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PATTERN OF RESEARCHES DONE ON ANTIMICROBIAL RESISTANCE IN ETHIOPIA

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ABSTRACT

Background: Antimicrobial resistance (AMR) threatens the effective prevention and treatment of an ever-increasing range of infections caused by bacteria, parasites, viruses and fungi. In recent years, since the rate at which resistance occurs has outpaced the development of new drug replacements, it has become necessary to use the currently available agents, optimally and appropriately. Apart from that assessing the awareness of health professionals in the issue and providing appropriate trainings on how to use the available antibiotics is a wise approach that could help us to challenge the challenges of AMR. Objective: The objective of this study was to assess the medical staff awareness towards the most common resistant bacteria species, the factors contributing to the lack of awareness, and the possible measures to address the awareness gap. Method: A structured questionnaire was administered to 205 health care professionals including physicians, pharmacists and nurses at Tikur Anbessa Specialized Hospitals, Addis Ababa-Ethiopia. Results: The study identified that most of the responding physicians and pharmacists considered Pseudomonas aeruginosa and methicillin resistant Staphylococcus aureus (MRSA) as the most frequently encountered resistant bacterial species. However, nurses recognized both MRSA and Extended Spectrum Beta Lactamase producing bacilii as the most prevalent resistant species. Physicians and nurses reported prolonged hospitalization as a factor likely to contribute to the increased incidence of bacterial resistance. About 58% of pharmacists indicated that the use of antibiotics without prescription as a significant reason for the development of bacterial resistance. Most of physicians reported that appropriate infection control is the most important measure to reduce bacterial resistance. Pharmacists (58.1%) recognized better adherence to the infection control guidelines as the most important factor that could reduce the risk of bacterial resistance. Conclusion: The findings of this study revealed that there was good awareness to the most common AMR etiologies and their risk factors among the different discipline health professionals. Even though there was a varying level of awareness among the health care professionals. Continuous medical education programs would be desirable to keep the health care professionals updated and diminish the future risk of excessive bacterial resistance.

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INTRODUCTION

Antibiotics and similar drugs are also called antimicrobial agents, which have been used for the last 70 years to treat patients with infectious diseases [1]. Antibiotics are those antimicrobial substances that target bacterial infections rather than infections caused by viruses and fungi [2]. However, the treatment of bacterial infections is facing a challenge as bacteria develop resistance to those antibiotic agents [3]. Antimicrobial resistance (AMR) is resistance of a microorganism to an antimicrobial drug that was originally effective for treatment of infections caused by it [4]. Microbes can acquire resistance through mutation or through horizontal transfer of genetic information [5].

AMR is driven by both appropriate and inappropriate use of anti-infective medicines for human and animal health and food production, together with inadequate measures to control the spread of infections [6]. Some studies showed that at any given time, 25% to 35% of hospitalized patients receive systemic antibiotics to treat active infections or to prevent potential infections [7]. Misuse of antibiotics have been associated with increased rates of AMR and increased healthcare expenditures [8].

The advent of AMR problem has resulted in the development and increased transmission of several significant pathogenic microorganisms [(e.g., Methicillin-resistant Staphylococcusaureus (MRSA), Vancomycin-resistant enterococci (VRE), Extended spectrum beta-lactamase, Carbapenem-resistant enterobacteriaceaeor Carbapenemase-producing Enterobacteriaceae that have the potential to negatively impact client/patient/resident morbidity and mortality [9].

The increasing clinical incidence of AMR is a major global health care issue [10, 11]. The patterns of AMR differ regionally and by country, mirroring patterns of infectious disease and antibiotic use [12]. Centers for Disease Control and Prevention (CDC) estimates that antibiotic resistance is responsible for more than 2 million infections and 23,000 deaths each year in the United States, at a direct cost of $20 billion and additional productivity losses of $35 billion [1]. In Europe, more than 25,000 patients die each year from antibiotic resistant bacteria (ARB) which infect about 4 million patients every year. One of the most worrisome developments is worsened rise of CPE over the last two years which represents an increasing threat to patientsafety in European hospital [13]. Africa bears the greatest infectious disease burden and considerable burden from AMR. Second-line drugs which are more expensive than first line drugs and many newer, patent-protected drugs are not available in much of Africa which worsens the situation [14]. In Ethiopia, the misuse of antimicrobials, unskilled practitioners, and drug consumers, coupled with rapid spread of resistant bacteria and inadequate surveillance contributed to AMR [15].

