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ORIGINAL RESEARCH ARTICLE

Prevalence of Antimicrobial Resistance in Saurashtra, Gujarat and Implications Toward Sustainable Healthcare

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Abstract Growing antimicrobial resistance (AMR) is one of the major worldwide healthcare problems at present. Antimicrobial resistance (AMR) is part of the natural process of evolution among microorganisms, but which is expedited manifold by the unregulated and over-the-counter use of antibiotics. This induces new and more severe resistance mechanisms in the microbes, which is quite difficult to treat with the routinely prescribed antibiotics, ultimately leading to prolonged infections, disease and even death of the host. WHO had, back in 2014, issued a strict warning in its report about the rising incidence and future threat of AMR globally. So, the present epidemiological survey was carried out to evaluate the growing incidence of antimicrobial resistance in Rajkot, a city located in the western part of India. The data was collected from various clinical settings e.g., hospitals, clinics and diagnostic centers, situated across the city, which was later statistically evaluated for clinical significance. The results clearly indicated towards the rising prevalence of resistance in some of the important clinical pathogens for example, *Escherichia. coli, Klebsiella pneumonia, S. aureus, Acinetobacter baumannii*, etc., against some of commonly used antibiotics e.g. ampicillin, piperacillin, ciprofloxacin, levofloxacin and aztreonam. This study clearly highlights the danger and challenge of treating antibiotic resistant infections in future, also drawing attention to a similar crisis probably existing in various parts of the world. It is very crucial to control this situation in relevance to SDG goals also, as minimizing the prevalence and effect of diseases is an important target to achieve in Goal-3, that aims to promote healthy lives and well-being for all.

Keywords Antimicrobial resistance (AMR) · Antibiotics · Epidemiology · Sustainable development goals · World Health Organization

Introduction

AMR is the ability developed by microorganism to inhibit or overcome the action of antimicrobial agents, which were previously effective against them [1]. AMR is part of the natural process of evolution among microorganisms, but which is expedited manifold by the unregulated and over-the-counter use of antibiotics [2]. This unwarranted exposure to antimicrobial drugs, induces new and more severe resistance mechanisms in the microbes, leading to prolonged infection, disability and even death in the host. Surprisingly the rising incidence of antibiotic resistance has been observed of late in non-clinical samples also [3]. The cost of health care for patients with resistant infections is higher than those with non-resistant infections, attributable to prolonged duration of illness, requirement of additional diagnostic tests to know the severity and use of more, and expensive drugs to treat such infection [4]. Even more dangerous is the scenario, when some pathogens develop resistance to more than one particular or class of antibiotics. This phenomenon is known as Multiple drug resistance (MDR) (http://www.tufts.edu). The additional threat of the horizontal transfer of the antibiotic resistant genes among the microbes, both inter and intra

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specific, is always looming large. This can lead to the generation of more antibiotic & multi drug resistant pathogens in the future, thus further increasing the burden of antibiotic resistance, disease and the cost of healthcare globally [5].

WHO, in fact, at its Jaipur declaration in 2011, has highlighted the rising prevalence and multi-faceted risks of AMR and stressed on the importance of a multi-sectorial approach to deal with the menace [6]. Certain estimates, like that of the Centre for Disease Control and Prevention (CDC), put the figure to the tune of approximately 10 million deaths and 100 trillion USD economic losses, every year worldwide, by 2050. Many mechanisms of resistance to antibiotics are prevalent and spreading in the microbial communities around the globe, increasing the difficulty in curing even common infections [2]. With the emergence and spread of the AMR, we are in all probability, heading towards a dangerous and post-antibiotic era, where the onus will be on discovering newer alternatives to the routine antibiotics. In fact, many scientists have already proclaimed that the next biggest health challenge facing the human race, would be caused by the antibiotic and multidrug resistant microbial infections, after Covid-19 [7].

