidelines, key messages includes protecting family by asking questions with health care personnel, cleaning hands, getting vaccination, being aware of sign and symptoms of infections, using antibiotics appropriately, practicing healthy habit around animal, preparation of food safely, staying healthy while traveling and preventing STDs.

6 Purposes and objectives of the study

The purpose of this study is to assess the self-reported use of antibiotics in Nepalese children aged between 0 to 12 years old. The objectives of this study are to assess the:

1. the knowledge of Nepalese parents towards antibiotics use in their children,
2. the self-reported use of Nepalese parents towards the antibiotics use in their children and
3. the differences in knowledge and self-reported antibiotic use of Nepalese parents according to demographic characteristics.

Based on this survey results, recommendations will be prepared for Nepalese parents about safe antimicrobials use according to the global recommendations.

7 Methods

The study process started in March 2018 by choosing the topic. Both authors were interested in the topic and after discussion, mutual interest was found to work with. The first author was interested in the issue of AMR in the initial period of nursing education more than a decade ago in Nepal. After working in different units of the hospital such as oncology, medical/surgical ward etc., the same issue about antibiotic resistance came across repeatedly. The second author has experience in a heart center in surgical intensive care unit and operation room for more than five years. While caring different heart disease patients, the author experienced critical cases. In some cases, the treatment periods were prolonged causing major financial and psychological burdens for the patient and family while in other cases causing the death of the patient.

The study process continued with literature review completed mainly by the first author, and operationalization of the research questionnaire by the second author. Both authors reviewed and accepted the survey questionnaire. The validation of the survey questionnaire was on the responsibility of the both authors. Both authors worked full-time, and the study completed in the “vacation time” as a part of master's studies. The first authors expended all the costs including travelling and materials expenses used for data collection. The data collected while she was in study leave. Therefore, no financial support received for conducting this survey.

7.1 Study setting

This survey completed in the rural setting of Nepal (Figure 4) in the Kawasoti Municipality. The Kawasoti municipality is located in the western region of Nepal and falls under the Nawalparasi district. The total number of the households in Kawasoti is 14104 in which the population of male counts for 28616 and for female 33805 (Kawasoti Municipality 2015).

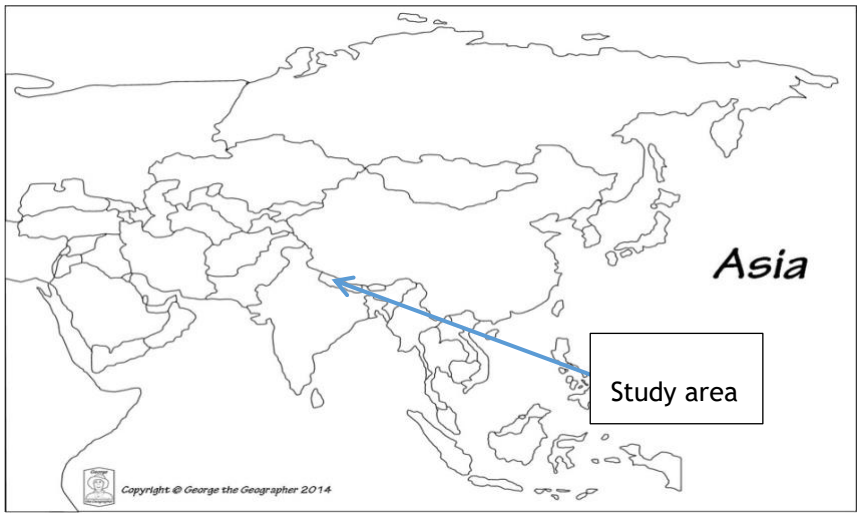

Figure 4: Study location (George 2014)

Geographically Nepal has hills and mountains covers 17%, Terai (plain area) covers 68% of areas and snow covering mountains covers 15% of total area of the nation (Amatya 2016). The diverse topography of the nation is a challenge to access health care services that force people to use available resources in that setting. In many cases, getting services from health post is beyond the reach of the public because of the lack of transportation facilities. Of those people living in the urban areas, not all are economically strong to get health services. The issue that many antibiotics are categorized as non-restricted prescriptive antibiotics in Nepal means that antibiotics are freely available without doctors' prescription (Ministry of Health and Population-Nepal, Kafle & others 2014). Such circumstances and practices mean that the use of antibiotics is in the hand of public probably contributing to the development of antibiotic resistance.

7.2 Study design

Cross sectional descriptive study design was chosen because it is used to find out the current practices as they naturally occur, to identify problems with current practice and to make judgement or to determine what others in similar situations have completed (Grove, Burns & Gray 2013, 215). In cross-sectional descriptive design, data is collected at a single point of time from group of people (Hickson 2013, 76; Grove et al. 2013, 221). This cross-sectional descriptive survey conducted among Nepalese parents as a targeted group to study their knowledge and use of antimicrobials in their children with the assistance of a survey questionnaire. To describe the sample and study of variables, descriptive statistics are conducted. Descriptive statistics such as Mean used to measure central tendency and Stander deviation (SD) is calculated to measure the dispersion (Grove, Gray, Bomer-Norton & Daniel 2019, 30).

7.3 Operationalization of a questionnaire

After literature review, validated questionnaire was adapted from the Mouhieddine and Tamim research from year 2015. Permission from the author was granted via e-mail on 2018.09.21 by Hani Tamim, PhD, associate professor of Internal Medicine, American university of Beirut Medical Center Lebanon. The questionnaire was adapted and edited to blend according to cultural and contextual setting of the Nepalese parents' group.

Operationalization is a methodological process for constructing measurable variables of the concepts of the instrument, which helps researcher to transform the idea or concept according to the study objectives (Curtis & Drennan 2013, 136). The study goals and objectives operationalized as a self-administrated survey questionnaire of 33 questions (Appendix I). Among 33 questions, questions 1 to 6, 9 to 33 modified from Tamim (2015). Questions 1 to 8 were background questions, 9 to 19 were self-reported practice about antibiotic use and 20-33 questions about knowledge toward antibiotic. Self-reported practice

about antibiotic use is divided into two parts. In first part, questions 9-13 used Likert scale, while in the second part questions 14-18 were multiple-choice questions. In order to meet the contextual setting of the respondents, the term “antibiotic” refers to antimicrobials. Questions 7 and 8 are self-administered questions. Question number 7 asking the number of children under the age of 12 in the respondent’s household. They selected as a vulnerable age group for active diseases such as upper respiratory tract infection. The question number 8 asked presence and type of domestic animals as a predisposing factor for recurrent infections in the household. In the questionnaire “antibiotics” was used to refer to antimicrobial medication because public understands this term better.

7.4 Data collection

Two-daycare centers in Kawasoti Municipality provided verbal consent for data collection in the planning phase of the study. However written consent was approved before collecting the data. One of the two-daycare centers showed no interest in the data collection. Therefore, only 35 parents in one daycare center participated in the study. To reach the designated number of participants, another 66 parents recruited to fulfill the questionnaire in the personal houses and local market. Totally 101 parents participated in the data collection. To identify the confusion, each survey questions was asked and fill-up by author herself. Objective of the nature of study and voluntary participation explained for the respondents before they conducted the survey (Helsinki Declaration; TENK 2019).

The data collected as face-to-face interview using the survey questionnaire in September 2018. The total time used for data collection was two weeks (November 19 to December 02, 2018). Data collection time was targeted to the winter season of the year to make sure that people understand the idea of the study. In that period of time, cold and upper respiratory tract infection was very common. By this, it aimed to improve the reliability of the data collection making possible for the respondents recalling how they are taking care of their sick children. Many participants were eager to know if they have been doing right thing for their children. In the daycare center, parents were interested about the topic and the author had to provide health education about certain health issues for e.g. how to prevent infections, what is antibiotics, functions, indications of antibiotic etc.

7.5 Data analysis

After reviewing the 103 survey questionnaires, two incomplete questionnaires excluded from the study. Altogether 101 answered questionnaires used for the analysis.