There is a difference in the causative organisms for similar diseases between the developed and developing countries [16]. It is believed, in most developing countries, gram negative bacteria remain the major source of infection while Gram positive organisms are for developed nations [17]. Increased risk for acquiring AMR organism is then related to host risk factors as well as to the amount of time that is spent in a setting where they are exposed to these microorganisms [9]. Bacteriological culture to isolate of the offending pathogen and knowledge about sensitivity pattern of the isolates remain the gold standard in the definitive microbiological diagnosis and management [18].

AMR can lead to increased mortality, morbidity, length of hospital stays, costs of treatment and loss of production in animals. Emerging AMR threatens to undermine the management of bacterial infections. Consequences of AMR may be felt harder in resource-poor settings as they may be unavailable or unaffordable [19]. Many studies focus on 5 most important areas for the control of AMR as recognized in the WHO 2001 strategy, which are: surveillance, rational use in humans, rational use in animals, infection prevention and control, and innovations [20]. Therefore, the purpose of this review is to describe the pattern of AMR in Ethiopia.

Tackling the persistence of Antimicrobial resistance

Microbial resistance to antimicrobials is a public health problem [21]. Misuse and abuse of antimicrobials in veterinary and human medicine is a worldwide phenomenon of AMR. The problems of AMR are typically magnified in hospital settings [10, 22] because antimicrobials are often started empirically in hospitalized patients while diagnostic information is being obtained. Physician also often do not revisit the selection of the antibiotic after more clinical and laboratory data become available [23]. The heavy use of antibiotics in the hospital exerts enormous selective pressure for the emergence and spread of antibiotic resistant bacteria. Consequently, bacterial resistance has reached an alarming level worldwide [24, 25].

The WHO has reported that there is a significant gaps in tracking of AMR in different part of the world [26]. An estimated 50% of antibiotic use in hospitals is deemed inappropriate, and consumption of antimicrobials correlates directly with the frequency of resistance at the country level [27]. CDC estimates that 1 out of 20 patients (2 million per year) acquire infections in the hospital. Nosocomial infections cost $4.5 billion a year in terms of extra treatment and days of hospitalization, directly cause 19,000 deaths, and contribute to 58,000 deaths annually [7].

Lack of automatic changes from intravenous to oral antibiotic therapy by clinical pharmacists in appropriate situations and for antibiotics with good absorption (e.g., fluoroquinolones, trimethoprim-sulfamethoxazole, linezolid, etc.), has also increased the risk of patients' safety [28]. Data from around the world confirm that ARB, including multidrug resistance, is increasing among many pathogens responsible for infections in health-care facilities and in the community [6]. For example, the number of blood stream infections increased 279% in small non-teaching hospitals, 196% in large non-teaching hospitals, by 124% in small teaching hospitals, and by 70% in large teaching hospitals during the 1980s [7].

Infections caused by resistant microorganisms often fail to respond to the standard treatment, resulting in prolonged illness, higher health care expenditures, and a greater risk of death [4]. AMR makes it difficult and more expensive to treat a variety of common infections, causing delays in effective treatment, or in worst cases, inability to provide appropriate therapy [6].

Assessment of AMR use is an important component of antimicrobial stewardship programs. The emerging clinical impact of AMR also requires urgent implementation for the global strategy for the containment of AMR. Hence, similar study will definitely disseminate current knowledge gaps and will provide information to stakeholders for action. AMR is a major issue for clinicians especially working in hospitals, through provision of current data in regard to the prevalence of antibiotic resistance, recommendations in regard to antibiotic selection for specific pathogens, and recommendations in regard to empiric antibiotic selection for common serious infections .

Currently, there is no formal report on the pattern of AMR in Ethiopia except some research focusing on specific antibiotics. Hence, the findings of this review will provide important information covering all type of bacterial agents and available antibiotic sensitivity patterns that are done to date in different regions of the country.

METHODS

Between April 2016 and July 2016, Google Scholar and PubMed databases were queried for articles containing the search terms presented in Table 1. As many research articles from Ethiopia were published in journals that are not indexed in MEDLINE, reference lists from identified articles were used to collate additional publications. The abstracts of all articles that met the inclusion criteria were reviewed. When insufficient detail was provided, the entire article was reviewed before determination for inclusion or exclusion.

