Overuse of antibiotics in high-income, middle -income, and low-income countries: patients' knowledge, attitude, behaviour, and factors affecting doctor's prescription behaviour and attitude of prohibiting antibiotics prescription. A Systematic Review.

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Abstract

Background: The excessive use of antibiotics have currently been recorded as a common phenomenon globally, and it has important public health repercussion. Consuming antibiotics every time an individual is suffering from a normal viral infection would make resistant to the antibiotics. And not be able to cure the disease, leading to harmful side effect for endorsing antibiotic resistance. The current study will be complementing all existing literature by systemic review of the available evidence on public knowledge, attitude, and behaviour regarding the misuse of antibiotics in the high, middle and low-income countries. This study also aims to investigate factors affecting physician's prescription behaviour and factors prohibiting the prescription of antibiotics.

Methods: A systematic review performed through pub med, and EBSCO-HOST scientific database January 2010 to March 2020 was considered including a cross-sectional study and focus group discussion. And investigating knowledge, attitude, behaviour about antibiotic use and factors prohibiting doctor's prescription behaviour.

Result: All the studies included in this review had definite objectives regarding patient, knowledge, attitude and behaviour associated with antibiotics use. These study had applied proper methodology for cross-sectional summary related to the search question. Most of the (22) reviews had appropriate methodology associated with a representative of the population. Six studies had not clear sample size and did not represent the entire population. Twenty studies had tested the validity and reliability test. A general question used by this survey categorised into four main themes.

Theme: 1. Knowledge and awareness of antibiotic use, 2: attitude and behaviour related to antibiotic use, 3: knowledge and awareness of AMR and 4: factors affecting physicians prescription behaviour and attitude of prohibiting antibiotics.

Conclusion: To maximise the use of surveys, the application in findings in survey and associated factors related to antibiotic use and AMR should primarily create public health intervention. A multifaceted approach is likely to improve more successful. The studies provide sufficient evidence which proves that a targeted approach in interventions has been successful in reducing antibiotic prescription and misuse.

Keywords: *Resistance; Antibiotics; Attitude; Knowledge.*

1. Introduction

1.1. Background

The excessive use of antibiotics have currently been recorded as a common phenomenon globally, and it has important public health repercussion.[1] 'Antibiotic' means "against life" and the treatment from it is proper for any kind of standard microbial infection.[2] The biochemical constituents in an antibiotic that a microorganism produces obstruct or kills the production of other microorganisms. It has used for the treatment of non-virus-related infections such as streptococcus pyogenic disease and strep throat.[3] The medication is not suggested for recurring sore throats mostly caused by common viruses. More diseases of viral infection cannot be benefitted from the treatment of antibiotic, for instance, influenza (flu), common cold, ear infections, Bronchitis, coughs, and sinus infection.[4]

Antibiotic a medication from an antimicrobial family and it has significantly used for killing as well as preventing the development of namely pathological bacterium, various fungus and pathological organism.[5] Antibiotic is said to be the most common medication in the collection of antimicrobial agents' that has used for treating any kind of infective diseases all over the world. Its administration establishes a wide-ranging set of actions that aims to enhance the usage by picking out the appropriate dose, duration and route for treatment. It reduces the undesirable viral occurrences comprising of bacterial resistance and toxicity.[6] Nevertheless, antibiotics not using in the correct manner; for instance, overusing could perhaps result in severe side-effect on the person's wellbeing.[7]

The first efficient antimicrobials were introduced in 1937. Subsequent to this introduction, there was seen to be an obstinate growing as well as the dispersion of this drug-resistant bacteria.[8] These bacteria are referred to as AMR (Antimicrobial resistance), which was effectively defined as a phenomenon, where the contagion was triggered by a microorganism similar to a bacterium that could extensively

endure drugs exposure which was capable of constraining their development.[9] However, consuming antibiotic every time an individual is suffering from a normal viral infection would make them resistant to the medicine and not be able to cure the disease leading to harmful side effects for endorsing antibiotics resistance.

The AMR study done in 2016 found out that approximately 700,000 people die every year around the world. This occurs mostly due to the infection that the antibiotic is unable to cure. A study states around 2050, 10 million people would have been dead globally as the result of AMR infection which might be a massive blow to the global economy costing around $100 trillion.[10] The individual cost in the USA for treatment being antibiotic-resistant is around $2 billion yearly.[11] This makes it clear that due to resistance from the antimicrobial medication, people worldwide are under the risk of infection. Commonly due to operations such as removal of the appendix, hip replacements, a routine surgery, as well as caesareans, people having become resistant putting them at a higher risk as they will have an enhanced stay in the hospital ensuing in premature death.[12] Patient's life can also be at risk when one misuses antibiotics as the side effects it causes could be ranging from an allergic reaction to diarrhoea.[13] It has recorded that around 25000[14] and 23000 people in Europe and the USA suffered death due to antibiotic resistance in a year.[15]

From the preceding research directed in Saudi Arabia, it acknowledged that there are varying factors that tend to influence the overuse of antibiotic.[16] These specific factors constitute of medical misperception of infection, diseases, patient's anticipated awareness and their entirely deprived receptiveness regarding the antibiotic's unnecessary usage and its severe outcomes.[17, 18, 19, 20] Having inadequate information about possible risks might also measure as a risk factor for antibiotics overuse.[21, 22] Furthermore, patients must be perceiving a pathological analysis and the doctor of medicine might refuse and does not recommend any antibiotics. Nevertheless, the patients being nonchalant due to the worry about their illness as well as the lack of understanding about using antibiotics.[23] This resulted in a making a large number of people unable to failing to complete antibiotics full course. As the patients tend to be recovering, they due to the lack of understanding save few of their pills.[24] Failing to complete a full course of antibiotic, and saving the medicine for upcoming self-medication leads to microorganism recovering resultant to resistance in antibiotic molecular development.[25] Most of the cases, people do not know about it. Not only that, some patients have misunderstood that, antibiotic also killed the viral infection.[26]

Indications from the legislative technology and science commission which states that the patients substantial demand for being prescribed the antibiotics by the doctors. This is because the AMR awareness amongst the public is not acceptable.[27] In high-income countries, there is a high rate of antibiotic usage in hospitals as well as the community, leading to the development of resistance.[28] Thus, this amounts to need for the development of a more advanced and costlier generation of antibiotic. In the low and middle-income countries, usage of antibiotics is equivalent to high increasing income as well as high-class hospitalisation facilities.[29]

The United Kingdom (UK) administration, in accordance with the AMR topic, has issued a policy in 2013-2018 that highly integrates enhancing the understanding AMR. The policy also incorporates enhancing of material regarding AMR, reducing the global microbial resistance as well as increasing awareness about antibiotics amongst the people which will be constituting the overall health development.[30] The UK policy comprises of convincing the efficacy of the given treatment as well as the resourcefulness for creating something new. It noted that the people of the United Kingdom were superficially aware of the antimicrobial resistance.[31]

About 91% of the respondents in the monitoring study seen to have come across the word antibiotic resistance. Yet, the survey conducted by the Euro Barometer recorded 92%[32] Of UK people for redundantly using antibiotics ultimately resulting in its ineffectiveness. In the year 2015, an annual report of the Public Health England refers to 74% of antibiotics in 2014 prescribed by GP.[33] All over the world, it found that a huge number of populations is ill-advised about the purpose and efficiency of antibiotics. Such as, for the treatment of viral infection, antibiotics are beneficial.[34, 35, 36, 37, 38, 39.]

To grow public awareness about the overusing of antibiotic and its effort for reducing, which is essential to discover appropriate solutions.[40, 41, 42, 43, 44] For instance, the Centre for Disease Control and Prevention (CDC) that sponsors for annual cognisance and sustaining the stewardship efforts amongst public health organisation, patient by evolving source materials[, 45, 46, 47] that also involve in massive contribution and intensification amongst people for investigating and evolving interference for policy-making to discourse antibiotic overuse.[48, 49, 50, 51] The international action plan made by WHO will help in enhancing public awareness and reducing problem[52]. The strategies of European and Norwegian countries showed an upsurge in general knowledge.[53, 54] A European investigation replicates a considerable variation amongst nation regarding public knowledge on antibiotics.[55]

In the previous study, the scholars have assessed public information, impertinence about the excessive usage of antibiotic. The current study will be complementing all the existing literature by systemic summarising of the available evidence on the patients' attitude, knowledge and behaviour regarding the misuse of antibiotics.

1.2 Aim

Aim of this study to assess patients' knowledge, attitude and behaviour regarding overuse of antibiotics in high income, middle income and low income countries. This study also aims to investigate factors affecting physicians' prescription behaviour and attitudes towards antibiotics misuse in those countries.

1.2.1. Objectives

The specific objectives of this study are:
- To systematically identify and summarise the available evidence regarding patients' knowledge, attitude, behaviour as well as other factors affecting prescription behaviour of doctors.
- To critically assess the quality of the evidence on available data findings.
- To propose recommendations to address misuse of antibiotics based on the findings of the systematic literature.

1.2.2. The research questions are as follow

- What is the patients' knowledge, perception and attitude regarding antibiotic overuse?
- How, if at all, do attitudes regarding antibiotic overuse shift after the patients engage in a different program?
- What recommendation could be an acceptable way of publicising knowledge on the sensible use of antibiotics to the people?
- What factors influence are doctors prescribing behaviour?