The data analysis started with entering data from hard copy survey questionnaire to Microsoft office Excel 2010 by both authors. After that, data was transferred to the Statistical Package for Social Sciences program (SPSS) version 23. To avoid any possible human error, one author

was repeating data while other was entering into the computer matrix program. Collected data analyzed using descriptive quantitative statistics for e.g. frequency and percentage for categorical variable; and Mean and SD for numerical variables. Mean value is calculated from 1 to 5 Likert scale that is strongly agree, agree, unsure, disagree and strongly disagree. Highest point referred to the right answer. To ease the interpretation of the results; totally agree and agree merged into agree while disagree and totally disagree merged into disagree. However, the analysis was done by using 1-5 Likert scale. Summation variables for first part of practice (self-reported antibiotic use) was calculated from 5 statements. Second part of practice consisted of 5 statements, which was analyzed using frequency and percentage. Knowledge was divided into three categories i.e. “function of antibiotics for the analysis” (7 statements), “recognition of antibiotics by trade name” (4 statements) and “adverse effect of antibiotics” (4 statements).

When choosing between parametric and non-parametric test, researcher should analyze the distribution of data. In parametric test of significance, the researcher must make assumptions. One of the most important assumptions is that the variable we have measured in the sample is normally distributed in the population to which our findings will be generalized. (Munro 2005, 109.) For assessing the normal distribution of the variables, normality test was conducted by Shapiro-Wilk’s W test (Grove et al.2013, 541). After conducting normality test for knowledge score (Shapiro-Wilk’s W test p=0.013, df =101) and practice score for Likert scale (Shapiro-Wilk’s W p=0.000, df=101), non-normal distribution of variables was found. Therefore, parametric technique was not suitable for the study. On the other hand, nonparametric test has no assumption about the distribution of the variable (Munro 2005, 123). Furthermore, if the variables are measured at nominal or ordinal level, nonparametric analysis is the best analysis technique (Grove et al. 2019, 310). In this study, the practice (part 1) and knowledge score were significantly skewed. Therefore, nonparametric test was the appropriate test for the study.

To find out the significance differences according to demographic characteristics with knowledge and practice, summation variable for practice and knowledge was calculated. Summation variable for practice and knowledge was calculated by using 5-statements (part 1) and 15-statements consecutively. Under non-parametric test, Kruskal- Wallis H test examine the differences among two or more groups at once using variation analysis while Mann-Whitney U test examine differences among two groups (Munro 2005, 152; Grove et al. 2019, 323-324). Mann-Whitney U test was used to analyze differences in knowledge and practice (part 1) with gender, employment, health care worker in the family, number of children and domestic animal. And Kruskal-Wallis H test was used to analyze difference in knowledge and self-reported use with age, occupation and education. For education, illiterate and elementary was merged into one category due to a smaller number of participants in illiterate category. For pairwise comparison, again Mann Whitney test was used with all categories of

education. While doing pairwise comparisons, there was possibility of type I error. Therefore, Posthoc test with Bonferroni correction was used to avoid type I error.

Pearson chi-square (X2) test was used to analyze differences in practice (part 2) with demographic characteristics. (Munro 2005, 110; Grove et al. 2019, 311.) There are mainly four underlying assumptions for chi- square test which are frequency data, adequate sample size, measures independent of each other and theoretical basis for the categorization of the variables (Munro 2005, 111) The statistical significance level was set at a P value less than 0.05 (Figure 5).

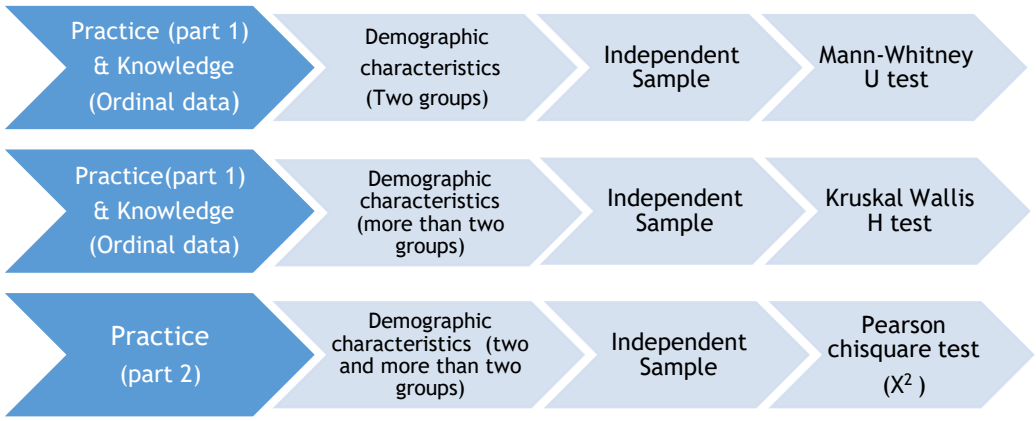

Figure 5: Statistical decision chart for analyzing differences in knowledge and practice according to demographic characteristics (Munro 2005; Grove et al. 2019)

8 Reliability and validity of the survey

Reliability has two aspects i.e. consistency and repeatability. Consistency means when a phenomenon remains same, it will be measured as the same even if measured by several observers or if used several measuring methods. In this survey Cronbach's alpha coefficient used to measure reliability of summated variables. If Cronbach alpha is 0.8 or more, the scale to measure knowledge and self-reported practice considered as having strong reliability. (Newell & Burnard 2011, 143-144.) In our study, in adopted research questionnaire Cronbach alpha of knowledge was reported a=0.80 and attitude a=0.64 (Kim et al. 2011; Mouhieddine 2015).

Repeatability means that the result remains the same in the several occasions when the phenomenon remains unchanged (Newell & Burnard 2011, 143-144). In order to measure the reliability, the consistency and the repeatability of the instrument, the questionnaire was pre-tested with two pilot respondents (n=2), one master level Nepalese student and another Nepalese Ph.D. student both living in Helsinki. After completion of pre-testing in Helsinki, further pre-testing was done in the actual setting of Nepal. The questionnaire was tested with three pilot Nepalese respondents (n=3), two master level students and one literate voluntary participant to make sure questions are understandable from the view of respondents to ensure face validity. After testing, following changes made, the answers placed from positive to negative order as suggested by one Nepalese pilot respondent. Such measures were applied to ensure face validity under content validity to make sure that actual respondent understand the context our survey was trying to measure. In addition, pretesting of the survey question also ensures readability of the survey method enduring that targeted sample could understand the concepts of the questionnaire. (Grove et al. 2019, 268-269.) While conducting data collection, the questionnaire translated from English to the Nepali language by the author (R.K.) who is a native Nepalese language speaker.

Validity means an instrument owns all the attributes to measure accurately that is supposed to measure (LoBiondo-Wood & Haber 2018, 264). For the study to be valid, the researcher has to obtain data via sound scientific methods. Bias and/or confounding variables have the potential to compromise the validity of the result. The more influence of these factors, the less valid the result will be. (Melnyk & Fineout-Overholt 2011, 83.) Validated questionnaire was further modified in order to blend into the cultural setting of the sample population in respect to the cross-cultural validity (Polit & Beck 2018, 241).

Of the 101 survey respondents, 35 responses collected from the daycare center and rest 66 from individual houses, workplaces and city center. Such variability of the participants means heterogeneity of the sample. By this heterogeneous convenience sampling, it is aimed to reach more variability in between-participants in compared to the homogenous sample. The reliability of the study may be stronger by this. (Grove et al. 2013, 289.) However convenient sampling provides ground for biases with little opportunity for control (Grove et al. 2013, 363; Grove et al. 2019, 243). On the other hand, adequate sampling is the keyway to ensure external validity, which is often magnified by ensuring the circumstances reflecting the real world (Newell & Burnard 2011, 148). In this study, the sample population is not representative, which means no generalizability of the result for the Nepalese parents but a specimen describing local challenges in the use of antimicrobials among children.

9 Ethical consideration

The ethical committee of Laurea's research and ethical board provided an ethical review for the planned study (Appendix 4) as required by Finnish National Board on Research Integrity (TENK 2019). According to TENK, responsible research of conduct must be followed to be ethically acceptable and reliable in order to obtain credible results. The researcher follows the principle of integrity, meticulousness and accuracy while conducting research during recording, presenting and evaluating results. The data collection method complies with scientific criteria and ethically sustainability. Results should report fairly and openly. Other researchers' works should respect and cite appropriately. The permission for using the map of the Asia was granted by George the Geographer on 2nd of June 2020 via email. The ethical issues should closely consider in all research related to the human subject (TENK 2019).