Study selection

The search terms identified 585 probable articles. Of these, only 585 English articles published between 1980 and may 2016 met the criteria for inclusion (Figure 1). All of those articles were studies on humans. Fourstudies [3%] concurrently tested human and clinical set up samples.

Inclusion and Exclusion Criteria

Inclusion Criteria

Articles were selected for further evaluation based on the following inclusion criteria: (i) relevance to antimicrobial resistance in bacteria, (ii) publication in English, and (iii) accessibility of the full-length article. As historical data was useful in informing us on the progress of AMR research in the study area, selection was not limited by the year of publication.

Exclusion Criteria

Duplicate references or publications reporting the same data in different journals were excluded. Those articles concerned on mycobacterium tuberculosis were excluded because of the availability of sufficient data on the pattern of drug resistant tuberculosis. Most articles (75%) on antibiotic resistance were identified by scanning reference lists of selected publications. Other relevant articles were obtained through personal references.

Study Variables

The fields considered for this review included author, year of publication, study period, region, study setting (rural, urban), study design (hospital-, laboratory- or community-based), age demographics (children, adults) or sample type collected, bacterium (genus) isolated, number of isolates obtained, number of resistant isolates and antibiotics tested.

Data extraction for analysis

For analysis: (i) study “settings” were classified as ‘mixed’ for samples drawn from both rural and urban populations; peri-urban and urban studies were pooled; (ii) study “designs” were considered ‘hospital-based’ if exclusively conducted in a hospital laboratory as part of patient management or if they contained AMR data extracted from hospital/patient records; ‘laboratory-based’ if they retrospectively analysed stored samples or clinical samples that were not used for patient management; ‘institution- based’ if conducted in the hospitals and other health care facilities or other facilities alone or ‘community- based’ if based on population-scale sampling irrespective of disease status; (iii) bacteria were collectively identified by their genus; and (iv) antibiotics with different trade names were identified using one name (thus cotrimoxazole included sulfamethoxazole/ trimethoprim while augmentin included amoxicillin-clavulanic acid). Given variation in study execution and reporting techniques, publications were carefully scrutinized when extracting data. Occasionally, this involved making the best possible judgments from the available data. Data extracted from included articles was summarized in SPSS Version 21.0.

Initial search terms included words used to filter out publications that did not address AMR. Refining terms were then applied to select only articles from the study region and on the pathogens of interest. Truncation marks (*) indicate that different extensions of the main stem of words were used.

Additional general information was garnered from reports by the Alliance for the Prudent Use of Antibiotics (APUA), the WHO, CDC and the Global Antibiotic Resistance Partnership (GARP).

RESULTS

Socio-demographic

Of the 128 articles focused on research in humans, 41.4% were from Amhara with those from Oromiya, Addis Ababa, Harar& Dire Dawa,Tigray and SNNPR accounting for the remaining 58.6% (Table 2; [8, 29-40]). Most of these were hospital based (89%) followed by lab-based (22%) studies reporting cross sectional or AMR data. Only four studies were considered community-based. Isolates were more commonly cultured from persons of all ages (48.4%) than solely from adults (25%), children (18%), pregnant women (5.5%) or neonates (3.1%) and represented higher distribution of mixed (93%) than urban (5.5%) settings; rural settings accounted for the remaining 1.5%. Of the 128 studies, 15.6% were conducted on participants with urinary tract infections followed by diarrhea (14.8%) and otitis media (10.2%) (Table 4; [32, 34, 39-151]).

Most articles (85.9%) were done prospectively while the remaining studies were conducted retrospectively.Most of the articles (21.9%) were using stool as a specimen for collecting sample followed by midstream urine collection accounting (18%).

Pathogens and resistances tested

Considering only one pathogen per study, Staphylococcus aureus (31 %) and E.coli (22.2%) were most commonly studied pathogens in humans, followed by Coagulase negative staphylococci (7%) and salmonella and shigella accounting (6.3%) each consecutively. These proportions remained unchanged when 93 studies that concurrently tested two pathogens and 59 studies that evaluated more than two pathogens were accounted for. In all, susceptibility results for these pathogens were reported for over 33 different antibiotics. However, for specific bacteria,Staphylococcus aureus, E. coli,Coagulase negative staphylococci, Salmonella and Shigella sp., isolates were most commonly (≥50% of studies) tested for resistance to ampicillin (Amp), Amoxicillin (Amox), chloramphenicol (Chl), ciprofloxacin (Cip), cotrimoxazole (Cot), gentamycin (Gen) and tetracycline (Tet) while Vibrio sp. for resistance to Amp, Chl and Tet.