1.3. Justification

Usage of antibiotics is very high all over the world and is the primary reason for resistance.[56] The doctors recommend most cases of antibiotics without any kind of diagnosis.[57] The primary issue for this redundant use was the unrecognisable information about the antibiotics amongst the people, especially in the low and middle-income nations. The people going through viral contaminations tends to improve without the assistance of the antibiotics. Nonetheless, the lack of awareness and improper knowledge makes people dealing with a viral infection to consume antibiotics pointlessly.

In high-income nations, second-generation antibiotics are easily accessible by the patients that are costlier than the first-generation medications. Yet, the frequency of illnesses in the low and middle-income countries is marked as high, which makes it unaffordable for the people.[58] The declaration by the WHO (World Health Organisation) that, the whole world is presently under the post-antibiotic stage. This is resulting in minor infection costing people's life, as the drug is not able to support this situation.[59] The chemist's in the middle and low-income nations such as India and Bangladesh,[60] manages to be unqualified regarding their knowledge about antibiotics. Sometimes, these people do not tend even to have a drug license.[61] These nations do have administration laws concerning antibiotics control; however, it has not correctly executed.[62] In addition to the laws and policies of the low and middle-income countries, some programs run regarding alertness of people on antibiotics. Since antibiotic resistance, are receiving the highest percentage of demise like the Sub Sahara where regulation about contemporary administration is not properly active.[63]

Resistant to antibiotics, a rapidly deteriorating issue considered to be of prime importance to the WHO. In 2015, WHO seen to deliver an International plan of action related to antibiotic and its appropriate usage. This initiative was taken up so that the present effect on the world could be minimised. For guarantying active awareness and making the people realise about the danger of antibiotic overuse was considered as a challenge for the patient and the doctor. Thus, this definite study is an imperative source of learning. Particularly for the low and middle-income nations as of the incompetent obtainability of locally related data and patient knowledge with information-based development standards.[64]

The physician, who has attained a lot of knowledge regarding diseases and medicines plays a vital role in this process. They can assist people in learning about the correct amount of dosage required for their illness.[65] They can also state if or not the medication is necessary of the ailment is just a self-limiting illness like viral infection.[66] The physician should be aware that, antibiotic should not be prescribed in their first visit.[67] And consequences of unreasonable uses of it should be made post readjustment.[68] However, as antibiotics are a source of income for experts and the medical institution, either as a service fee[69]or a drug promotion recompensing.[70]

In nations such as Asia, Africa, Eastern and Southern Europe and South America, people tend to take self-medication and antibiotics is the predominant one of the drugs.[71] Living in these nations, easily assess the medication due to the absence in operative implementation of law.[72] Instead of getting proper awareness about antibiotics, people are getting influenced are purchase the medication without proper supervision. From the US CDC-studies, it noted that in the low and middle-income countries tend to acquire their information about drug usage by means of sales and antibiotic awareness.[73]

There is very less alertness regarding the antibiotic resistance, especially in low-income nations, thus this paper is essential for measuring individual knowledge as a requirement for suitable antibiotics usage. People awareness about the drugs will assist in advocating more acceptable medication usage. As information seems to be associated with the effects linked with the degree of attitude, socio and demographic factors as well as the belief system of people for reducing the complete information gap making them more aware about the proper use.[74] For improving the public knowledge, Norwegian ministry of health and care services decided to introduce a campaign for public information about the significances and challenges of antibiotics and this strategy was adopted by the low and middle-income nation of the world.[75]

1.4. Ethical and GDPR review

Systematic review not being primary research in this study, hence General Data Protection Regulation (GDPR) is not a barrier. The systematic review is stated not to collect any kind of individual sensitive or intimate information but utilised for publicly available documents. Moreover, irregularly it needs principled official approval, and the institutional review board for the ethical and moral conduct of study typically does not contains a standard for a systematic review. Nevertheless, it entails considerable resources and measured as a cost-benefit investigation with the primary scope for possible benefits of the shareholders.

2. Methodology

2.1. Eligibility criteria

2.1.1. Inclusion criteria

This systematic review included quantitative studies and qualitative studies involving the general population, public, parents, University students and medical doctors who inquired about knowledge, awareness, and attitude of antibiotic use or AMR. This review considered low, middle and high income selected countries. As well as factors affecting doctors' prescription behaviour. Only peer-reviewed publications in English published between January 2010 and March 2020 were considered eligible for inclusion.

2.1.2. Exclusion criteria

This review excluded search studies that could not electrically identify. Due to the abstract of those studies does not fulfil the criteria of the research question. As well as it was considered three sets of criteria. A. Features of the studies, writer, and year of publication, Country, study design, sample size, administration, and tools development. B. Themes emerging from a common question asked in the survey to determine the level of knowledge and awareness of antibiotic, attitude, behaviour, and AMR or any relevant issues. C. Key findings in the studies.

2.2. Search strategy

A systemic search of scientific literature to identify publication from the internal database done. Search term developed along with three domain, namely antibiotics or antimicrobial resistance, knowledge or awareness and survey on the questionnaire. To international database PubMed, EBSCO-host searched using the search term as details in figure 1. The search term for international publications applied to title, abstract, keyword and full text. To domestic journal, namely health science research institute journal and health and social science journal were electronically searched.

2.2.1. Study selection

The search result was analysed to find out potentially eligible studies. The publications shorted by title and abstract. Only eligible studies selected for full-text review. During this stage, all the irrelevant studies which are lack of pertinence and data already found in other publications and duplications excluded. Then, assessed from the selected articles for inclusion using inclusion and exclusion criteria.

Database	Search term					
	Antibiotics/antimicrobial resistance		Knowledge/awareness		Survey/questionnaire	
PubMed	"antibiotic*".m_titl. OR "anti-bacter*".m_titl. OR "antibacter*".m_titl. OR "antimicrobe*".m_titl. OR "antibacterial drug* ".m_titl. OR "anti-bacterial drug* ".m_titl. OR "antimicrobial drug* ".m_titl. OR "antibacterial agent* ".m_titl. OR "anti-bacterial agent* ".m_titl. OR "antimicrobial agent* ".m_titl. OR (antibiotic* adj3 resistan*).m_titl. OR (anti-bacter* adj3 resistan*).m_titl. OR (antibacter* adj3 resistan*).m_titl. OR (antimicrob* adj3 resistan*).m_titl. OR ("bacterial drug*" adj3 resistan*).m_titl. OR ("microbial drug*" adj3 resistan*).m_titl. OR Anti-Bacterial Agents/ or Drug Resistance, Bacterial/) OR (antibiotic* adj3 us*).m_titl. OR (antibiotic* adj3 misuse*).m_titl. OR (antibiotic* adj3 overuse*).m_titl. OR "self-medicat*".m_titl. OR Self Medication/	AND	"knowledge*".m_titl. OR "understand*".m_titl. OR "aware*".m_titl. OR "perception*".m_titl. OR "perceiv*".m_titl. OR "attitud*".m_titl. OR "view*".m_titl. OR "opinion*".m_titl. OR "belie*".m_titl. OR "concern*".m_titl. OR "fear*".m_titl. OR "accept*".m_titl. OR "perspectiv*".m_titl. OR "worr*".m_titl. OR "concept*".m_titl. OR KNOWLEDGE/ or HEALTH KNOWLEDGE, ATTITUDES, PRACTICE/ or PATIENT MEDICATION KNOWLEDGE/ or PERCEPTION/ or SOCIAL PERCEPTION/ OR Attitude to Health/ OR Attitude/ or PUBLIC OPINION/ or "Surveys and Questionnaires"/ OR FEAR/	AND	"assess*".m_titl. OR "evaluat". m_titl. OR "determin*".m_titl. OR "explor*".m_titl. OR "apprais*".m_titl. OR "estimat*". m_titl. OR "analy*".m_titl. OR "examin*".m_titl. OR "measure*".m_titl. OR "survey*". m_titl. OR "questionnaire*". m_titl. OR "inspect*".m_titl. OR "Surveys and Questionnaires"/
EBSCO-HOST	TITLE-ABS (antibiotic* OR anti-bacter* OR antibacter* OR antimicrob* OR {antibacterial drug*} OR {antimicrobial drug*} OR {antibacterial agent*} OR {anti-bacterial agent*} OR {antimicrobial agent*} OR anti-bacter* W/3 resistan* OR antibiotic* resistan* OR antimicrob* W/3 resistan* OR {bacterial drug*} W/3 resistan* OR {microbial drug*} W/3 resistan* OR antibiotic* W/3 usage* OR antibiotic* W/3 misuse* OR antibiotic* W/3 overuse* OR self-medicat*)	AND	TITLE-ABS (knowledge* OR aware* OR understand* OR attitude* OR view* OR perception* OR perceiv* OR opinion* OR belie* OR concern* OR fear* OR accept* OR perspectiv* OR worr* OR concept*)	AND	TITLE-ABS (evaluat* OR determin* OR explor* OR apprais* OR estimat* OR analy* OR examin* OR measure* OR survey* OR questionnaire* OR inspect*)	

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Fig. 1: Search Term.

2.2.2. Data extraction

a) Studies Characteristic: Author, Publication Year, Aim and Objectives, Country, Design of the Study, Sample size, the general population, public, parents, University students and medical doctors, eligibility criteria and data collection tools.
b) Themes developing from mutual question inquired during the survey to assess the knowledge level on antibiotics, attitude and awareness on its usage, aspects barring doctor's behaviour, antibiotic resistance on the pertinent issues.
c) Major findings and conclusion.