The principle subject of the research is directly related to human i.e. parents of children. Principles of Psychologists, code of Ethics for Nurses and the American Psychological Association (APA 2010) provide guidelines for protection of right of human subjects in biological and behavior research. The rights of human subjects are (1) the right to self-determinants; (2) the right to privacy; (3) the right to autonomy and confidentiality; (4) the right to fair treatment and justice; and (5) the right to protection from discomfort and harm (Grove et al. 2013, 163-164).

In this study, self-determinants safe-guarded by asking the individual for the permission before conducting survey. In the informed consent, information provided to the participants for the free will of participation for the survey that respects autonomy. Voluntary participation is ensured by making sure that no external enforce is applied. The right to privacy determined by making sure to determine the right to determine the time, extent and general circumstances to share information with or withheld from others (Grove et al. 2013, 169; TENK 2019). In this study, the human personal privacy ensured by making participants to choose time limit for the survey and time of the survey according to his/her will. Question concerning personal profession was not answered from all the participants due to cultural factor. Their decision was accepted as their right to share their information regarding personal matter.

According to the regulation (2016/679) of the European Parliament and the council states, the protection of natural person during data processing is fundamental right and protection of personal data is concerned subjects' rights (Official Journal of The European Union 2016). In this study, no sensitive or personal data (e.g., name, identification number, e-mail addresses) collected and no register completed. During the data management, questionnaires enclosed in a secure place so that unauthorized persons have no access to the original data. After 6 months of publication of the survey study, the collected questionnaires will be destroyed.

The right to autonomy and confidentiality confined by making sure that the subject from which data collection remained concealed by using numbers for the participants for e.g., 1, 2 and so on. After collection of data, anonymity was maintained throughout the processing of data by making sure that unauthorized person has no access to the raw data (Grove et al. 2013, 172). The right to fair treatment ensured by collecting data from all the possible participants regardless of social, cultural, racial and sexual biases in the society (Grove et al. 2013, 173). In this research, all the potential participants included regardless of age, gender, social status and cultural status. Participants were chosen from the population.

In addition, data collection was completed according to the available schedule one can provide according to his/her life situation. The right to protect from discomfort and harm based on the ethical principle of beneficence which means one should do good and above all do not harm (Grove et al. 2013, 174). In our research, temporary discomfort seen regarding answering of certain questions. Some level of anxiety and embarrassment was faced by the participants while responding to some questions. Therefore, personal reassurance was provided not to reveal their personal data. Furthermore, secure place was chosen to share their information to avoid any harassment while answering survey questions.

10 Results

10.1 Demographic characteristics of parent

Of the 101 respondents, almost half (48.5%) of the responding families were between 20-30 years of age and rest were over 41 years. The majority (69%) were female, and the rest (31%) were male. Most of the respondents reported to have university degree (39.6%). Only 9.9% respondents were illiterate. Most of the participants (58.4%) were employed whereas 39.6% reported as unemployed. In the occupation, most of the participants reported as housewives (36.6%) and 25% of participants were farmers. Only 17.8% had health care worker in the family. Most of the participants (97%) reported having one or two children and the rest had 3-4 children. Only, 33.7% had domestic animals mostly dog, cow, chicken and goat (Table 1).

Variables	Characteristics	Frequency (Percentage)
1. Age of Respondent	1. 20-30 2. 31-40 3. >41 Total	49 (48.5%) 38 (37.6%) 14(13.9%) 101(100%)
2. Gender	1. Male 2. Female Total	31(30.7%) 70(69.3%) 101(100%)

Variables	Characteristics	Frequency (Percentage)
3. Education	1. Illiterate 2. Elementary 3. Secondary 4. University Total	10 (9.9%) 19 (18.8%) 32 (31.7%) 40 (39.6%) 101 (100%)
4. Employment Status	1. N/A 2. Unemployed 3. Employed 4. Student Total	1 (1.0%) 40 (39.6%) 59 (58.4%) 1 (1.0%) 101(100%)
5. Occupation of respondent	1.N/A 2. Housewife 3. Farmer 4. Teacher 5. Others* Total	17 (16.8%) 37 (36.6%) 25 (24.8%) 7 (6.9%) 15 (14.9%) 101(100%)
6. Health care worker in family	1.Yes 2. No Total	18(17.8%) 83(82.2%) 101(100%)
7. Number of Children under 12 years	1. 1-2 2. 3-4 Total	98(97.0%) 3(3.0%) 101(100%)
8. Domestic Animal	1. Yes 2. No Total	34(33.7%) 67(66.3%) 101(100%)

Table 1: Demographic characteristics of Nepalese parents

(N/A =Not applicable; *Others = Business, beautician, receptionist, tailor, cashier, social worker, cook, barber, technician, labor, driver, medical personnel)

10.2 Self-reported antimicrobial use in the children

The self-reported use of antimicrobial medicine was measured in two parts. In the first part, five summation variables with Likert scale, measured self-reported use of antimicrobial medicine in children. In the second part, five summation variables with multiple-choice questions, measured self-reported use of antimicrobial medicine in children.

10.2.1 Self-reported antimicrobial use (part 1)

Of the 101 respondents, 92.1% reported that they seek doctors' prescription of antibiotics for their children (mean= 4.72, SD 0.896). Most of the respondents, 82.2% reported giving antibiotics according to instruction of health care personnel (mean 4.32, SD 1.435). Only 29.7% respondents would stop giving antibiotics when their children start getting better (mean 3.82, SD 1.717). Most of the respondents, 88.1%, reported that they would not give same antibiotics to another sick child suffering from the same symptoms (mean 4.7, SD 0.819). Only 8.9% of respondents would keep antibiotic stock at home (mean 4.59, SD 1.088).

The internal consistency measured by Cronbach α for five summation variables was α= 0.523. The total mean for the five summation variables of "sum of practice" (part 1) was 4.43 and SD 0.722. The frequency distribution of summation variables was not normally distributed (Table 2).

Summation variable for self-reported use of antimicrobials (Mean=4.43, SD= 0.722 & α= 0.523)	N (%)	Mean (SD)
Buying antibiotics for a sick child without doctors' prescriptions to help them get better quickly. Agree Unsure Disagree* Total	 5 (5.0%) 3 (3.0%) 93 (92.1%) 101 (100%)	4.72 (0.896)
Giving antibiotics according to instruction of health care personnel. Agree* Unsure Disagree Total	 83 (82.2%) 2 (2%) 16 (15.8%) 101 (100%)	4.32 (1.435)
Normally stopping antibiotics when my child starts feeling better. Agree Unsure Disagree* Total	 30 (29.7%) 2 (2%) 69 (68.3%) 101(100%)	3.82 (1.717)
Usually giving same antibiotics to another sick child suffering from the same symptoms. Agree Unsure Disagree* Total	 4 (4%) 8 (7.9%) 89 (88.4%) 101 (100%)	4.79 (0.819)
Usually keeping antibiotics stocks at home for later use. Agree Unsure Disagree* Total	 8 (8.9%) 4 (4.0%) 90 (89.1%) 101 (100%)	4.59 (1.088)

Table 2: Self-reported use of antimicrobials in children (part 1) (*Indicates correct response)

10.2.2 Self-reported antimicrobial use (part 2)

The most frequent answer for "How do you get antibiotics for your children?" was doctors' prescription (92.1%). Almost half (47.5%) of the respondents used antibiotics for fever followed by fever and cold (23.8%) and others 24.8%) (others indicates diarrhea, cold, stomach-ache, urinary tract infection, skin disease, pneumonia, fever and diarrhea, fever and stomach-ache, fever and urinary tract infection, urinary tract infection and skin infection,

fever and pneumonia, fever, cold and pneumonia, skin disease and pneumonia, not yet given antibiotics & home remedies). Furthermore, most of the parents "always" (64.4%) consulted doctor if their children get sick. When asking reason for not consulting doctor, only one quarter (24.8%) answered that there is no need for a doctor followed by unavailability of doctor (14%) and others (9.9%) (others indicates money, no time, home remedies, no need for doctor and home remedies & medical personnel in family). The most frequent answer of waiting time periods for starting antibiotics was 1-2day (46.8%). Only one quarter (25.7%) started antibiotics directly and another 1/4 (23.8%) waited for 3-4 days (Table 3).