In the Indian subcontinent and especially India, the antibiotic resistant microbial infections have been observed to be continuously on the rise. To counter the threat posed by it, a joint initiative has been formed between the Department for Biotechnology (DBT), under Indian Government and Research Councils United Kingdom (RCUK), under UK Government to map the entire spectrum of AMR in the country and based on it, devise strategies and therapies for tackling and preventing it. Along this line, an elaborative report released by it, 'The DBT scoping report on antimicrobial resistance in India in 2017, states that some of the more common antibiotics, against which resistance is exhibited by more than 70 percent isolates of various clinical pathogens e.g., *E. coli*, *K. pneumoniae*, *A. baumani*, and *P. aeruginosa*, are the fluoroquinolones and 3rd generation cephalosporins [8].

Developing countries, comparatively are more prone to the rising incidence of AMR, due to prevalence of certain factors like lack of awareness about infectious diseases and prevention, inaccessibility to healthcare facilities, localized treatments which are costly and unaffordable to majority, self-prescription and over-the-counter use of antibiotics etc. [9]. Dumping of inadequately treated effluents from the pharmaceutical industry, especially in countries where drugs are manufactured in bulk, is seen one of the major causes for this [10]. The greater access to antibiotics and drugs, and on most occasions even without prescriptions, again more common in the developing countries is considered as one of the principal reasons, for increasing the menace and prevalence of AMR [11]. Not only that, the lack of awareness regarding usage of clean water, sanitation, hygiene, coupled with poor accessibility to affordable drugs, vaccines, etc., all associated with possible administrative and legislative apathy, had made this issue more threatening [12]. As a response to these, WHO has initiated a special global awareness campaign, termed as World Antibiotic Awareness Week (WAAW) from 2020, to make people and the health workers aware of best practices in sanitation hygiene etc., so the contribution of these factors towards AMR can be controlled and also reduced.

In the state of Gujarat also, such pattern of resistance has been reported in bacterial isolates, from various places, to some of the common antibiotics, for example, ciprofloxacin, cefuroxime, cefotaxime, ceftazidime etc. [13]. So, it is quite evident that the issue of AMR is both locally and globally alarming and it should be dealt with very urgently and firmly [14]. Viewing this situation, many international health organizations like WHO, CDC, EMA etc. in collaboration with the national government and other public health agencies, are trying to frame policies and regulations to tackle the growing threat of antimicrobial resistance around the globe [15]. To support such initiatives and research in this regard, a true estimate of the prevalence of the antimicrobial and multi-drug resistance in any region, backed properly by epidemiological survey, assumes great significance. As far as Rajkot, a city situated in the region Saurashtra of Gujarat state of India, such surveys have not been undertaken before. Keeping this in mind, the present study was initiated to know the prevalence of AMR in Rajkot city, along with determining the more resistant pathogens, and the specific antibiotics they are resistant against.

Materials and Methods

The methodology adopted for the prospective survey of the prevalence of the antimicrobial drug resistance in Rajkot included data collection from the various hospitals, clinics and diagnostic laboratories situated across different locations of the city analysis of the data. The survey was intentionally and carefully designed so that the hospitals and laboratories selected covered the entire city, namely Amruta hospital, Arpan hospital, Ashirwad hospital, Century cancer hospital, Genesis hospital, Giriraj hospital, Lotus hospital, Medisurge hospital, NeuGen diagnostic lab and Salus hospital. Few more medical setups were targeted, but any data could not be retrieved from there, due to the non-cooperation of the personnel. So, the collection of the data had to be limited only to the before mentioned hospitals and labs, which included total of 40 infections and spanning over a duration of approximately 30 days.

A specific set of questionnaires was also prepared for the purpose of data collection and survey. Later the data collected was analysed statistically for its clinical significance.

Certain common questions were asked to the respondents in the clinics, hospitals and labs for example, as shown in Table 1.

Various clinical reports pertaining to the resistant infections of the patients, were also obtained from the hospitals and diagnostic labs detailing various important facts e.g. the culturing and isolation of the pathogens from the patient specimens e.g. urine, blood, pus and stool, the colony count, identification of the bacterial species, and determining its response towards antibiotics. This report, in most of the cases also additionally included the basic and demographic information of the patients like age, gender, locality, environment, sample type, life style, predisposition to disease, etc. All this information was meticulously used and analysed in the study.