2.2.3. Result

An electronic search comprises two international databases recorded. A total of 1120 records 791 from PubMed data and 329 from other sources. After duplicate removal, there were 1095 articles for abstract screening. Nine hundred twenty-nine articles excluded, as they are not relevant. They were leaving 166 records to search for full text. Twelve full papers that were not electronically available. And nine duplicate were excluded. One hundred sixty-six full papers reviewed for eligibility, and 117 publications excluded for not being relevant to the review objectives. Finally, 28 studies met the eligibility criteria and included for analysis.

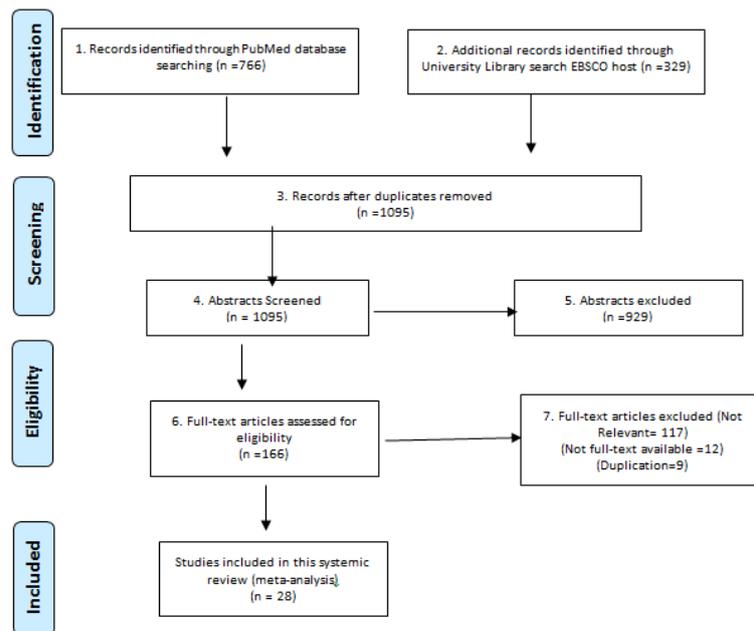A PRISMA flow is describing the study recruitment process for the systemic review shown in Chart 1.[76]

Chart. 1: PRISMA Flow of Systematic Review of the Study.

2.2.4. Characteristic of studies

This study associated with an excessive antibiotic in high middle and low-income countries regarding patients' knowledge, attitude and factors prohibiting doctors' trend of prescription. In this study, seven high-income countries included namely England, UAE, Norway, Qatar, Poland, Australia and Korea. Ten middle-income countries included namely Brazil, India, China, Kosovo, Jordan, Malaysia, Romania, Srilanka, Kenya and South Africa. And two low-income countries, namely Nepal and Mozambique.

In this review, twenty-seven quantitative and one qualitative (12) studies included. 23 studies had applied suitable methodology of cross-sectional survey linked with objectives (1,2,3,4,5,6,7,8,9,10,11,13,14,15,16,17,18,19,20,21,22,23,28). There was one longitudinal observation study (24) among the three studies were observational analytic cross-sectional study (25,26 and 27). This study accepts that simple random sampling is optimal as it accurately represents the people, but it is consuming time and resource. It was applied in 10 studies (1,4,8,9,16,20,22,23,24,25). In six studies, the sampling technique did not mention (2,10,12,14,15,21), multistage stratified random sampling was done in two studies (3,27), convenient sample design done in three studies (5,11,13). Three-stage cluster sampling done in two studies (7,26), random cluster sampling (17,18), Estimated minimum sampling was done in one study (6). One study mentions purposive sampling (19). As well as probabilistic sampling was done in study no 28. Recruiting sample such as an adult member who has a clear understanding of the language used in the survey is difficult for ensuring high quality in many surveys.

All studies published in peer- review journals. In table 1, summarises characteristics of those studies. They published from January 2010 to March 2020. The majority of studies conducted in the single country while three (5,15,26) of the study conducted in multiple countries. A comparative study regarding antibiotic consumption and knowledge among Australian and Srilanka (5). Rural health behaviour survey among a middle and low-income country of South East Asia (26), KAP (Knowledge, Attitude and Practice) survey regarding antibiotic use among pilgrims attending in hajji mosque gathering from a different country (15). Regarding study design, one study was an interventional study which assumed the outcome of the campaign and educational intervention on the proper use of antibiotics (3). Sample size varied depending on the sample frame and approached applied by each study. 22 studies mention that sample size was calculated based on statistical method and population data (1,3,4,5,6,7,8,9,11,13,15,16,17,18,19,20,22,23,24,25,26,27). Sample size varies from minimum 36 (12) to a maximum 11192 (18). For sampling criteria, these study recruited adult 18 years or over (3,11,15,24) and individual aged at 22 to 80 years (4). And aged 16 years or above (16).

Additional criteria such as respondent understand the local language and familiar with the term of antibiotics, e.g. (Arabic 11, 15). Almost all studies described specific administrative method (1,3,4,5,6,7,8,9,10,11,13,14,15,16,17,18,19,20,22,23,24,25,26,27,28) Following method of questioner administration were identified in this review :- Interview survey face to face (7,9,10,13,15,19,20,21,24,25,26,27) Focus group discussion (12) use of telephone by trained interviewers (28). By self-administration questioner through postal (3,4,5,6,11,17,18,22,23). Internet method (14) Smartphone (18) handed over (1,8). Using multiple methods when no single method is adequate to address research objective, can minimise low response rate prevent coverage measurement of non-response error. Each method may have its advantage and disadvantage; for example, self-administered survey present challenges of interpreting the question as it is one-way communication which can introduce measurement error. Face to face interview can prevent measurement bias.

Table: 1: Characteristic of the 28 Studies

No	Author	Year of Publication	Country	Inclusion Criteria	Number of Respondent/ Sample Size	Sampling Technique	The objective of the study	Key Findings
1	Ammar Jairoum	2019	United Arab Emirates	University Students	1200 Student	Simple Random Sampling	Assess the KAP of antibiotics of the university students.	□ KAP score stood at 56% □ 91.4% of the students had appropriate knowledge about bacteria-killing antibiotics.
2	Kyung-Hyun Choi	2011	Korea	Physician	250	Not mention	The use of antibiotics in primary care	□ Use of antibiotics was dependent upon the knowledge level of the respondents.

							for respiratory tract infections.	
3	Beata Mazinska	2017	Poland	Household member (Mobile/Landline Number)	5400	Multistage stratified random sampling	To analyse the level of knowledge and awareness about antibiotics and AMR among the European population.	□ Majority of households using physician prescribed antibiotics. However, 38% used antibiotics in the past 12 months.
4	Voidazan S	2019	Romania	20 year to 40 years age	996	Simple Random Sampling	To collect efficient data to study the knowledge and attitude of the people regarding antibiotics.	□ 65.9% preferred physicians' consultation before consuming antibiotics. □ 22.9% of the respondents used expired antibiotics.
5	M. H. F. Sakeena	2019	Australia and Srilanka	Pharmacy students	476 from Australia and 466 from Srilanka	Convenient sampling Design	To analyse the knowledge and attitude of pharma students in Australia and Sri Lanka.	□ 89% of the Australian population and 77% of the Sri Lankan population used antibiotics based on prescription only.
6	Poonam Shah	2019	Nepal	Medical and non-medical students	1222	Estimated minimal sampling size	To assesses the level of KAP in medical and non-medical students.	□ 54% had adequate knowledge about antibiotic use in case of viral infection.
7	Inocencio Mate	2019	Mozambique	Over 18 years	1091	Three-stage cluster sampling	To analyse the KAP regarding antibiotic use in the population above 18 years of age.	□ Around 20.9% of the students used non-prescribed antibiotics. □ 87.3% of the antibiotics bought from pharmacies over the counter.
8	Ammar Jairoum	2019	UAE	Medical and non-medical students	Medical - 600 & Non-medical -600	Simple Random Sampling	To compare the KAP of antibiotics among medical and non-medical students.	□ Average knowledge score of both the group of respondents was 59% □ 76% is the overall attitude of the students.
9	Drita Zajmi	2017	Kosovo	Kosovo Resident	811	Simple Random Sampling	To evaluate the level of KAP about antibiotic use among the public in Kosovo.	□ 58.7% of the resident has used antibiotic in the past year. □ Around 70.4% of the respondents used physician prescribed antibiotics only.
10	Marit Waaseth	2019	Norway	Population explored among Pharmacy customers	877	All individuals who entered the pharmacy at the appointment time	To analyse the level of knowledge of pharmacy owners in Norway.	□ Majority of 57% responders had high knowledge of antibiotics use. □ 90% know about antibiotic resistance. □ 30% stated that antibiotic Kill virus.
11	Ghadir Fakhri Aljayyousi	2019	Qatar	More than 18 Years who understand English and Arabic	596	Convenience Sampling Design	To assess the knowledge of appropriate use of antibiotics among the Qatari students and their families.	□ 82% of the participant uses non-prescriptive antibiotics. □ 73% of the owners knew that antibiotics were ineffective against bacteria.
12	Anita Kotwani	2010	India	Physicians	36	N/A	To assess the knowledge of physician regarding antibiotic use.	□ Doctors followed prescriptive knowledge of antibiotics and raised concerns on the misuse.
13	Dr Abuabker Elbur	2016	Saudi Arabia	Adult more than 18 years of parent	400	Convenience Sampling Design	To evaluate the effectiveness of antibiotic for treating infections in respiratory tracts.	□ 31% of respondent said the use of antibiotics was satisfactory. □ The misuse of antibiotics in children is dependent on the knowledge of the parents.
14	Sawsan Kurdi	2019	Saudi Arabia	16 or above Resident of Saudi Arabia can speak Arabic	570	Not mention sample technique Online survey	To evaluate the use of antibiotics and the effectiveness of antibiotic prevention laws	No considerable difference before and after law enforcement in purchasing and use of antibiotics.
15	Saber ezli	2018	Macca Saudi Arabia	More than 18 Years attending haji mass gathering 21.09.15 to 28.09.15	1476	Sampling Technique not disclose	Empathetic tourists' familiarity and awareness regarding antibiotic	□ 43% of respondents believing the antibiotic can cure every disease. □ Antibiotics reused by 54.1%. □ Non-prescription antibiotics used by 87.3%. □ 54% of individuals have not checked the expiration date in the drug.
16	Waseem Hajjar	2017	Saudi Arabia	Patient of URTI	400	Simple Random Sampling	To examine the causes and responsiveness amongst patient dealing with upper respiratory tract infection about antibiotic misuse	□ 45.5% of respondents use the drug without any prescription. □ 17.3% forces their medical doctors to recommend an antibiotic. □ Around 51.7% of the people stop the intake of antibiotic as they are better.