Self-reported use of antimicrobial medicine	Options	N (%)
Parents getting antibiotics for children by	1. Doctor's prescription 2. Pharmacist's advice 3. doctor's prescription and pharmacist's advice 4. Non-medical person's advice 5. Personal choice 6. I do not know Total	93 (92.1%) 2 (2%) 5 (5%) 0 (0%) 0 (0%) 1 (1%) 101 (100%)
Reason for giving antibiotics to children	1.Fever 2. Fever and cold 3. Others* 4. I do not know Total	48 (47.5%) 24 (23.8%) 25 (24.8%) 4 (4%) 101(100%)
Consulting a doctor when children is sick	1. Always 2. Most of the time 3. Often 4. Sometimes 5. Never Total	65 (64.4%) 19 (18.8%) 14 (13.9%) 1 (1%) 2 (2%) 101 (100%)
Reason for consulting a doctor when children get sick	1. Not applicable 2.Unavailability of doctors 3. No need for doctor 4. Others** Total	52 (51.5%) 14 (13.9%) 25 (24.8%) 10 (9.9%) 101 (100%)
Waiting time before starting antibiotics when children get sick	1. Directly 2.1-2 days 3. 3-4 days 4. >4 days 5. Directly and 1-2 days 6. Directly and 3-4 days 7. I do not know Total	26 (25.7%) 44 (43.6%) 24 (23.8%) 1 (1%) 2 (2%) 1 (1%) 3 (3%) 101 (100%)

Table 3: Self-reported use of antimicrobial (part 2)

10.3 Parental knowledge about antimicrobial medicine

Parental knowledge about antimicrobial is analyzed in three sections i.e., function of antibiotics, recognition of antibiotics by tradename and adverse effect of antibiotic.

10.3.1 Functions of antibiotics

More than half (53.5%) of the parents knew that antibiotics kill bacteria. On the other hand, only few parents (15.8%) knew that antibiotics are not effective against viral infection. Almost 1/3 had no knowledge that antibiotics are effective against viral or bacterial infection. When asking if antibiotics cure all infections, less than half guardians/ parents (43.6%) knew that antibiotics do not work for all infections. Furthermore, only few participants (25.7%) were aware that antibiotics do not reduce pain and inflammation. More than half of the participants' (68.3%) believed that antibiotic reduce fever. Less than half (46.5%) knew that antibiotics do not cure stomachache and disinfect digestive tract. In contrary, most of the participants (79.2%) knew that same antibiotics are not effective against different infections.

The summation variable for functions of antimicrobials consisted of seven statement with internal consistence α= 0.357.(Grove, Bruns and gray 392.) The total mean of summation variable for function of antibiotics was 3.2 and SD 0.588. The frequency distribution of summation variables was normally distributed (Table 4).

Summation variable for functions of antibiotics (Mean=3.2, SD= 0.588 & α= 0.357)	N (%)	Mean (SD)
Antibiotics killing bacteria. Agree* Unsure Disagree Total	 54 (53.5%) 36 (35.6%) 11 (10.9%) 101(100%)	3.78 (1.188)
Antibiotics treating viral infections. Agree Unsure Disagree* Total	 46 (45.5%) 39 (38.6%) 16 (15.8%) 101 (100%)	2.46 (1.315)
Antibiotics curing all infections. Agree Unsure Disagree* Total	 26 (25.7%) 31 (30.7%) 44 (43.6%) 101 (100%)	3.39 (1.356)

Summation variable for functions of antibiotics (Mean=3.2, SD= 0.588 & α= 0.357)	N (%)	Mean (SD)
Antibiotics reducing pain and inflammation. Agree Unsure Disagree* Total	 37 (36.6%) 38 (37.6%) 26 (25.7%) 101 (100%)	2.84(1.309)
Antibiotics reducing fever. Agree Unsure Disagree* Total	 69 (68.3%) 17 (16.8%) 15 (14.9%) 101 (100%)	2.03(1.323)
Antibiotics are medicine that curing stomachache and disinfect digestive tract. Agree Unsure Disagree* Total	 19 (18.8%) 35 (34.7%) 47 (46.5%) 101 (100%)	3.51 (1.354)
Same antibiotic using to treat different infection including (upper respiratory tract, urinary, skin, genital, etc.) Agree Unsure Disagree* Total	 9 (8.9%) 12 (11.9%) 80 (79.2%) 101 (100%)	4.4(1.225)

Table 4:Knowledge of parents about function of antibiotics (* Indicates correct response)

10.3.2 Recognition of antibiotics by tradename

When assessing the recognition of antibiotics by tradename, more than half of the respondents (55.4%) knew that Paracetamol® is not an antibiotic. However, only 44.6% knew that Brufen® is not an antibiotic. In addition, 3/4 or more had no knowledge if Amoxicillin® (74.3%) or Aspirin® (80.2%) is an antibiotic.

The summation variable for recognition of antimicrobials by tradename included four variables with internal consistency α= 0.60. The total mean of four summation variable for recognition of antibiotics was 3.46 and SD 0.765. The frequency distribution of summation variable was normally distributed (Table 5).

Summation variable for recognition of antibiotics by tradename (Mean=3.46, SD=0.765 & α= 0.60)	N (%)	Mean (SD)
Amoxicillin® is an antibiotic. Agree* Unsure Disagree Total	 21(20.8%) 75(74.3%) 5 (5%) 101 (100%)	3.28 (0.198)
Aspirin® is an antibiotic. Agree Unsure Disagree* Total	 4 (4%) 81 (80.2%) 16 (15.8%) 101(100%)	3.24 (0.789)
Paracetamol® is an antibiotic. Agree Unsure Disagree* Total	 13 (12.9%) 32 (31.7% 56 (55.4%) 101(100%)	3.79 (1.373)
Brufen® is an antibiotic. Agree Unsure Disagree* Total	 16 (15.8%) 40(39.6%) 45(44.6%) 101(100%)	3.54 (1.323)

Table 5: Knowledge of parents about recognition of antimicrobial by tradename (® Refers to retail name of medicines) (* Indicates correct response)

10.3.3 Adverse effect of antibiotics

When assessing the adverse effect of antibiotics, more than half (59.4%) knew that antibiotics overuse leads to antibiotics resistance. In addition, half or more of the participants were aware that antibiotics may induce allergic reaction, antibiotics may cause side effects and the effectiveness of the antibiotics is reducing if a full course of antibiotic is not completed.

The summation variable for the adverse effect of antibiotics consists of four statement with internal consistency α= 0.30. The total mean of four summation variable for the adverse effect of antibiotics was 3.78 and SD 0.753. The frequency distribution of summation variables was normally distributed (Table 6).

Adverse effect of antibiotics Mean= 3.78, SD= 0.753 & α= 0.30	N (%)	Mean (SD)
Antibiotic overuse leading to antibiotic resistance. Agree * Unsure Disagree Total	 60 (59.4%) 32 (31.7%) 9 (8.9%) 101(100%)	3.91(1.201)

Adverse effect of antibiotics Mean= 3.78, SD= 0.753 & α= 0.30	N (%)	Mean (SD)
Antibiotics inducing an allergic reaction. Agree* Unsure Disagree Total	 50 (49.5%) 26 (25.7%) 25 (24.8%) 101(100%)	3.4 (1.415)
Antibiotic not causing side effects. Agree Unsure Disagree* Total	 25 (24.8%) 23(22.8%) 52 (51.5) 101(100%)	3.5 (1.514)
Antibiotics effectiveness reducing if full course of antibiotics is not completed. Agree* Unsure Disagree Total	 74 (73.3%) 19 (18.8%) 8 (7.9%) 101(100%)	4.33 (1.225)

Table 6: Knowledge of parents regarding adverse effect of antibiotics (* Indicates correct response)

10.4 Differences in knowledge and self-reported use of antimicrobial medication of Nepalese parents according to demographic characteristics.

10.4.1 Differences in Practice according to demographic characteristics

Kurskal Wallis H test (see Table 7) with a significance level of 0.009, refers that three age groups differ significantly on practice about purchasing antibiotics without doctors' prescription. Looking at the mean ranks, age group of 31-40 scored highest (56.50) followed by age group >30 (53.18). Mean ranks of age group of 20-30 scored lowest (46.11). Pairwise comparison was done with Mann Whitney test to compare all possible comparisons. For the comparison to be significant, the significant level of 0.0167 (0.05/3=0.0167) was used instead of 0.05 according to Bonferroni correction in Posthoc analysis. The first comparison was completed with 20-30 and 31-40 age groups. Significance level of 0.003 indicates that there were significant differences between these two-age groups. The second comparison between 20-30 and >41 age groups (p=0.216) was not significant when used Bonferroni correction. In the third test, comparison was done with 31-40 and >41 age group (p=0.099) was also not significant. Therefore, these data referred that parents of 31-40 age group showed better practice in purchasing antibiotics with doctors' prescription than parents of aged 20-30 and >41. There was no significant difference with parents of age 20-30 and >41. Also, there was no significant difference with parents of age 31-40 and >41.