For the purpose of this review, comparisons between reported resistance levels were not performed given the large variability in reported variables and reporting styles. In general, AMR in the country was reported to be increasing, presumably driven by multiple factors (Table 1). Importantly, while most authors made claims about the mechanisms that were likely to contribute to the observed AMR patterns, no studies were identified that actually investigated or quantified the contributory roles of any of these factors within the region.

DISCUSSION

Preface

The goal of this review was to assess the current knowledge of pattern of AMR for gram positive and gram negative bacteria found in Ethiopia. After collating the data and conducting exploratory analyses, it is found difficult to make meaningful comparisons from studies due to the differences in styles of reporting of results. Here, a general view of the progress is made in AMR research in Ethiopia. A potential ways to address these gaps to improve the quality of AMR data and build a pool of evidence-based data for the country is reported at the end. These are likely to improve understanding of the mechanisms that contribute most to AMR, the pattern and the trends of AMR in the short- or long-term. When crucial information was required but lacking, authors were not contacted via email to provide clarification rather such information were excluded. This is can affect the reports roughly as only 6 articles were excluded.

Trend of AMR research in Ethiopia

The gradual increase in publications from 1988 to date suggests that AMR research is gaining increasing attention within Ethiopia (Table 3). While most of the reported AMR research was conducted in Amhara and Addis Ababa, an increase in AMR research was observed in other regions although fewer publications were identified from them. It is possible that researchers from Ethiopia have focused their AMR research on Uropathogens. A very limited data from Afar, Somali, Benishangul and Gambella may be due to historical political events that could have disrupted health-related surveillance or research studies if these existed. Therefore, lack of attempting to gather such data may affect the findings of this research. Notably, even in regions from which more publications were derived, research progress on AMR in some disease conditions appears slow relative to the global awareness of AMR, supporting the seemingly low prioritization of this problem in Ethiopia[30]. This is worrisome considering that a sizable portion of health budgets in these regions are allocated to the acquisition of antibiotics for the prevention or treatment of infectious diseases, including diarrhea.

Furthermore, human diseases are a primary concern, particularly when those affected are the most economically productive sub-populations. Nevertheless, in the case of zoonotic food and water-borne diseases, control of human disease relies, in part, on the control of animal diseases. With projected increases in human and food animal populations in the coming decades, increased interactions between humans and animals are inevitable, particularly where land for expanding populations is scarce [88]. Presumably, animals can also serve as reservoirs of antibiotic resistant enteric bacteria, underscoring the importance of integrating animal and human research to maximize benefits for both sectors (i.e., a One Health focus) [152]. Despite this need, this study focuses on humans because of the limited review period. Based on this review, research in Ethiopia has been focused on AMR prevalence and patterns; a trend that has persisted since the 1970s.

The frequency of studied bacteria corresponds with the frequency of their implication in infectious diseases in the region, their potential for transmission to humans and their high rates of resistance to available treatment regimens (Amp, Chl, Cip, Cot, Gen, and Tet). Probable drivers and potential mitigation actions were universally discussed by study authors. Nevertheless, no study directly tested these ideas or assessed the effectiveness of AMR interventions. Similarly, none of the studies tested associations between these putative risk factors and reported prevalence of AMR; consequently, although mechanistic explanations were suggested and may be intuitively reasonable, they remain speculative. While the potential role of risk factors such as antibiotic use is undisputed, a consistent focus on cross-sectional prevalence data does not build understanding of the proportional contributions and distributions of each of these factors in different environments and subpopulations. Thus, while useful for qualitative purposes, unstructured and uncoordinated prevalence data is insufficient for estimating changes overtime and for designing focused interventions [30]. The following issues present the greatest challenges to drawing inferences from the existing research.