No	Author	Year	Country	Population	Sample size	Sampling method	Objective	Findings
17	Weiyi Wang	2019	China	University Students 16 to 18 Years	10925	Cluster random sampling	To unfolding that the drug is Xiaoyanyao as antibiotics	□ Misconceptions among 34.7% pupils that consumption of antibiotic is a Xiaoyanyao.
18	Yanhong Hu	2018	China	University student	11192	Cluster randomised sampling method	To effectively considering the attitude and knowledge about the usage of antibiotic during self-limiting diseases.	□ Around 29.1% of the people showed traits; 54% of which are taking self-medication with 27% using antibiotic and 21% is keen to visit a doctor from which 58% of the medical experts prescribe antibiotics.
19	Jian Wang	2019	Shanghai, China	Guardians who took children for vaccination	1368	Purposive sampling	To evaluate the information and attitude regarding using of antibiotic.	Around 83.5% of the parents felt that the common cold did not require any antibiotics usage.
20	Jing Cheng	2018	Anhui, China	Rural resident	2760	Random sampling	To scrutinise the information regarding antibiotic.	91.6% surveyed people believed in antibiotic a drug that is efficient for killing viruses. Around 77.5% states that combining antibiotic will be more effective.
21	Shreya Agarwal	2015	India	Parents who visited the outpatients department	872	Not mention	To inspect the attitude, information by observing the usage of antibiotics	□ 73.6% of them stated that miss usage of antibiotics could cause problems in children □ 85.2% acknowledged them not practising antibiotics use without a prescription.
22	Ghadeer A. R. Y. Suaifan	2012	Jordan	Medical and non-medical students	679	Random sampling	For evaluating the existing behaviour, information, attitude about the using of antibiotics.	□ 61% of students were not completing their previous course of the drug. □ 31.2% demanded antibiotic prescription from the clinician.
23	Koh Chee Teck	2016	Malaysia	parent attending in primary health clinic	320	Simple Random Sampling	To measure the behaviour, attitude and knowledge and practice of parents	□ 69.1% had very little knowledge regarding antibiotic. □ Antibiotic-resistant awareness of 67.5%.
24	Sylvia Omulo	2017	Kenya	Household participant over 18 year	□ 200 Entry □ 149 Exit	Simple Random Sampling	To evaluate the antibiotics and its using.	□ Antibiotics effectiveness for cold and flu was estimated by 66% and 74% from the entry and exit survey.
25	K Ramchurren	2019	South Africa	Patient attending in outpatient	386	Systematic random sampling	For assessing KAP concerning antibiotic use amongst outpatient.	□ 53% had adequate information on the antibiotic. □ 70% of patients were aware of antibiotic used for bacterial infections.
26	Marco J Haenssgen	2019	Chiang Rai and Slavan village	Over 18 years of the general rural population	2141 adult	Three-stage stratified cluster random sampling	To define antibiotic-related information and practices in the general population of two LMICs.	□ Villagers being aware of antibiotics 95.7% in Chiang Rai; 86.4% in Salavan
27	Cliodna A M McNulty	2019	England	15 Years Plus UK resident	1691	Multistage random sampling	To designate communal understanding and usage of antibiotics	□ 83% predicted antibiotic killing bacteria. □ 14% reported the left-over antibiotics, and 33% reserved those for future use.
28	Jessica Quintao Pereira	2018	Brazil	An adult over 18 years	4000	Probabilistic sampling	To evaluate antibiotic consumption rate of self-medication	□ Using antibiotics through self-medication around One-fifth of respondent □ 81% used the drug after a physician prescription.

2.2.5. Assess the quality of 28 articles

The result of the quality assessment of 28 eligible studies by using Axis tools is presented in figure 3 and 4. This analysis found that all publications had clear study objectives which focus on assessing the level of knowledge, attitude, and behaviour related to antibiotic overuse and factors prohibiting doctor's prescription behaviour of antibiotics. All studies had appropriate methodology related to objectives. There are 18 studies (1,3,4,6,8,9,11,12,13,14,15,19,20,22,24,25,27,28) that reported estimation of sample size using justified statistical method. Most of the studies clear defined reference population. There are some studies that not representative of entire population (4.6,10,14,22,23,25).

These studies tested both the validity and reliability of the questionnaire and provided the statistical significance of the key variable. (1,3,4,5,8,9,10,11,14,15,17,18,20,21,22,23,25,26) Regarding the reporting of survey results, almost all studies presented adequate basic data, and all result for the describe method except this study which did not show basic data (2). Ghadir Fakhri Aljayyousi (2019) was the study which address and categorise non-responders and which reported profile of non- respondents to the survey.

Regarding conflict of interest and ethical review twelve studies clearly declared funding source (1,3,6,10,12,16,17,18,19,23,26,27). Another sixteen studies did not declare the funding source, which may influence the interpretation of the result. Among the thirteen studies

provide information on ethical clearance on whether they attained consent of the survey participant (1,4,7,8,9,10,12,15,17,19,20,27,28). Rest fifteen studies did not provide information on ethical approval.

These studies discussed limitation including selection bias (4,6,10,14,22,23,25). Information bias such as recall bias present in nine studies (7,14,16,18,20,22,24,26,27). Measurement bias present in 11 studies (1,3,4,5,6,11,16,17,18,22,23). Social disability bias present in article 18 and acquiescence bias only present at article no 20.
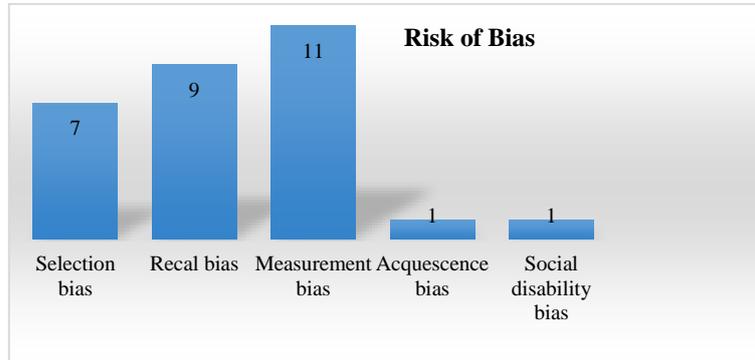

Fig. 2: Risk of Bias.

According to Axis quality assessment, the tool does not provide a numeric scale for evaluation. Still, it is flexible enough for the user to judge overall the quality of the paper. However, in this review, all articles are classified into three types. Based on methodology result discussion those are as follows: A. Fully qualified, B. Partly qualified, C. Unqualified. Fully qualified means the studies are qualified in all parts. There are no studies which reach the qualification. Partly qualified considers the studies that are eligible for some parts. In this review, this study was not fully qualified in methodology (2). Some studies are unqualified because they are missing an essential part of the quality assessment; for example, some studies had inappropriate selection processes (4,6,10,14,22,23,25) influencing representativeness of the study. These seven studies unqualified because they are missing an important part of quality assessment. That means this study did not represent the entire population. Some studies did not have validity and reliability test of measurement.