Results

The survey was carried out by collecting data, mainly in the form of information and report from clinical settings comprising of at least ten different hospitals and diagnostic labs in Rajkot. The data reflected the drug susceptibility and resistance pattern of several clinical bacterial strains, which was further analysed by using appropriate methods for significance. The results obtained in the study pointed out to the following important facts.

Resistance Pattern Exhibited by the Different Isolates in Various Clinical Samples

Urine Sample

E. coli, the Gram-negative bacteria, isolated from the urine sample of male more than 50 years of age was found mostly resistant to levofloxacin, ciprofloxacin, ticarcillin, whereas in males less than 50 years of age, it was found to be mostly resistant to aztreonam, piperacillin, cefepime, ceftazidime. The bacteria isolated though, from urine sample of both elderly men and women exhibited a common resistant pattern to ampicillin, ciprofloxacin and levofloxacin.

Pus Sample

E. coli from the pus sample in both men and women was found to be more resistant to ampicillin and piperacillin. *S aureus, isolated* from the same source, was found to be more resistant to cefazolin, cefoxitin, ceftriaxone, piperacillin in males and in case of female, the resistance was found to be majorly against ciprofloxacin, amoxicillin and penicillin-G. *Klebsiella pneumoniae* from pus sample, irrespective of the gender and age, was found to be mostly resistant to ceftriaxone, cefoperazone, cefoxitin and amoxicillin.

Blood Sample

In blood sample*, S. aureus* was found to be resistant to oxacillin and cefazolin in females. Significant data was not available to verify the resistance pattern of the *S. aureus* in case of male blood samples. Though the same isolate showed a notable resistance pattern to benzylpenicillin, amoxicillin and ampicillin, in case of blood samples obtained from children.

Common Resistant Species and Their Antibiotic Resistant Pattern

Common Resistant Species

The detailed analysis of the reports of patient with bacterial infections, collected from different clinical settings across the Rajkot city, revealed that the most common resistant bacterial pathogenic species was *E. coli,* followed by *S. aureus and P. aeruginosa.* (Fig. 1). Approximately ten cases were reported, wherein antibiotic resistant *E. coli* was isolated from the samples, whereas the number of cases caused by resistant *S. aureus and P. aeruginosa* were approximately six and four respectively. Resistance pattern exhibited by the remaining isolates, e.g. *Klebsiella* spp., *Enterococcus*

Table 1 Questionnaire asked to the respondents during the survey

Sr. No	Questions asked
1	The average influx of the patients?
2	General information e.g. their origin, gender, age etc.?
3	Proportion of indoor patients in that group?
4	The severity of the infections, like percentage of sensitive and resistant bacterial infections in the diseased people?
5	Whether any correlation was found between the severity of the infection with the living environment of the patients or the time of the year?
6	Any sign or direction of the infections, becoming more resistant in case of co-morbidity in the patients?