Mann Whitney U (see Table 7) test with a significance level of 0.034, refers that family with health care worker or without health care worker differs significantly on sharing antibiotics with another sick children. Comparing the mean ranks with or without health care worker in the family, family without health care worker scored highest (52.67) than family with health care worker (43.28). These data suggested that the family without health care worker shared significantly less antibiotic than the family with health care worker.

	Demographic characteristics	Mean rank	Kruskal Wallis H (p value)	Mann Whitney U
Antibiotic purchase with doctor's prescription when children gets cold	Age class of the respondent 1.20-30 2.31-40 3.>41	 46.11 56.50 53.18	 0.009	
Not sharing antibiotics with another sick children suffering from same symptoms	With Health care-worker in the family Without Health care-worker in the family	43.28 52.67		0.034

Table 7: Significant level of practice (part 1) according to demographic characteristics

In chi square test of practice (part 2), none of the results shows significance difference in practice (part 2) according to demographic features.

10.4.2 Differences of Knowledge score according to demographic characteristics

The Kruskal-Wallis H test (see Table 8) with significant level 0.017, indicates that the three groups with different educational backgrounds differs significantly on their knowledge score. Among the three groups, mean rank of respondents with university level scored highest (61.25), followed by elementary/illiterate (44.29) and secondary level (44.27). Pairwise comparison was done with Mann Whitney test to compare all possible comparisons. For the comparison to be significant, the significant level of 0.0167 (0.05/3=0.0167) was used instead of 0.05 according to Bonferroni correction in Posthoc analysis. The first comparison was completed in illiterate/elementary and secondary education (p=0.960) was not significant when used Bonferroni correction. The second comparison between illiterate/elementary and university education (p=0.020) was also not significant. The third comparison was done with secondary and university education. Significance level of 0.013 indicates that there was significant difference between these two groups. Therefore, these data referred that parents with university level of education scored higher in knowledge about antibiotics than parents with secondary and elementary education/ illiterate parents. There was no significant

difference in knowledge level between parents with elementary/illiterate and secondary level of education. Also, there was no significant difference with elementary/illiterate and university level of education.

The Mann Whitney U test (see Table 8) with significance level of 0.031, indicates that the two groups according to the number of children differs significantly on their knowledge score. Among the two groups, mean rank for the family with 3-4 children scored highest (85.83), followed by the family with 1-2 children (49.93). These data referred that the family with 3-4 children scored significantly higher knowledge score than the family with 1-2 children.

	Demographic characteristics	Mean rank	Kruskal Wallis H P-value	Mann Whitney U P-value
Knowledge score	Education: 1.Illiterate & Elementary 2.Secondary 3.University	 44.29 44.27 61.25	0.017	
Knowledge Score	Number of children: 1. 1-2 2. 3-4	 49.93 85.83		0.031

Table 8: Significant level of knowledge score according to demographic characteristics.

11 Discussion

To our knowledge, this is the first known study of knowledge and practice of antibiotics in parents conducted in Nepal. This study could provide comprehensive knowledge and self-reported practice about antimicrobial use of the parents. Before understanding the results of this survey, it is crucial to understand the main demographic characteristics of the parents. It was noteworthy that 86% parents were in between the age of 20-40 and only 14% parents aged >41 which means more than 4/5 of the parents were young. Almost all 97.9% had 1-2 children in their family and majority of the respondents had either secondary or university level of education that may have impact in our survey result. In addition, this survey was conducted in the urban setting where accessibility of mass media and availability of information could be easier than in the rural area.

In demographic characteristics, questions about number of children and domestic animal were self-administered. The intention of these self-administered questions was to find out

any potential impact on parents' knowledge and self-reported use of antimicrobials. In this study, there was significant differences between number of children with knowledge score which is also addressed by Kuzujanakis (2003). There were not any significant differences in parental knowledge and self-reported use of antibiotic according to domestic animal.

In this study, statistically significant differences were found between knowledge score of antibiotics with parental education which is consistent with previous studies (Zahreddine et al. 2018; Yu 2014; Samar 2020; Cantarero-Arévalo et al. 2017; Kuzujanakis 2003). Also, it suggested that majority of respondents aged 31 to 40 purchased antibiotics on doctors' prescription. However, when analyzing knowledge about antibiotics, Mate (2019) reported that people with higher age has less knowledge about antibiotics in contradiction to the study by Kuzujanakis (2003). Furthermore, in this study, family without health care worker shared significantly less antibiotic than the family with health care worker which was contradictory according to Khoury (2018). In addition, the family with 3-4 children had better knowledge than the family with 1-2 children which is in consistent with the study by Kuzujanakis (2003).

It was interesting to identify public practices contributing to the development of AMR. In this survey, questions such as buying antibiotic without doctors' prescription, stopping antibiotic when children feel better, sharing antibiotics and keeping antibiotic stock at home were asked to find out the practices of antibiotic use that could potentially accelerate AMR. In this study, only 5% would give antibiotic without doctors' prescription. Such practices vary countrywise for e.g., in Lebanon, Saudi Arabia, Yemen, Kuwait, Mongolia, China, Cameroon, Indonesia and Uganda, 35%-68% self-medicated with antibiotics without doctor's prescription (Awad 2015; Togoobaatar et al. 2010; Yu 2014; Chan 2018; Grace-Ange 2019; Mohanna 2010; Mouhieddine 2015; Mohammad 2019; Kurniawan 2017; Ocan 2017; Al-Shibani et al. 2017). On the other hand, in Cyprus and Greece, only 6% and 10% self-medicated with antibiotic (Rouusounides 2011; Panagakou 2011).

In this study, majority (92%) disagreed on buying antibiotic without doctors' prescription. Also, in order to find out the reliability of the reported answer, open ended question was further asked explaining the same issue. Same percentage i.e., 92% reported correct answer i.e., "doctor prescription". Such repeatability ensured reliability of the reported answer through test-retest reliability test (Grove et al. 2013, 389). Furthermore, it was noteworthy to observe that 92% parents gave antimicrobials according to the doctors' prescription which is more than Lebanese study i.e., 65% (Mouhieddine 2015), Malaysian community i.e., 80% (Fatokun 2014) and Kosovo study i.e., 70% (Zajmi 2017). In addition, in this study, 68% parents would not stop giving antibiotics when their child start feeling better explaining compliance with the doctors' prescription. Such compliance was also observed in the study conducted in India (Agarwal 2015), where 83% parents were always compliant with doctors' prescription. On the contrary, a study done in Kuwait stated that only 58% would complete

the course (Awad 2015). In this study, 30% would stop antibiotic when child starts feeling better which is consistent with the study by Alili-Idrizi (2014) i.e.,31% and worse than the study by Salazar (2012) i.e., 5%. On the other hand, in United Arab Emirate (UAE) 80.5%, Malaysia 85% and Indonesia 42% would stop antibiotics when symptoms are improving (Salama 2018; Chan 2006; Kurniawan 2017).

In this study, it was reported that only 4% would share antibiotic to another sick children suffering from similar symptoms which is better than the study in Lebanon, Palastine, Malaysia and Macedonia where 26%, 27%, 24% and 43% respectively would share antibiotic with sick family members (Mouhieddine 2015; Zyoud 2015; Chan 2006; Alili-Idrizi 2014). Also, in present study, only 9% would keep left over antibiotics for later use. In Malaysia, Palestine, Macedonia and UAE, 15%-61% would keep leftover antibiotic for later use (Chan 2006; Zyoud 2015; Alili-Idrizi 2014; Salama 2018).

In this study, obvious lack of knowledge about antimicrobials is visible. However, parental use of antibiotic is far better than their knowledge about antimicrobials. Less than half (46%) reported that antibiotic treats viral infection. Also, in Sweden, Peru, UAE and Kuwait, 21%-54% stated that antibiotics treat viral infections (André et al. 2010; Salama 2018; Awad 2015; Paredes 2019). Furthermore, CDC (2019) also reported that the most common cause for prescribing antibiotic is of viral origin which account for at least 50% of antibiotic prescription.