Introduction						Methods					
Author (Year of Publication)	Were the Aims/Objectives of the study clear?	Was the study design appropriate for the stated aim(s)?	Was the sample size justified?	Was the Target/reference population clearly defined? (Is it clear who the research was about?)	Was the sample frame taken from an appropriate population base so that it closely represented the target/reference population under investigation?	Was the selection process likely to select subjects/participants that were representative of the target/reference population under investigation?	Were measures undertaken to address and categorize non responders?	Were the risk factors and outcome variable measured appropriate to the aims of the study?	Were the risk factors and outcome variable measured correctly using instruments/measurements that had been trailed, piloted or published previously?	Is it clear what was used to determined statistical significance and/or precision estimates? (e.g., p values, Cis)	Were the methods (including statistical methods) sufficiently described to enable them to be repeated?
Ammar Jairoum (2019)	Y	Y	Y	Y	Y	N	N	Y	Y	Y	Y
Kyung-Hyun Choi (2012)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Beata Mazinska (2017)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Voidazan S (2019)	Y	Y	N	Y	N	N	Y	Y	Y	Y	Y
M. H. F. Sakeena (2019)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Poonam Shah (2019)	Y	Y	N	Y	N	N	Y	Y	Y	Y	Y
Inocencio Mate (2019)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Ammar Jairoum (2019)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Drita Zajmi (2017)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Marit Waaseth (2019)	Y	Y	N	N	N	N	Y	Y	Y	Y	Y
Ghadir Fakhri Aljayyousi (2019)	Y	Y	N	N	N	Y	N	Y	Y	Y	Y
Anita Kotwani (2010)	Y	Y	Y	Y	N	N	N	N	N	N	Y
Dr. Abuabker Elbur (2016)	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	Y

Fig.3: Quality Assessment of the Studies

Sawsan Kureli (2019)	Y	Y	N	N	N	N	N	Y	Y	Y	Y
Saber ozli (2018)	Y	Y	Y	Y	Y	Y	N	N	Y	Y	Y
Waseem Hajjar (2017)	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	Y
Wenyi Wang (2019)	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	Y
Yanhong Hu (2018)	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	Y
Jian Wang (2020)	Y	Y	Y	Y	Y	Y	N	CT	Y	Y	Y
Jing Cheng (2018)	Y	Y	Y	Y	Y	Y	N	CT	Y	Y	Y
Shreya Agarwal (2015)	Y	Y	Y	Y	Y	N	N	CT	Y	Y	Y
Ghadeer A. R. Y. Suaifan (2012)	Y	Y	N	Y	N	N	N	N	Y	Y	Y
Koh Chee Teck (2016)	Y	Y	N	Y	N	N	N	CT	Y	Y	Y
Sylvia Opoku (2017)	Y	Y	N	Y	N	N	N	CT	Y	Y	Y
K Ramchsrron (2018)	Y	Y	N	Y	N	N	N	Y	Y	Y	Y
Marco J Haenssgen (2019)	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	Y
Claolna A M McNulty (2019)	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	Y
Jessica Quintana Pereira (2018)	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	Y

Fig. 4: Quality Assessment of the Studies.

Quality assessment of 28 included studies using the Appraisal Tool for Cross-Sectional Studies (AXIS).

	Author (Year of Publication)	Results Were the basic data adequately described?	Does the response rate raise concerns about non response bias?	If appropriate, was information about non responders described?	Were the result internally consistent?	Were the results for the analysis described in the methods, presented?	Discussion Were the authors' discussions and conclusions justified by the results?	Were the limitations of the study discussed?	Others Were there any funding sources or conflicts of interest that may affect the authors' interpretation of the results?	Was ethical approval or consent of participants attained?
1	Ammar Jairoum (2019)	Y	N	N	Y	Y	Y	Y	N	Y
2	Kyung-Hyun Choi (2012)	N	N	N	Y	Y	Y	N	N	N
3	Beata Mazinska (2017)	Y	N	N	Y	Y	Y	N	N	N
4	Voidazan S (2019)	Y	N	N	Y	Y	Y	Y	N	Y
5	M. H. F. Sakeena (2019)	Y	N	N	Y	Y	Y	N	N	N
6	Poonam Shah (2019)	Y	N	N	Y	Y	Y	Y	N	N
7	Inocencio Mate (2019)	Y	N	N	Y	Y	Y	Y	N	N
8	Ammar Jairoum (2019)	Y	N	N	Y	Y	Y	N	N	Y
9	Drita Zajmi (2017)	Y	N	N	Y	Y	Y	Y	N	Y
10	Marit Waaseth (2019)	Y	N	N	Y	Y	Y	Y	N	Y
11	Ghadir Fakhri Aljayyousi (2019)	Y	Y	Y	Y	Y	Y	Y	N	N
12	Anita Kotwani (2010)	Y	N	N	Y	Y	Y	Y	N	Y
13	Dr. Abuabker Elbur (2016)	Y	N	N	Y	Y	Y	N	N	N
14	Sawsan Kurdi (2019)	N	N	N	Y	Y	Y	Y	N	N

Fig. 5: Axis Quality Tool for Quality Appraisal Continue.

	Author									
15	Saber ezli (2018)	Y	N	N	Y	Y	Y	N	N	Y
16	Waseem Hajjar (2017)	Y	N	N	Y	Y	Y	Y	N	N
17	Weiyi Wang (2019)	Y	N	N	Y	Y	Y	N	N	Y
18	Yanhong Hu (2018)	Y	N	N	Y	Y	Y	N	N	Y
19	Jun Wang (2020)	Y	N	N	Y	Y	Y	N	N	Y
20	Jing Cheng (2018)	Y	N	N	Y	Y	Y	Y	N	Y
21	Shreya Agarwal (2015)	Y	N	N	Y	Y	Y	N	N	Y
22	Ghadeer A. R. Y. Suaifan (2012)	Y	N	N	Y	Y	Y	Y	N	Y
23	Koh Chee Teck (2016)	Y	N	N	Y	Y	Y	Y	N	Y
24	Sylvia Omulo (2017)	Y	N	N	Y	Y	Y	Y	N	Y
25	K Ramchurren (2018)	Y	N	N	Y	Y	Y	Y	N	Y
26	Marco J Haenssgen (2019)	Y	N	N	Y	Y	Y	Y	N	Y
27	Cliodna A M McNulty (2019)	Y	N	N	Y	Y	Y	Y	Y	Y
28	Jessica Quintao Pereira (2018)	Y	N	N	Y	Y	Y	Y	Y	Y

Fig. 6: Axis Quality Tool for Quality Appraisal.

3. Thematic analysis

With the systematic literature search of high income, middle income and low-income countries regarding antibiotic use, thematic finding scenario of different countries analysed as follows:

3.1. Theme 1: knowledge and awareness of antibiotic use

In the United Arab Emirates (UAE), 91.4% of the respondent knew that antibiotic could treat bacterial infection.[77] This finding is nearly similar to that of Norway study 90%[78] but higher than found in studies Saudi Arabia 31%,[79] India 28%,[80] this rate was also much higher than found in Jordan 70.4%,[81] Romania 60.65%,[82] Qatar 73%.[83] This finding even higher than knowledge of antibiotics have observed in Poland 80%,[84] Nepal 86.9%,[85] and England 83%.[86] Such a high prevalence of knowledge in UAE, England, and Norway reflect that most of the high-income country had adequate knowledge about antibiotics.

Also, Nepal though it is a low-income country, it has sufficient knowledge. But other countries like Jordan, Romania, Qatar, India, and South Africa had no good knowledge about antibiotics. It is an important point that India had very poor knowledge which is a term increase risk of antibiotic resistance adverse effect and economic burden in India also Jordan, South Africa, Qatar and Romania.

There is a misconception that antibiotic can treat viral infection. In high-income country UAE, 30% of respondent had a misconception that antibiotic can treat viral infection.[77] This finding was consistent with a study conducted in Norway 30%.[78] This result was inconsistent with other studies that showed high misconception regarding antibiotic could treat viral infection. In China, 91.6% respondent believe that antibiotic can kill the virus and can be used to cure a viral infection. That shows high misconception of antibiotics in this middle-income country, namely China.[87] These findings were inconsistent with Romania 22.89%[82] and England 35%.[86] It was also noteworthy that in

Nepal 46%,[85] Qatar 55%,[83] Saudi Arabia 55.8%[88] Of the respondent had a misconception that antibiotic can kill the virus. Besides, in Jordan 67.2%[81] and South Africa 55%[89] had misconception on the same topic.

In a nutshell, China had more misconception in compare with Qatar, Jordan, UAE and Nepal. Romania though it is middle-income country had less misunderstanding in comparison with the above countries. Among high-income countries England, Norway, UAE has less misconception, but Poland has more misconception that antibiotic can kill the virus. That implies that a rigorous assessment of the respondent where knowledge is lacking would help develop an educational program.

The 2014 and 2017 survey report in England stated that 14% to 15% respondent knew that cold and influenza treated adequately with antibiotics. That indicates an improvement of knowledge because 27% to 32% respondent knew that antibiotics work on most of the cases cough and cold in an earlier survey. And 30% respondent knew that a course of antibiotic is not necessary if symptom removed. In the year 2014 compared with 22% to 24% in 2008 and 2009 survey.[86]

In a particular case of Qatar, 60% of the respondents identified the speedy recovery from cough and cold by the consumption of antibiotics. According to Univariate logistics, it found that there were no determining predictions about the demographic effects of the knowledge of antibiotic use.[83]

It found that in Poland, women had a higher knowledge about antibiotics than men. Also, highly educated respondents gave better answers than respondents having little knowledge about antibiotic use.[84]

Studies in Saudi Arabia showed that on comparing educational levels above and below secondary study level respondents and also respondents with higher and lower-income, the higher-level education and income category respondents had sufficient knowledge about antibiotics. Another study associated the level of knowledge about antibiotics and the knowledge level of parents in Malaysia.[90]

In a study conducted in India, it found that parents with a higher level of formal education had better knowledge about misconceptions related to antibiotics. Similar associations recognised in respondents in England, UAE, and Norway.