Study execution

Study and sampling design

Of the four study designs (hospital, laboratory, institution and community-based), AMR studies involving humans were predominantly hospital or laboratory-based. Samples and isolates for these studies were obtained primarily from patients seeking treatment at health facilities and, in general, reported high prevalence of AMR. While hospital sampling is more convenient and less expensive than field-level random sampling, it likely represents populations that owing to failures in self-medication with variable-quality antibiotics are pre-selected for resistant strains of bacteria thereby inflating reports of AMR prevalence [152]. Similarly, where the hospital environment facilitates infection transmission, as in the case of non-typhoidal Salmonella, hospital and community prevalence may differ, particularly in communities that rely on non-antibiotic forms of therapy [30, 153]. Consequently, while hospital samples provide an important means of characterizing AMR, their generalizability to the general population is limited. Randomized and independent sampling, akin to methods employed in community-based studies; need to be considered as the basis for future sampling efforts [154].

Laboratory protocols

Different laboratory assays were used for antibiotic resistance testing, with automated systems coming into use after the year 2000. Occasionally, modifications to these assays were used such as single- or double-disc diffusion, controlled agar diffusion and gradient agar diffusion (E-test), and instances occurred where two tests were employed [48]. This was either done in combination (to simultaneously determine antibiotic sensitivity and minimum inhibitory concentrations or when testing was done in different laboratories) or separately (each test for a specific set of antibiotics as was the case where certain antibiotics were not included in automated systems). Where combined testing was reported, however, it was unclear how disparities between tests were resolved in the event that this occurred, or which of the test results were reported (if done in different labs). In general, there are reported modifications of the common laboratory assays and it was unclear how these were standardized to ensure agreement between tests [155].

Non-standardized reporting

There is large variability in the scope of reported data and in some cases limited detail on the description of study methods and results. This could have been due to page limitations imposed by specific journals and/or the absence of a structured reporting system for AMR research. Most of the gaps in this study's data arose from inadequate description of (i) study period (date and duration), (ii) population demographics, and (iii) laboratory procedures (isolation techniques, controls and standards). These elements, discussed below, may be critical in detecting subtle yet significant differences between populations, procedures and time points, differences that may otherwise not be appreciated when AMR data is considered generally.

[156]Depending on the nature and duration of a study, events (both natural and man-made) can intervene during the course of a study period to skew prevalence data in either direction. For instance, outbreaks of enteric diseases, commonly observed during floods or drought can increase health facility attendance and/or antibiotic usage thereby amplifying AMR prevalence during such periods [157]. Providing 'time data' while identifying factors associated with AMR during study periods thus becomes crucial in explaining patterns or deviations that would otherwise be interpreted incorrectly.

Population demographics

Factors such as age, gender, ethnicity, environment and health status can limit the generalizability of AMR data. Children, who often are at a higher risk of infections, are likely greater consumers of certain types of antibiotics than others and could, contribute more to the AMR prevalence for some antibiotics as compared to adults. Gender roles, on the other hand, can have an indirect bearing on AMR by affecting health-seeking behavior. For instance, health-services utilization by men can be lower than among women whose child-rearing roles present opportunities for seeking treatment particularly when a child is sick [158]. Cultural traditions and practices can also explain differences in AMR levels and profiles [159]. AMR prevalence can also vary by study setting [160]. Similarly, rural populations may have, among other differences, poorer sanitary conditions, greater human-animal interactions, limited access to treatment facilities and fewer varieties of effective antibiotics [161]. All which can impact their AMR prevalence and profiles when compared to urban populations. Laboratory procedures subtle variation in laboratory protocols can impact the interpretation of antibiotic sensitivity results [162]. There are multiple steps involved in quantifying antibiotic susceptibility/resistance, and consequently multiple potential sources of variation among studies that can impact the validity of AMR data [163].

The individual and collective contribution of each of these factors cannot be appreciated fully in the absence of guidelines that ensure consistent reporting of such variables. A means for incorporating this data when reporting AMR data is needed. The opportunities to implement a structured AMR surveillance system are probably limited for the country owing to competing national priorities and scarcity of resources. Nevertheless, it is still feasible for scientists in these regions to adopt a structured reporting mechanism for AMR studies so that the data collected can be used to make meaningful comparisons between different studies, geographic locations and points in time [152]. Given widespread adoption, such guidelines should make it possible to compile AMR trends, highlighting variation between regions and guiding the implementation of focused interventions based on data from what would otherwise be scattered amongst reports. The potential benefits of such a venture stand to be appreciated by research groups and public health policy-makers in the country [164].

LIST OF TABLES

Table 1: Key search terms used in PubMed and Google Scholar.