In this study, more than half (53%) reported that antibiotic kills bacteria. Also, in UAE, Kuwait, Indonesia, Sweden, Macedonia and Saudi Arabia, 16.7% to 73% reported that antibiotic kills bacteria (Kurniawan 2017; André et al. 2010; Awad 2015; Salama 2018; Alili-Idrizi 2014; Al-Shibani et al. 2017). On the other hand, only 16% acknowledged that antibiotics were not effective against viral infections which is less than study in Macedonia i.e. 24% (Alili-Idrizi 2014). People are confused about whether antibiotics are effective against bacteria or virus (André et al.2010; Agarwal 2015; Awad 2015). In fact, in layman term, there is no difference between these two terms. Therefore, they use same term as “germ” for both bacteria and virus. Such uncertainty could explain the reason for finding difficulty to choose correct answer for whether antimicrobial is effective against virus or bacteria.

Inadequate knowledge revealed when people were asked about antibiotics by trade name. Almost half of them knew that Brufen® and Paracetamol® were not antibiotic. Whereas in Lebanon, 78% and 45%, respectively knew that Panadol® and Profen® were not an antibiotic (Mouhieddine 2015). In Saudi Arabia and Palastine, more than 90% knew that Paracetamol® is not an antibiotic (Al-Ayed 2019; Zyoud 2015). In addition, in this study, 74.3% were unsure if Amoxicillin® is an antibiotic while in the study conducted in Saudi Arabia less than 30% were

unsure (Al-Ayed 2019). In this study, only 20.8% could identify Amoxacillin® as an antibiotic which is in consistent with the study by Teck (2016) in Malaysia and far less than study in Palestine 55.6% (Zyoud 2015) and Indonesia 85% (Kurniawan 2017).

In present study, majority of parents (68%) reported that antibiotic reduce fever. In Macedonia, 65% answered correctly on "antibiotics are the same medication as Paracetamol ®" (Alili-Idrizi 2014). Agarwal (2015) and Al-Ayed (2019), in India and Saudi Arabia respectively, reported that fever is the most common cause for antibiotic prescription. On the contrary, in the study conducted in Cyprus, 87% disagreed on fever being cause for antibiotic prescription (Rouusounides et al. 2011). Also, in Lebanon, common cold was the main reason for giving antibiotics (Mouhieddine 2015). In present study, people have more knowledge about the adverse effects of the antimicrobials. Also, almost half knew that antimicrobials have side effect and could cause allergic reaction which is less than the study done in Cyprus (Rouusounides et al. 2011) and in Indonesia (Kurniawan 2017) where 93% and 63% respectively acknowledged about the potential side effect. In Macedonia, Indonesia and Saudi Arabia, 70%, 63% and 35% respectively were aware about allergic reaction (Alili-Idrizi 2014; Al-Shibani et al. 2017; Kurniawan 2017).

In present study, majority of parents knew about the antibiotic resistance that comply with the study by Fatokun (2014), Panagakou (2011) and Yu (2014). Most parents (73%) also knew that effectiveness of antimicrobials is reduced if full course is not completed which is more than the study in Macedonia 60%, in UAE 62% and in Saudi Arabia 55% (Alili-Idrizi 2014; Al-Shibani et al.2017; Salama 2018). Also, almost 60% agreed that antibiotic misuse increase antibiotic resistance which is in consistent with the study by Yu (2014). In UAE, Malaysia and Cyprus, 44%-90% reported that antibiotic misuse increase AMR (Salama 2018; Fatokun 2014; Rouusounides et al. 2011).

The reason behind having poor knowledge about antimicrobials could be many for e.g., inadequate information about antimicrobial in school curriculum, cultural aspects of trusting health care workers, unavailability of accessible mass media connection etc. It is noteworthy, to mention that since this survey has limited number of participants, only 101 respondents out of more than 14 thousand households, the result of the survey cannot be generalized for the entire city. Furthermore, convenient sampling could provide less opportunity to control for biases, that could have effect on the result as well (Grove et al. 2019, 242; Grove et al. 2013, 363).

12 Strength and Limitation

To our knowledge, this is the first known study to assess parental knowledge about antibiotic use in children. Upper Respiratory Tract Infection is the most common infection in winter season. Therefore, the study was also conducted in the winter season so that it is easier for parents to recall information about the way they are treating their children. Furthermore, the study was conducted by direct face to face interview. However, the respondents in this study (N=101) doesn't represent the population of the entire city (Kawasoti, Nepal). Therefore, the result generated by this study may not be generalized. In addition, using a convenient sampling could hinder representative of the actual sample population. It is noteworthy that the study is conducted in urban area of the Municipality. In the urban setting with educated sampling, access to mass media and receiving information might be easier than in the rural setting with less educated sample. Therefore, more studies with adequate sample participants, both with children and adult, are necessary to find out reliable and valid information.

13 Recommendation and Conclusion

This study has revealed that although parental practice about antibiotic is much better, knowledge about antibiotic is inadequate. Therefore, following recommendations are prepared:

1. People were not aware if antibiotic treats viral or bacterial infection. Therefore, information should be provided to differentiate between them stating that viral infections are self-limiting.
2. Most of parents reported that fever is the main cause for antibiotic prescription. Therefore, it should be focused that presence of fever do not always need antibiotic treatment. According to ECDC (2018) guidelines, it is mentioned that most of the winter illnesses get better in two weeks depending upon the illness.
3. Almost 3/4 parents were unsure if Amoxicillin® is an antibiotic which is one of the most commonly used antibiotics. Based on such result, doctors should explain about the medication and use of them while prescribing them.
4. Almost 1/3 (30%) would stop giving antibiotic when their children feel better which refers to the low knowledge about proper use of antibiotics. That is why, crucial role of the full course of antibiotics should be explained. Also, health care practitioner should emphasize the consequences of incompletion of antibiotic course.
5. In a long-term goal, curriculum of the school should include information about functions of antibiotics, proper use of antibiotics and consequences of antibiotic overuse and misuse.

6. AMR Campaign: AMR campaigns should be initiated from the grass root level, enabling local resources to implement in the actual field or community.
7. Information should be provided to prevent any infection such as personal hygiene, preparation and storage of food in right way etc.

Our findings could provide corner stones for the future investigations that could allow information to generalize information nationwide. Because AMR is a global phenomenon that could affect every individual in the world, the importance of awareness cannot be stressed enough. Moreover, this study also revealed inadequate knowledge about antibiotic. Therefore, available resources should be used to educate people about antibiotic and AMR.

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Figure

Tables

Appendices

Appendix 1: Operationalisation of research questionnaire

Set of questions	Operationalisation of variables	Questions and alternatives for the answers	References
A. Demographic characteristics of respondents	1. Age range of the Nepalese parents/ guardians.	1. Age of the respondent 1. 20-30 2. 31-40 3. >41	1. Applied (culturally validated by Mouhieddine 2015, Awad/2015, Manzinska 2017, Self-modified
	2. Gender of the Nepalese parent / guardian.	2. Gender 1. Male 2. Female	2. Applied (culturally validated by Mouhieddine 2015, Awad/2015, Manzinska 2017, Self-modified
	3. Educational background of the Nepalese parent /guardian.	3.Educational level 1. Illiterate 2. Elementary 3. Secondary 4. University	3. Applied (culturally validated by Mouhieddine 2015, Awad/2015, Manzinska 2017, Self-modified
	4. Work status of the Nepalese parents/ guardian.	4. Employment status 1. Unemployed 2. Employed 3. Student 4. Others	4. Applied (culturally validated by Mouhieddine 2015; Awad 2015; Manzinska 2017; Self modified
	5. Work background of the Nepalese parents / guardian.	5. Occupation: open ended answer	5. Applied (culturally validated by Mouhieddine 2015; Awad 2015; Manzinska 2017; Self modified
	6. Healthcare worker in the family.	6. Is there any healthcare worker in the family? 1. Yes (if yes choose from the options below) a. Nurse; b. Doctor; c. Pharmacist; d.Veterinarian; e. Other 2. No	6. Applied (culturally validated by Mouhieddine 2015. Awad 2015; Manzinska 2017; Self modified
	7. Number of children at vulnerable age group for active disease (upper respiratory tract infection).	7. Number of children under 12 years. 1. 1-2 2. 3-4 3. >4	7. Self-administered