Studies have revealed that the female population in India and China have more misconceptions about antibiotics rather than Poland. Also, it analysed that Chinese students following social science stream have more misconceptions regarding antibiotics rather than students pursuing medical science. The students' knowledge of antibiotic is very limited in China 34.7%.[91]

However, in low-income countries, for example, Nepal, it was found that 53.5% of the population of survey knew that antibiotics do not work against chest infections and 3.6% knew that antibiotics do not speed up the recovery process of cough and cold. The medical student had better knowledge than a non-medical student. Final year medical students in Nepal had a higher understanding of antibiotic use and also reflected upon the spread of awareness for antibiotic misuse in the 1st year medical students of Nepal.[85]

Studies conducted in Malaysia proved that 69% of the population have inadequate knowledge regarding antibiotics.[90] A similar pattern analysis established in the respondents of Kenya where there is an absence of public healthcare system in the community due to which the knowledge survey yields that the idea of the respondents about antibiotics ail from own judgements rather than concepts.[92] In South Africa, 53% of people knew antibiotic.[89]

3.2. Theme 2: attitude and behaviour related to antibiotic use

According to studies, even though over the counter trade of antibiotics is not allowed by law in Golf Commission Country (GCC). 68% pharmacy in Abu Dhabi, 78% in Riyadh and 87% in Saudi Arabia sold antibiotics without prescriptions.[93] UAE, similarly to other countries, there is concern regarding the haphazard prescriptions of antibiotics. And even self-administration for mild symptom for which antibiotic does not need.[77] In UAE average attitude score was 76%. On an average participant score higher in attitude followed by knowledge of antibiotics.[94] In the UAE, 29.7% of people use antibiotics for cold flu and sore throat. On the other hand, approximately 41% of respondent expected a prescription for an antibiotic against flu, but less often against sore throat 23%, cold 19%, toothache 15% and cough 10%.[84] In Romania, nearly the same as Poland, 39.2%[82] of people take antibiotics for cold and flu. In Qatar, Jordan, Nepal, more than 60% respondent takes antibiotic for cold, flu, sore throat. In Nepal 68.4%,[85] Qatar 60%,[83] Jordan 62.8%[81] respectively. In China, 40% respondent use antibiotics for sore throat.[95] Interestingly in Kosovo, only 23.8% respondent use antibiotics for sore throat.[96]

In Poland, a very low rate of 3% of purchase antibiotics without prescription shown.[84] This result was inconsistent with other studies in China 97%,[95] Haji mass camp in Saudi Arabia 87.3%,[97] Saudi Arabia 78.7%[93] and Qatar 82%.[83] Besides comparatively low in Romania 29.7%[82] and Mozambique 20.9%.[98] It is notable that in England only 1.6% respondent take antibiotics without any prescription.[86]

So, in Poland and England, fewer people use antibiotics without prescription. Whereas in Jordan, Saudi Arabia, Qatar, more people buy antibiotics without prescription. The study found that the highest number 97%[95] of antibiotic users in China taking antibiotics without doctors' prescription.

Due to misconception about antibiotics, 44.5% respondent in UAE stop taking antibiotics when patients feel better.[77] These findings were much higher than the study conducted in England 13%,[86] Romania 9.94%.[82] These findings are inconsistent with Qatar 65%,[83] China 44.7%,[87] Poland 47%.[84] It is a point of concern that in Nepal, 85.2% of respondent stop taking antibiotics when they feel better. However, their knowledge score was high. It reflects the patient's attitude score was poor. So, the misconception was less in England, Romania and Mozambique compare with other selected countries.

UAE and England, both knowledge and attitude score were good whereas in Qatar though knowledge score is good but in terms of attitude, 60% respondent negative attitude towards antibiotic use. In Qatar, married and university graduated participant was more likely to have a positive attitude towards antibiotic use. In India, though knowledge score is low attitude score is high and satisfactory. In China, both knowledge and attitude score was low. In Nepal, knowledge score is good, but the attitude was poor.

3.3. Theme 3: knowledge and awareness of AMR

Antibiotic resistance studies in UAE showed that majority population believed that there is irrational use of antibiotics in the country. Nearly 45% of the respondents were aware that antibiotic resistance is an issue in UAE. However, the percentage of resistance was lower in Romania at 85.14%,[82] Norway at 90%[78], Malaysia at 67.5%[90] And China at 85%[95]. Kosovo 42%[96] and South Africa 44%[89] recorded even lower rates of antibiotic resistance knowledge among the people. In India, only 15.5%[80] respondents were aware of the term antibiotic-resistant, which is the lowest rate compared to other studies. It is evident from the study that respondents from India, Kosovo, Saudi Arabia and South Africa have inefficient knowledge about antibiotic resistance.

It also found that Romania had comparatively better knowledge about antibiotic resistance. Romanian respondents obtained through social media, physician records, television, and radio. Respondents believed that the resistance to antibiotics could control through restricted consumption of antibiotics. And also, to consume antibiotics prescribed by physicians only. They even knew that over dosage of antibiotics could make it less effective.

Therefore, there was a high level of knowledge regarding antibiotic resistance in the population of Norway, China, and Romania. An experiment assessing the knowledge of participants with a high level of awareness of antibiotics showed that they had a positive impact (P< .001)[78,93.] The educational level of health professional background particularly plays an important role in the knowledge about antibiotic-resistant.

3.4. Theme 4: factors affecting physicians prescription behaviour and attitude of prohibiting antibiotics

The education level of physicians influenced by the efficiency of antibiotics prescribed for the treatment of disease. Internal health specialists and paediatricians are less likely to prescribe antibiotics to their patients.[99] Patients are unsatisfied with the consumption of paracetamol and oral saline in the treatment process for diarrhoea and fever. Doctors assume that patients request for medicine which they have never taken. That is why doctors prescribe antibiotics. Private practising doctors do not want to lose patients as potential customers. It is a general unethical practice in doctors that prescribing only ORS to patients of diarrhoea might make the patients leave to other doctors. It observed that 17.30% of patients in Saudi Arabia forced physicians to prescribe antibiotics.[88] A similar trend followed in china were 19.30% of patients requested doctors to prescribe them antibiotics.[100] In Jordan, 31.2 % of patients requested doctors for prescribing antibiotics.[81] Therefore, it recommended that private practitioners prohibit the use of antibiotics.

Doctors reasoned that they did not have enough time to check each patient individually. Nor did they have a tie to go through patient history as well. Therefore, to save time and money, they prescribe antibiotics to patients. Another reason to prescribe antibiotics is to clear out the stock before the expiry of the products.[101]

Influence from the representatives of the health care sector is another factor that determines the prescription of antibiotics in the private sector. Wealthy pharmaceutical companies also influenced the prescription of antibiotics by doctors. Such influences are illegal and have adjudicated in courts. That proves there are unethical governance issues in the private sector health care system where the pharma companies put pressure over the decisions of the doctors.[102] Due to the absence of regulatory rules in Korea,[103] India[80] and Brazil[6] the issue of antibiotic misuse prevails. Healthcare sectors and private practitioners must be supplied with the appropriate guidelines for antibiotic misuse. Such policies must be prepared by the advice taken from microbiologists and laboratory professionals. There should also be strict rules and regulations applied on the over the counter sales of antibiotics prescription of doctors. The patient must also be given the appropriate information regarding the misuse of antibiotics.[101]

4. Discussion

The systematic review will develop essential features in the methodology of studies that would help in creating a tool to measure the level of knowledge and attitude and behaviour antibiotic use of public and antimicrobial resistance. It is essential to set objectives to guide the study design. The study materials gathered as specific target objectives focussed on assessing the level of knowledge and attitude with antibiotic use and awareness of AMR related factors. A cross-sectional survey can help the study in assessing the research in the population in the form of knowledge about antibiotics under the efficient resource constraints and measuring exposure and outcome at the same time. One can find a possible association between exposure and outcome. However, a causal relationship easily identified through longitudinal studies in which temporary relationships can be addressed. Qualitative and quantitative knowledge together give better information about AMR. A cross-sectional study is a cheap and less time consuming compared with longitudinal studies.[104] Synthesis of qualitative and quantitative studies reflect more accurate information about public knowledge and belief about AMR than using quantitative information alone.

Wei Yi Wang made design in line with country context is important. For example, the Chinese population is highly misconception about the use of antibiotics and has recorded a high antibiotic misuse disorder among the university students of China.[91] Therefore, the study requires a strategic design to ensure the proper interpretation of the respondent's response to the survey of their ability to identify antibiotics from xiaoyanyao. Improper consumption of antibiotics can cause adverse drug effect in the body of the consumer.[105] Also, to align the study with the response for awareness campaign of the antibiotics, the context needs to be identified.[84] Twenty studies out of 28 studies performance measured for validity and reliability. Also, some questionnaire developed by other studies. Due to the difference in population, culture, health systems, and terminology of the studies, the test for viability and reliability becomes essential for gaining local context.