Initial search terms	Refining terms
"Antibiotic resistan*"	"south* Ethiopia*"
"Antimicrobial* resistan*"	"east* Ethiopia*"
"Drug* resistan*"	"Hospital*"
"Multi-drug resistan*"	"North* Ethiopia*"
"Multidrug resistan*"	"West* Ethiopia*"
"Multiple-drug resistan*"	"Northeast* Ethiopia*"
"Multiple drug* resistan*"	"Northwest* Ethiopia*"
"Antibiotic* susceptib*"	"Southwest* Ethiopia*"
"Antimicrobial* susceptib*"	"Southeast* Ethiopia*"
"Drug* susceptib*"	"Cent* Ethiopia*"
"Multi-drug susceptib*"	"enterobacteria*"
"Multidrug susceptib*"	"enter* pathogen*"
"Multiple-drug susceptib*"	"diarrh* pathogen*"
"Multiple drug* susceptib*"	

Table 2: List of risk factors that are thought to contribute to the state of antimicrobial resistance in Ethiopia as suggested both by studies on AMR in humans.

Factors that explain the prevailing state of AMR in Ethiopia and/or persistence of AMR	Factors that contribute to the reduction of AMR	Citation
Ease of access (cheap, widely available) to antibiotics	High cost of antibiotic	[8, 29-40]
Antibiotic use practices, including self-medication, high frequency of antibiotic use, sub-therapeutic use or indiscriminate use	Limiting antibiotic availability	
Over-prescription at health facilities due to limited diagnostics resources	Periodic withdrawal of antibiotics from public use	
Severe infections requiring different antibiotics	Parenteral administration of antibiotics	
Human importation of antibiotic resistant bacteria	Infrequent or prudent use of antibiotics	
Nosocomial or community transmission of resistant bacteria		
Resistant bacteria imported via contaminated food or animal-animal contact		
Animal-human close co-existence increasing contact and Housing contamination		
High antibiotic use in animals in small production systems, poor farm management practices disseminating resistant bacteria		
Contamination during handling animal products.		

Table 3: Trend (based on year of publication) shown for human studies from different regions of the country.

Publication Year	Frequency	Percent
Studies done before 2000	3	2.3
Studies done between 2001 and 2005	6	4.6%
Studies done in between 2006 and 2010	8	6.3%
Studies conducted between 2011 and 2015	103	80.5%
Studies done after 2016 till may 2016	8	6.3%
Total	128	100.0

Table 4: Distribution of publications from the regions of countries studied shown by age of study subjects.

Variables	Addis Ababa	Tigray	Amhara	Oromiya	SNNPR	Harar & Diredawa	Total	Citation
Adults	5	1	11	10	1	4	32	[39-70]
All ages	10	4	32	7	2	7	62	[32, 50, 61, 71-124]
Children	6	1	7	7	1	1	23	[34, 103, 120, 125-147]
Neonates	3		1	-	-	-	4	[47, 115, 143-151]
Pregnant women	1		2	-	1	-	7	[47, 115, 147-151]
Total	25	9	53	24	5	12	128	
Percent	19.5%	7%	41.4%	18.8%	3.9%	9.4%	100%	

Table 5: Frequency of studies based on study design.

Study design	Frequency	Percent
Prospective studies	110	85.9
retrospective studies	18	14.1
Total	128	100.0

Table 6: Frequency of studies based on their use of type of specimen.

Type of Specimen Used	Frequency	Percent
Recto-vaginal swabs	2	1.6
All available clinical specimens	11	8.6
Blood	13	10.2
CSF	5	3.9
Ear discharge swabs	7	5.5
External ocular specimens	3	2.3
Mid-stream (“clean catch”) Urine	23	18.0
Stool	28	21.9
Wound Pus	13	10.2
Others	21	16.4%
Total	128	100.0