Set of questions	Operationalisation of variables	Questions and alternatives for the answers	References
	8. Domestic animal as a predisposing factor for recurrent infection.	8. Is there any domestic animal in your home? 1. Yes a. Dog b. Cow c. Goat d. Chicken e. Others 2. No	8. Self-administered
B. Self-reported practice towards antibiotic use	9. Measuring the self-medicating practice on antibiotic use.	9.When my child gets cold, I would buy antibiotics without doctors' prescription to help them get better quickly. 1.Totally agree =1 2. Agree =2 3. Uncertain =3 4. Disagree =4 5. Totally disagree =5	9. Applied (culturally validated by Mouhieddine 2015, Zyoud (2015), self-modified)
	10. Measuring how parents / guardians follow medical advice.	10. I would give antibiotics according to instruction of health care personnel. 1.Totally agree =1 2. Agree =2 3. Uncertain =3 4. Disagree =4 5. Totally disagree =5	10. Applied (culturally validated by Mouhieddine 2015, Zyoud / 2015, self-modified)
	11. Explains if parents/guardian follow medical advice explicitly in that certain case.	11, I would normally stop giving antibiotics when my child starts feeling better. 1.Totally agree =1 2. Agree =2 3. Uncertain =3 4. Disagree =4 5. Totally disagree =5	11, Applied (culturally validated by Mouhieddine 2015, Awad/2015, Zyoud / 2015)
	12. Explains the attitude on sharing antibiotics.	12. I would usually give same antibiotics to another sick child suffering from the same symptoms. 1.Totally agree =1 2. Agree =2 3. Uncertain =3 4. Disagree =4 5. Totally disagree =5	12. Applied (culturally validated by Mouhieddine 2015, Awad/2015, Zyoud / 2015, modified by researcher)
	13. Explains what they do with leftover antibiotics.	13. I would usually keep antibiotic stocks at home for later use. 1.Totally agree =1 2. Agree =2 3. Uncertain =3 4. Disagree =4 5. Totally disagree =5	13. Applied (culturally validated by Mouhieddine 2015, Awad/2015, Zyoud / 2015)

Set of questions	Operationalisation of variables	Questions and alternatives for the answers	References
	14. Defines ways of getting antibiotics from the different options.	14. How do you get antibiotics for your children? 1. Doctor prescription 2. Pharmacist's advice 3. Non-medical person's advice 4. Personal choice	14. Applied (culturally validated by Mouhieddine 2015, self-modified
	15. Finds out the main reason to use antibiotics.	15. What is the reason for you to give antibiotics to your children? 1. Fever 2. Diarrhea 3. Cold 4. Stomach-ache 5. Others	15. Applied (culturally validated by Mouhieddine 2015, self-modified
	16. Finds out how often do parents seek medical advice from doctor.	16. Do you consult a doctor when your child is sick? 1. Always 2. Most of the time 3. Often 4. Sometimes 5. Never	16.Applied (culturally validated by Mouhieddine 2015, self-modified
	17. Finds out the cause for not seeking doctor's advice.	17. What is a reason for not to consult a doctor when your children get sick? 1. Money 2. Unavailability of doctors 3. No need for a doctor 4. No time	17. Applied (culturally validated by Mouhieddine 2015, self-modified
	18. Finds out duration before starting antibiotics.	18. How long do you wait before starting antibiotics when you children get sick? 1. Directly 2. 1-2 days 3. 3-4 days 4. >4 days	18. Applied (culturally validated by Mouhieddine 2015, self-modified
C. Knowledge towards antibiotic use	19. Finds out if parents are aware of how antibiotic work.	19. Antibiotics kill bacteria. 1. Totally agree =1 2. Agree =2 3. Unsure =3 4. Disagree =4 5. Totally disagree =5	19. Applied (cuturally validated by Mouhieddine 2015, Zyoud / 2015
	20. Clarify the misconception about antibiotic use.	20. Antibiotics treat viral infections. 1. Totally agree =1 2. Agree =2 3. Unsure =3	20, Applied (cuturally validated by Mouhieddine 2015, Zyoud / 2015

Set of questions	Operationalisation of variables	Questions and alternatives for the answers	References
		4. Disagree =4 5. Totally disagree =5	
	21. Finds out if they are aware of using antibiotic appropriately.	21. Antibiotics cure all infections. 1. Totally agree =1 2. Agree =2 3. Unsure =3 4. Disagree =4 5. Totally disagree =5	21, Applied (cuturally validated by Mouhieddine 2015, Zyoud / 2015
	22. Measures process about how antibiotic works	22. Antibiotics reduce pain and inflammation. 1. Totally agree =1 2. Agree =2 3. Unsure =3 4. Disagree =4 5. Totally disagree =5	22, Applied (cuturally validated by Mouhieddine 2015, Zyoud / 2015
	23. Clarifies the current trend for using antibiotics	23. Antibiotics reduce fever. 1. Totally agree =1 2. Agree =2 3. Unsure =3 4. Disagree =4 5. Totally disagree =5	23, Applied (cuturally validated by Mouhieddine 2015, Zyoud / 2015
	24. Measures concept for antibiotic use	24. Antibiotics are medicines that cure stomach-ache and disinfect digestive tract. 1. Totally agree =1 2. Agree =2 3. Unsure =3 4. Disagree =4 5. Totally disagree =5	24, Applied (cuturally validated by Mouhieddine 2015
	25. Finds out if they know about trade name of antibiotic	25. Amoxicillin is an antibiotic. 1. Totally agree =1 2. Agree =2 3. Unsure =3 4. Disagree =4 5. Totally disagree =5	25. Applied (cuturally validated by Mouhieddine 2015, self-modified
	26. Finds out if parents recognize antibiotic on the basis of trade name	26. Aspirin is an antibiotic. 1. Totally agree =1 2. Agree =2 3. Unsure =3 4. Disagree =4 5. Totally disagree =5	26. Applied (cuturally validated by Mouhieddine 2015
	27. Finds out if parents recognize antibiotic on the basis of trade name	27. Paracetamol is an antibiotic. 1. Totally agree =1 2. Agree =2 3. Unsure =3 4. Disagree =4 5. Totally disagree =5	27. Applied (cuturally validated by Mouhieddine 2015
	28. Finds out if parents recognize	28. Brufen is an antibiotic.	28, Applied (cuturally

Set of questions	Operationalisation of variables	Questions and alternatives for the answers	References
	antibiotic on the basis of trade name.	1. Totally agree =1 2. Agree =2 3. Unsure =3 4. Disagree =4 5. Totally disagree =5	validated by Mouhieddine 2015
	29. Finds out if they are aware of causing factor for developing antibiotic resistance	29. Antibiotic overuse leads to antibiotic resistance. 1. Totally agree =1 2. Agree =2 3. Unsure =3 4. Disagree =4 5. Totally disagree =5	29. Applied (cuturally validated by Mouhieddine 2015
	30. Reveals awareness about antibiotic side effects.	30. Antibiotics may induce an allergic reaction. 1. Totally agree =1 2. Agree =2 3. Unsure =3 4. Disagree =4 5. Totally disagree =5	30. Applied (culturally validated by Mouhieddine 2015
	31. Finds out if parents are aware about potential risk.	31. Antibiotic do not cause side effects. 1. Totally agree =1 2. Agree =2 3. Unsure =3 4. Disagree =4 5. Totally disagree =5	31. Applied (culturally validated by Mouhieddine 2015
	32. Measures if they aware about proper use of antibiotic.	32. Antibiotics effectiveness is reduced if a full course of antibiotics is not completed. 1. Totally agree =1 2. Agree =2 3. Unsure =3 4. Disagree =4 5. Totally disagree =5	32. Applied (culturally validated by Mouhieddine 2015, Awad/2015, Zyoud / 2015, self-modified)
	33. Measures parent's knowledge about antibiotic use in different diseases.	33. Same antibiotic can be used to treat different infection including (upper respiratory tract, urinary, skin, genital, etc.) 1. Totally agree =1 2. Agree =2 3. Unsure =3 4. Disagree =4 5. Totally disagree =5	33. Applied (cuturally validated by Mouhieddine 2015, Awad/2015, Zyoud / 2015, self-modified)