The study proved the key findings that the behaviour of respondents based on doctor's prescription, which widened the gap between antibiotics use and awareness. There is only one study which analyses the outcome of the survey with further implications. The result of the campaign conducted in Poland allows for slight optimism. In Poland, a positive implication seen in conducting the awareness campaign. Half of the population in Poland responded with a change in mind set about antibiotic use after attending the campaign. Among the respondents in Poland there was an optimistic trend noticed on the Euro barometer survey (2013-2016). A trend in sustainability in the knowledge of antibiotics also observed. All the studies tried to establish a relationship between the low level of knowledge of antibiotics and the characteristics of the population. Also, the studies assessed the level of knowledge among all demographics of society be it race, sex, caste etc. the findings of the study proved that the level of awareness about antibiotic use was in association with the knowledge level of the population. Other determinant associations found were the relationship between exposer to information and awareness. There is a significant association between levels of knowledge with a level of awareness.[80,85] This relationship noted between the knowledge of antibiotics and the behaviour associated with it. The lack of knowledge and misuse ratio was more in population with lower income.[80] Among participant with health professional background and had a high level of knowledge score on knowledge of antibiotic and antibiotic resistance is high.[78]

The lack of knowledge observed to be higher in low and middle-income countries than in higher-income countries. Data about incorrect behaviour were higher than what the result showed in the previous review. The incorrect knowledge of the general population regarding the use of antibiotics can overrule their decisions of using antibiotics for illnesses such as flu and the common cold. Evidence has also shown that patients can also influence the physicians in prescriptions of antibiotics.[81,88,106] Hence the GP plays a pivotal role in antimicrobial drug misuse. Doctors should not be overwhelmed by patient request. However, the relationship between the doctor and patient may influence the choice of the doctor of prescribing antibiotics, even when the patient does not need it.[101]

The results of the study clearly showed that a certain section of the population has been consuming antibiotics without prescriptions. Such unethical practices make it difficult for the GP to control urges and also develop antibiotic resistance. Therefore, there is an urgent need to develop educational campaigns to improve among the masses the unethical practice of antibiotic consumptions.

Alignment of the global action plan on AMR lead to surveillance on knowledge and awareness level can lead to effectively contribute to intervention design that can change the behaviour of patients on the use of antibiotic. It overall could potentially work to minimizing the AMR.[107]

This has been reviewed through the many studies that many limitations are generated within the association knowledge, performs, and awareness with the use AMR in community.

This is important to develop strategies based on survey evidence regarding change of antibiotic utilization pattern. Scholars, as well as specialist within the field, should converse needed queries within the survey module of AMR. One of the critical points is linkage within the knowledge level and awareness level regarding behaviour that is affected through the many elements. These accessed regarding free health care and cultural level elements.[108]

The survey can be a surrogate measure use to probe into possible causes of the problem. Survey evidence can use for public advocacy. However, among these studies, only a few studies linked the survey with a communication campaign and evaluate policies.[84]

Phycology is capable of handling AMR misuse. There has been a contribution from sociologists in controlling the misuse of AMR following the disciplines and reviews from phycology. The study also considers the perception of the general physician towards the prescription of antibiotics. And, the appropriate intervention required to shape the perception of the general physician. The perception of the public and healthcare professionals helps policymakers in designing interventions for the general physicians for creating awareness and healthy practices in the prescription of antibiotics to the public. The initiative must aim at improving communication skills among physicians.[101]

Social capital concerns the existence of social norms of the society and the corporations of people cooperating according to the established norms of the society which shape the behaviour of the people regarding antibiotic misuse.

The knowledge of public and junior practitioners can have an impact on the future of AMR. The knowledge of social science students and the first-year medical science students have comparatively less knowledge than final year medical students in China.[95]

It observed that the role of society in deciding the behaviour of antibiotic abuse and tendencies is important. In countries like India, the consumption of antibiotics is high due to the high risk of infectious diseases in the middle and low-income population. Also, in India as well as other low and middle-income countries, the obtaining of non-prescriptive antibiotics is easy. Therefore, it is a common trait of society in antibiotic abuse.[80] Antibiotic use practice is mostly context as specific. Surveys in high income developed countries have shown that societies with better socio-economic status have a higher tendency of using prescriptive antibiotics. However, the practice of non-prescriptive antibiotic misuse and resistance in the community of sub-Saharan Africa are largely undescribed.[108] Studies in England showed that the knowledge of antibiotics is highly correlated with educational qualifications and social status. The lack of knowledge found to be highly predominant in minority ethnic groups such as black Asians. Therefore, there is a need to target such ethnic groups to cultivate awareness in them. Various research in England proved that there are variously modified and translated leaflets present for the targeted intervention.[86]

However, the specific sampling method may introduce selection bias. To the measurement error raised concern about the level of the understanding question to arise, such as the term antibiotic or can understand local language[83,97.] The study aims at creating selection criteria for those respondents who are familiar with antibiotics. However, based on the specific groups, the selection criteria should be taken into consideration. The Inclusion criteria ensured the validity and reliability of the questionnaire.

However, there remain some limitation, for example, although the search strategy was as large as possible. Some studies had likely left out. Another point was that review was unable to capture the link AMR tool and actual knowledge and behaviour of antibiotic use on the broader population. This review cannot address this issue. Primary data collection, either quantitative survey or qualitative interview, is needed for this action. Besides, a more complex review design, for example, the real review is likely to be answering this question. Further systemic review that explored the tools in a specific subpopulation is huge value on AMR field.

The strength of the study lies in the evaluation methodology of the questionnaire as the cross-sectional survey. The systemic review is assessing new methodologies of assessing and monitoring statistical data for AMR awareness. Firstly, it provides a quality assessment of the cross-sectional surveys, which is important for tool development and data collection. The axis tool provides qualitative assessment review. Secondly, the previous reviews focus on the result of the studies. The survey review will establish a bridge between the gap of the 28 studies and the factors associated with antibiotic misuse and AMR.

The implication of the research considers that the antibiotics widely used as a standard medication solution, so resistance to the drug is also common. The results of the research proved that the population was far away from achieving complete awareness about the misuse of antibiotics. Recommendations such as educational campaigns in the society suggested improving knowledge about antibiotic misuse in the community. Also, another initiative would be to advise physicians to inform patients about the correct and efficient use of antibiotics and build a positive behaviour towards overuse of drugs.

5. Conclusion

Access to better study examples such as knowledge, population, and awareness of antibiotics can lead to a reduction in the levels of AMR in the low and middle-income countries. Valid household base assessment requires clear survey objective. This systemic review covers four thematic areas.

It observed that in high-income countries, interventions had been taken place by community and household level population to reduce the use of antibiotics misuse in the country. The target of the intervention should be the prescription of antibiotics for infectious disease for better significant results. A multifaceted approach is likely to improve more successful. The studies provide sufficient evidence which proves that a targeted approach in interventions has been successful in reducing antibiotic prescription and misuse. However, the gap in the study found to be at the communication sphere between the attitude and knowledge of the public's choice of consumption of antibiotics, both legal and illegal in low and middle-income countries.

Accurate survey tools contribute to valid evidence which can be used to form policy for a specific intervention to improve population knowledge and awareness on antibiotic use and AMR. High-level knowledge of antibiotics among England and Norway are observed. In Romania, the majority of the respondent had adequate knowledge, and most of them considered that the use of non-prescribed antibiotics had a harmful effect. More misconceptions and lower level of knowledge identified among Srilanka undergraduate students compare with Australian undergraduate student. In Mozambique, China, India and Saudi Arabia regarding knowledge of antibiotics found in the very poor level. Especially in India and Saudi Arabia, most of the antibiotics sold on pharmacy without a prescription. Significant data found in hajji mass study 87.3% of pilgrims used non-prescribed antibiotics even most of them did not check the expiry date of medication. Majority of the Kosovo population had inappropriate knowledge of antibiotics and used antibiotics as self-medication. The utmost goal of this survey

would be to enhance the application of this knowledge to target a specific group as well as to target specific intervention and measure according to country-specific as follows:

1) Studies among the Norwegian respondents showed that the population had a high level of knowledge of antibiotic resistance. That proves that the public is well aware of the threats the over dosage of antibiotics has over the immunity structures of the body. However, there is a gap between the knowledge of the rationale behind the resistance of antibiotics. There is a need for strategic action plans for public officials without efficient knowledge and a health professional background. The intervention must also focus on parents with young children and low medical knowledge.[78]

2) Even though there are integrative interventions in England regarding antibiotic misuse, the people still influenced by the basic knowledge held by them. The target intervention lacks in reaching out to adolescent and young adults with harmful misconceptions about antibiotic misuse.[81] Digital campaigns in social media, gaming software and email and text marketing identified to be more effective than leaflet distribution.[90] Europe provides an educational resource project for school children in the name of the e-bug project. England's public health system as also launched digital campaigns on television, radio and social media to raise global awareness on antibiotic misuse. It also supported by political structures imposing the threat of antibiotic misuse in the polity of the nation. The study hopes to detect the levels of antibiotic misuse in young adults of the next generation. Another key step could be to improve the prescription of antibiotics by the physicians by distributing the evidence of antibiotic effects among them. The future of the national action plan expects an improvement in the trends of appropriate antibiotic use in the next five years.