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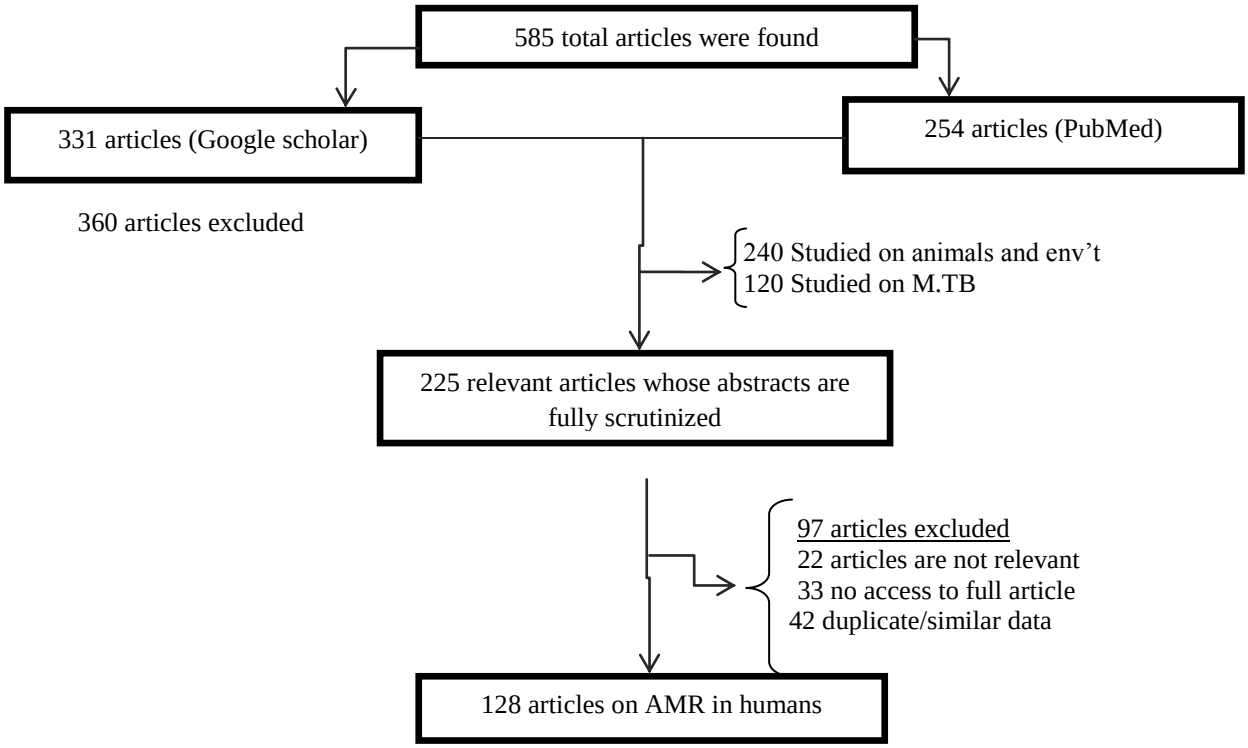

Figure 1: Flow diagram summarizing the selection of publications for review. Two exclusion steps were applied. Total articles excluded (underlined) and reasons for exclusion are shown.

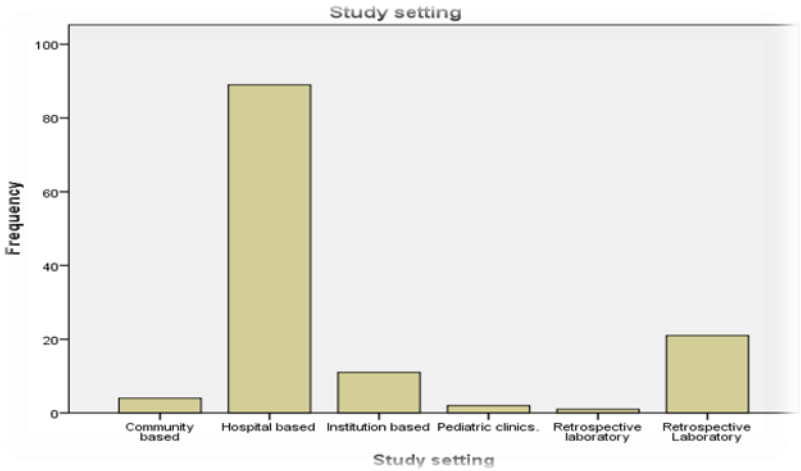

Figure 2: Distribution of Studies based on Study settings.