Appendix 2: Survey questionnaire

A. Demographic characteristics of respondents (Parents/Guardian)

1.	Age of the respondent	1. 20-30 2. 31-40; 3. >41
2.	Gender	1. Male; 2. Female
3.	Educational level	1. Illiterate 2. Elementary 3. Secondary; 4. University
4.	Employment status	1. Unemployed 2. Employed 3. Student
5.	Occupation:	
6.	Is there any healthcare worker in the family?	1. Yes (if yes choose from the options below); a. Nurse b. Doctor c. Pharmacist d. Others 2. No
7.	Number of children under 12 years	1. 1-2 2. 3-4
8.	Is there any domestic animal in your home?	1. Yes 2. No

B. Self-reported practice towards antibiotic use

a. Please answer the statements about self-reported practice towards antibiotic use by circulating the number between

totally agree 1 2 3 4 5 totally disagree

9.	When my child gets cold, I buy antibiotics without doctors' prescription to help them get better quickly.	1	2	3	4	5
10.	I give antibiotics according to instruction of health care personnel.	1	2	3	4	5
11.	I normally stop giving antibiotics when my child start feeling better.	1	2	3	4	5
12.	I usually give same antibiotics to another sick child suffering from the same symptoms.	1	2	3	4	5
13.	I usually keep antibiotic stocks at home for later use.	1	2	3	4	5

b. Please answer the questions about self-reported practice towards antibiotic use by circulating suitable options

14.	How do you get antibiotics for your children?	1. Doctor prescription 2. Pharmacist's advice 3. Non-medical person's advice 4. Personal choice

15. What is the reason for you to give antibiotics to your children?	1. Fever. 2. Diarrhea 3. Cold 4. Stomach-ache 5. Urinary tract infection 6. Skin diseases
16. Do you consult a doctor when your children are sick?	1. Always 2. Most of the time 3. Often 4. Sometimes 5. Never
17. What is a reason for you not to consult doctors when your children get sick?	1. Money 2. Unavailability of doctors 3. No need for a doctor 4. No time
18. How long do you wait before starting antibiotic when your children get sick?	1. Directly 2. 1-2 days 3. 3-4 days 4. >4

C. Please answer the statements about your knowledge towards antibiotic use by circulating the number between

totally agree 1 2 3 4 5 totally disagree

19. Antibiotics kill bacteria.	1	2	3	4	5
20. Antibiotics treat viral infections.	1	2	3	4	5
21. Antibiotics cure all infections.	1	2	3	4	5
22. Antibiotics reduce pain and inflammation.	1	2	3	4	5
23. Antibiotics reduce fever.	1	2	3	4	5
24. Antibiotics are medicines that cure stomach ache and disinfect digestive tract.	1	2	3	4	5
25. Amoxicillin is an antibiotic.	1	2	3	4	5
26. Aspirin is an antibiotic.	1	2	3	4	5
27. Paracetamol is an antibiotic.	1	2	3	4	5
28. Brufen is an antibiotic.	1	2	3	4	5
29. Antibiotic overuse leads to antibiotic resistance.	1	2	3	4	5
30. Antibiotics may induce an allergic reaction.	1	2	3	4	5
31. Antibiotic do not cause side effects.	1	2	3	4	5
32. Antibiotics effectiveness is reduced if a full course of antibiotics is not completed.	1	2	3	4	5
33. Same antibiotic can be used to treat different infection including (upper respiratory tract, urinary, skin, genital, etc.)	1	2	3	4	5

Appendix 3: Request letter

Arrangement to collect data from _____ institution in Nepal in autumn 2018 for a study: "Nepalese parent's knowledge and self-reported use of antimicrobial medicine in the children of 0-12 years"

Dear Sir/ Madam,

As per the requirement of Laurea University of applied science curriculum, master's degree students have to conduct an initial study on selected topic. It is our pleasure to inform you that, Ms. Rajya Kasichhawa and Ms. Usha Shrestha would like to collect data for their masters' study from Nepal.

We would be very much grateful if you could help them by providing an opportunity to collect required data and information.

Thanking you for the kind co-operation.

_____

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_____

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Appendix 4: Informed consent

Parent/Guardian Informed Consent

Identification of Investigators & Purpose of Study

Welcome to participate in a study on antibiotic use. The study is the thesis study of Rajya L. Kasichhawa and Usha Shrestha, the nurses and master's degree student from Laurea University of Applied Sciences. The purpose of the study is to assess Nepalese parent's knowledge and self-reported practice regarding antibiotic use of children 0-12 years.

Study Procedures

Should you decide to participate in this research study, you will be asked to sign this consent form once all your questions. This study consists of an interview, which will be placed on suitable place like at your home or children kindergarten. You will be asked to provide your opinions in a series of question regarding antibiotic use.

Time Required

Participation in this study will require 15-20 minutes of your time.

Confidentiality

You will be identified in the study by a number. The researchers retain the right to use and publish non-identifiable data. When the results of this study are published, or discussed in conferences, no information will be included that would reveal your identity. All data will be stored in a secure location and accessible only to the researcher. After completion of study all information that matches up individual will be destroyed.

Participation in the study is completely voluntary, and you are free to discontinue from this study at any point. Participation in the study will cause no harm for you or on your personal life.

For further information about this study, please contact the researchers;

Rajya L. Kasichhawa & Usha Shrestha
Registered Nurse, Master's student

+977 98 XXXXXXXX (Nepal), +358 44 XXX XXXXXX

rajya.kasichhawa@student.laurea.fi

usha.shrestha@student.laurea.fi

Appendix 5: Giving consent

I have read the information above about this consent form and here by, I agree to participate in this study. I am aware of, what being requested to do as a respondent for this study.

Name of respondent (parents/guardians)

Name of researcher

Appendix 6: Letter from ethical board

LAU REA Together we are stronger

Ethical statement

10.10.2018

Laurea Research Ethical Board

Ethical statement for the Kasichhawa Rajya and Shrestha Usha thesis work "Nepalese parent´s knowledge and self-reported practice about antibiotic use in children 0-12 years"

Donors: Mikko Julin, Marilla Kortesalmi
Time: 10th October 2018

Ethical board dealt with the ethical statement request of the thesis work Kasichhawa Rajya and Shrestha Usha "Nepalese parent´s knowledge and self-reported practice about antibiotic use in children 0-12 years".

The thesis aims to work on strengthening knowledge about the use of antimicrobials by surveying the knowledge and the self-reported practices about the antibiotic use of the Nepalese parents of children aged between 0 to 12 years.

The thesis is a nature of a survey and will be conducted in Nepal in Kawasoti municipality in two day care center and public area. Despite of the cultural differences there should a permission to do so in the day care centers. On the thesis plan there is an indication that permission is granted by professor Hanni Tamin, but it remains unclear the role of the permission. The Appendix 1. is a request letter to collect data, but there are no references on the thesis plan text of how this request is to be used and will it include other documents such as this thesis plan. The permission issues must be solved before the action starts.

The data analysis is well described on the thesis plan. What is missing, is the data management plan. On the inform consent, which is clear and informative enough, is a statement that indicates the data handling issues. However, the thesis plan is missing the data management plan. This is very important ethical aspect and should be described throughly on the plan. Also, if a participant wants to know of how the data is handled, there should be readiness to reveal in details the data management steps.

The informed consent is vital in these kind of studies and it is clear on this thesis plan. However, it remains unclear on this thesis plan, that what language will be used on the data collection. If it is English then all is clear, if it is not English, but e.g. Nepali language, who will do the translations and how is it confirmed that the translation matches to the English versions? This applies to all the documents and should be dealt with care already on the thesis plan.

The privacy of the participants is also one of the key elements. It must be made clear that any of the participants cannot be recognized from the published data. This is mentioned on the Informed consent paper, but on the thesis plan there is no explanation of how it will be done. It is important to understand that there are many other ways to reveal personality besides the name of the participant. This have to be considered and described on the thesis plan level.

Overall this thesis plan is interesting and ambitious. Since the topic might interest many other as well the thesis authors could consider the Open science approach, data available for the others. This could be talked with the thesis tutor. With the remarks completed the study is ready to start in ethical wise.

On behalf of the Laurea Research Ethical Board,

Mikko Julin

Marilla Kortesalmi

Appendix 7: Nepali language Logo for safe handling of antibiotics use copyright© Rajya Kasichhawa and Usha Shrestha 2020