3) It observed that an urgent requirement of a plan for public healthcare initiative for regulation and control of antibiotic and AMR in the healthcare system of UAE. Also, appropriate standards in public health and educational awareness in medical and non-medical universities required to set up.[94]

4) On November 18 2008, the European countries has managed to cooperate with the countries to establish a regulatory platform for prevention and awareness of antibiotic misuse and AMR awareness. Poland has actively jointed the initiative and to maintain a regular program to reduce misuse of antibiotics.[84]

5) Saudi Arabia recommended developing efficient educational programs and campaign for the population about antibiotic resistance and the real cause after the prohibition of the law. Also, there is a need for an increase in the accessibility of primary health care system of medical insurer's providers.[93] A misconception has existed about use and indication of antibiotic. There is also a need for Educational programs which can improve the knowledge attitude and behaviour of people towards antibiotic use. The use of print and electronic media can also be a contributing campaign factor for spreading awareness about antibiotic misuse.[91]

6) More studies should be performed during next year in Brazil to analyse if the reduction of the use of antibiotic is just an immediate effect or continuous process.[6]

7) Due to the higher level of infectious disease in middle-income countries like India, the use of antibiotic is widespread. Because of relaxed law in India and other middle-income countries, it is essential to improve respondent knowledge and promote a healthier attitude and practices. The Government should implement proper application of the law to buy and sell of antibiotics. Firstly interaction between respondent and health professional can help to increase the public views regarding use and indication of antibiotics and the importance of completing the course of antibiotic. Mass media may be an essential component in disseminating appropriate information to the general population. Secondly, that strength laws should be in force by the Government that prohibit the availability of antibiotic as over the counter drugs. Also, the pharmacist should be encouraged to give specific antibiotic as mention in the prescription in India.[80]

8) The consumption of antibiotics in the medical student of china reflect the consumption of antibiotics in the public of China. There is an urgent need for strengthening of the national education policy to spread awareness of antibiotics.[95]

9) In Kosovo, to increase people knowledge regarding antibiotic use, medical professional plays an important role. They must take into consideration as a powerful tool to improve appropriate use. Antibiotic stewardship programs should be arranged at an academic level.[109]

10) In a low-income country like Nepal medication course, more activities can be organised for both medical and non-medical students. For example workshop, seminar, competition on knowledge of antibiotic use, media approaches such as TV program, printed news could be an effective way of disseminating knowledge as the appropriate use of antibiotics in the general population.[85]

11) In Mozambique, it observed pharmacies sold non-prescribed antibiotics to the public. This practice is of concern and illegal. As the law of Mozambique prohibits the sale and consumption of antibiotics without prescription.[98] Similar trends observed in the Sub Saharan African countries. This is different from high-income countries where the physician prescribes most of the antibiotics. The unethical sale of antibiotics highlights the inefficiency of the legislation and enforcement system of the country where the pharmacists were unaware of the laws regulating the sale of antibiotics.[101, 109, 110] It is essential to intervene in the medical system with multifaceted reinforcements for frequent inspections together with educational policies. Also, due to flexible law, it is not difficult to obtain antibiotics without prescription in Mozambique, India, Brazil, China, Nepal, Bangladesh.[80, 98] There is a lack of knowledge in the general public of Kenya regarding antibiotic misuse and awareness of AMR. There is an urgent need for educational intervention pertains to antibiotics, and there use which can be a remedy for the prevailing situation. There is a need for intervention in the education and medical system of south Asian countries for the control and regulation of antibiotics. The antibiotic misuse to minimise, there is a need for coordinated action at the national and regional level, which includes judicious use of antibiotics and proper patient education and counselling in Romania.[82]

6. Acknowledgment:

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Annexe

List of acronyms
Acronym Term
KAP   Knowledge Attitude Practice
GDPR   General Data Protection Regulation

AMR	Antimicrobial resistance
UAE	United Arab Emirates
GCC	Golf Commission Country
CDC	Centers for Disease Control and Prevention
WHO	World Health Organization

Details of 28 reviewed articles:

SL	Details of Articles
1	Jairoun A, Hassan N, Ali A, Jairoun O, Shahwan M, Hassali M. (2019). 'University students' knowledge, attitudes, and practice regarding antibiotic use and associated factors: a cross-sectional study in the United Arab Emirates', *Int J Gen Med*, 12, 235-246. https://doi.org/10.2147/IJGM.S200641
2	Choi, K. H., Park, S. M., Lee, J. H., & Kwon, S. (2012). 'Factors affecting the prescribing patterns of antibiotics and injections', *Journal of Korean medical science*, 27(2), 120–127. https://doi.org/10.3346/jkms.2012.27.2.120
3	Mazińska, B., Strużycka, I., & Hryniewicz, W. (2017). 'Surveys of public knowledge and attitudes with regard to antibiotics in Poland: Did the European Antibiotic Awareness Day campaigns change attitudes?'. *PloS one*, *12*(2), e0172146.
4	Voidăzan, S., Moldovan, G., Voidăzan, L., Zazgyva, A., & Moldovan, H. (2019). 'Knowledge, Attitudes And Practices Regarding The Use Of Antibiotics. Study On The General Population Of Mureş County, Romania'. *Infection and drug resistance*, 12, 3385–3396. https://doi.org/10.2147/IDR.S214574
5	Sakeena, M., Bennett, A. A., Carter, S. J., & McLachlan, A. J. (2019). 'A comparative study regarding antibiotic consumption and knowledge of antimicrobial resistance among pharmacy students in Australia and Sri Lanka'. *PloS one*, *14*(3), e0213520. https://doi.org/10.1371/journal.pone.0213520
6	Shah, P., Shrestha, R., Mao, Z., Chen, Y., Chen, Y., Koju, P., Liu, X., & Li, H. (2019). 'Knowledge, Attitude, and Practice Associated with Antibiotic Use among University Students: A Survey in Nepal'. *International journal of environmental research and public health*, 16(20), 3996. https://doi.org/10.3390/ijerph16203996
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8	Jairoun, A., Hassan, N., Ali, A. *et al.* (2019). 'Knowledge, attitude and practice of antibiotic use among university students: a cross sectional study in UAE'. *BMC Public Health* **19**, 518 (2019). https://doi.org/10.1186/s12889-019-6878-y
9	Zajmi, D., Berisha, M., Begolli, I., Hoxha, R., Mehmeti, R., Mulliqi-Osmani, G., Kurti, A., Loku, A., & Raka, L. (2017). 'Public knowledge, attitudes and practices regarding antibiotic use in Kosovo'. *Pharmacy practice*, 15(1), 827. https://doi.org/10.18549/PharmPract.2017.01.827
10	Waaseth, M., Adan, A., Røen, I. L., Eriksen, K., Stanojevic, T., Halvorsen, K. H., Garcia, B. H., Holst, L., Ulshagen, K. M., Blix, H. S., Ariansen, H., & Nordeng, H. (2019). 'Knowledge of antibiotics and antibiotic resistance among Norwegian pharmacy customers - a cross-sectional study'. *BMC public health*, 19(1), 66. https://doi.org/10.1186/s12889-019-6409-x
11	Aljayyousi GF, Abdel-Rahman ME, El-Heneidy A, Kurdi R, Faisal E. (2019). 'Public practices on antibiotic use: A cross-sectional study among Qatar University students and their family members'. *PLOS ONE* 14(11): e0225499. https://doi.org/10.1371/journal.pone.0225499
12	Kotwani A, Wattal C, Katewa S, Joshi P C and Holloway K. (2010). 'Factors influencing primary care physicians to prescribe antibiotics in Delhi India'. *Family practice*. 27. 684-90. 10.1093/fampra/cmq059.
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14	Kurdi S, Faran A, Eareeni E, Alhalal N, Joseph R, Wali H and Alshayban D. (2019). 'Assessment of Knowledge and Attitude Toward the New Antibiotic Dispensing Law and its Effect on Antibiotic Use in Saudi Arabia'. *Saudi Pharmaceutical Journal*. 28(2020) 58-67
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16	Hajjar W, Alnassar S, Al-Khelb S, Al-Mutairi S, Al-Refayi N & Meo S. A. (2017). 'Antibiotics use and misuse in upper respiratory tract infection patients: Knowledge, attitude and practice analysis in University Hospital, Saudi Arabia'. *JPMA. The Journal of the Pakistan Medical Association*, 67(9), 1387–1392.
17	Wang W, Wang X, Hu Y J, Wu D, Lu J, Xu Y, Sun C & Zhou X. (2019). 'The Misconception of Antibiotic Equal to an Anti-Inflammatory Drug Promoting Antibiotic Misuse among Chinese University Students'. *International journal of environmental research and public health*, 16(3), 335. https://doi.org/10.3390/ijerph16030335
18	Hu Y, Wang X, Tucker JD, Little P, Moore M, Fukuda K & Zhou X. (2018). 'Knowledge, Attitude, and Practice with Respect to Antibiotic Use among Chinese Medical Students: A Multicentre Cross-Sectional Study'. *International Journal of Environmental Research and Public Health*. 15(6):1165.
19	Wang J. Sheng Y, Ni J, Zhu J, Zhou Z, Liu T, Zhang X & Zhao Q. (2019). 'Shanghai Parents' Perception And Attitude Towards The Use Of Antibiotics On Children: A Cross-Sectional Study'. *Infection and drug resistance*, 12, 3259–3267. https://doi.org/10.2147/IDR.S219287

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23	Teck KC, Ghazi HF, Bin Ahmad MI, et al. (2016). 'Knowledge, Attitude, and Practice of Parents Regarding Antibiotic Usage in Treating Children's Upper Respiratory Tract Infection at Primary Health Clinic in Kuala Lumpur, Malaysia: Pilot Study'. *Health Serv Res Manag Epidemiol*. 3:1-8 doi:10.1177/2333392816643720
24	Omulo S, Thumbi SM, Lockwood S, Verani JR, Bigogo G, et al. (2017) 'Evidence of superficial knowledge regarding antibiotics and their use: Results of two cross-sectional surveys in an urban informal settlement in Kenya'. *PLOS ONE* 12(10): e0185827. https://doi.org/10.1371/journal.pone.0185827
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