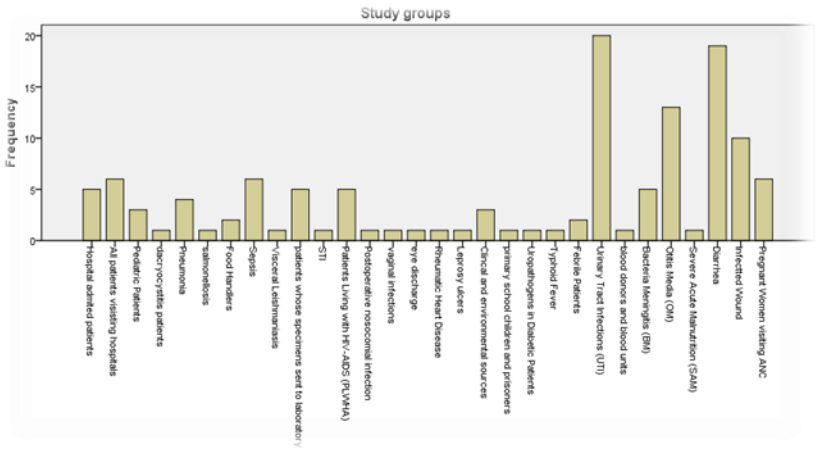

Figure 3: Distribution of Studies based on Study groups (disease conditions).

CONCLUSION

There is a growing body of literature describing AMR in Ethiopia and these studies are useful for identifying the kinds of resistance that are present in the country. Unfortunately, the focus on non-random samples and potentially pre-selected flora combined with a very diverse array of methodologies make it impossible to estimate trends in prevalence and incidence from this body of literature. A more structured reporting strategy is needed to aid future efforts in this regard. Ultimately, however, a significant investment is needed to develop a structured and rigorous country-wide antibiotic resistance surveillance network. In the interim, understanding of the AMR challenge in Ethiopia can substantially be improved by moving beyond descriptive studies to hypothesis-based projects that evaluate intervention strategies. Emphasis on quantitative assessment of risk factors rather than simply making assumptions on how AMR is influenced in study populations would be extremely valuable because inquiries such as these will inform policy far better than accumulation of even more descriptive and incomparable AMR studies.

OPERATIONAL DEFINITIONS

First line drugs:
A drug considered to be the first choice to treat a specific condition.

Health care professionals:
A health professionals are qualified persons who deliver proper health care in a systematic way professionally to any individual in need.

Gram positive bacteria:
Gram-positive bacteria are those that are stained dark blue or violet by Gram staining.

Gram negative bacteria:
Are bacteria that do not retain crystal violet dye in the Gram staining protocol.

Multi drug resistant:
Is a condition enabling disease-causing microorganisms to resist distinct drug, first and for most, but also chemicals of a wide variety of structure and function targeted at eradicating the organism.

Resistant (R):
A bacterial strain is said to be resistant to a given antibiotic when it is inhibited in vitro by a concentration of this drug that is associated with a high likelihood of therapeutic failure.

Second line drugs:
Any therapeutic agent that is not the drug of choice or the drug normally used to treat a particular condition if first line therapy fails.

Susceptible (S):
A bacterial strain is said to be susceptible to a given antibiotic when it is inhibited in vitro by a concentration of this drug that is associated with a high likelihood of therapeutic success.

ACRONYMS

AMOX	:	Amoxicillin
AMP	:	Ampicillin
AMR	:	Antimicrobial Resistance
APUA	:	Alliance for the Prudent Use of Antibiotics
ARB	:	Antibiotic Resistant Bacteria
CDC	:	Center for Communicable Diseases Prevention And Control
CHL	:	Chloramphinicol
CIP	:	Ciprofloxacin
COTRI	:	Cotrimoxazole
CPE	:	Carbapenemase-producing Enterobacteriaceae
CRE	:	Carbapenem-resistant enterobacteriaceae
E. Coli	:	Escherchia Coli
MAR	:	Multiple Antibiotic Resistances
MDR	:	Multidrug Resistant
MIC	:	Minimum Inhibitory Concentration
MLST	:	Multi-locus Sequence Typing
MRSA	:	Methicillin-Resistant Staphylococcus Aureus
OPD	:	Outpatient Department
SNNPR	:	Southern Nations, Nationalities and people' of Ethiopia
Sp	:	Species
UTI	:	Urinary Tract Infection
WHO	:	World Health Organization

COMPETING INTERESTS

The authors declare that they have no competing interests.

AUTHORS' CONTRIBUTIONS

MT discovered the area, designed the study and collected the documents and wrote the draft; **MA** reviewed and revised the whole manuscript. Both authors read and approved the final manuscript.

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