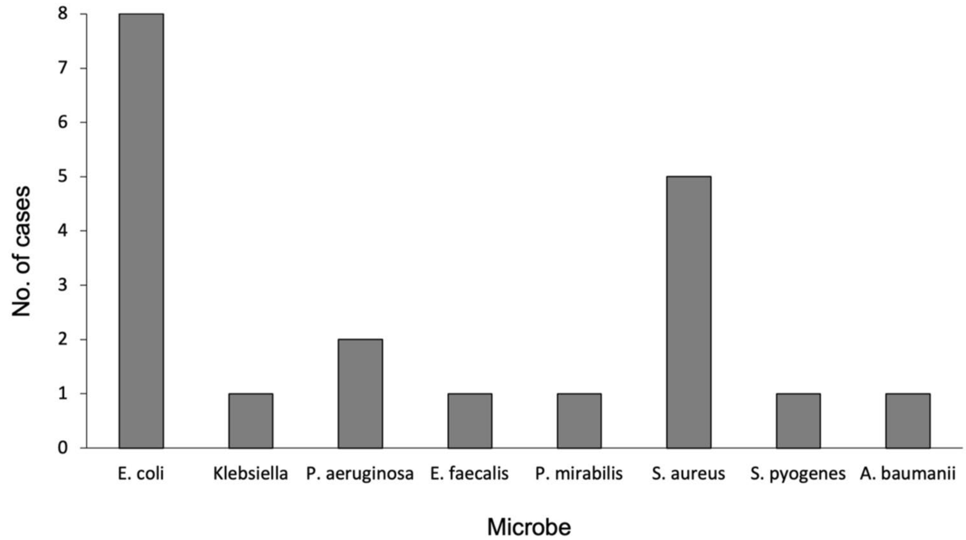

Fig. 1 Prevalence of antimicrobial resistance observed in the various pathogenic species reported in the study

faecalis, *Acinetobacter baumanii*, etc. were almost identical, each causing around, on an average 1–3 infections. This points to the fact that though the range and frequency of antimicrobial resistance might be enhanced in certain species like *E. coli* and *S. aureus*, but the fact that slowly different kinds of bacterial species are acquiring the AMR traits, cannot be denied.

Antibiotic Resistance Pattern

The resistant isolates, isolated from the clinical infectious samples, were found to be more resistant against certain specific antibiotics for example ampicillin, piperacillin, ciprofloxacin, levofloxacin and aztreonam.

Number of Infections Caused by Resitant Bacteria Reported from Various Hospital Across City

Figure 2 highlights the total no of cases reported from different hospitals and laboratories across Rajkot city. Giriraj hospital reported the maximum number of cases (seven), followed by Lotus, Arpan and Medisburg hospitals with five cases each. Four cases each were reported from hospitals namely, Ashirvad, Genesis and Century. Amrita hospitals reported 3 cases, whereas 2 cases were reported from Neu-Gen laboratoy and the least number of resistant cases (only one) was reported from Salus hospital. This figure clearly hints at the rising pravalence of antimicrobial resistance in Rajkot city.

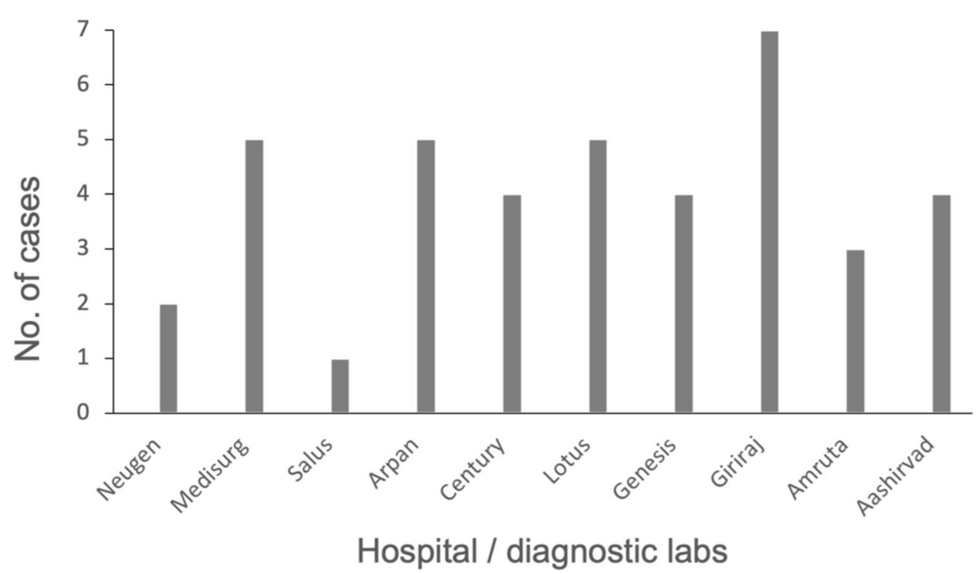

Fig. 2 Antibiotic resistant bacterial infections reported from various hospitals and diagnostic labs of Rajkot city

Comparative Evaluation Between Number of Infections Caused by Drug Resistant and Sensitive Bacteria, Reported Across Various Healthcare Facilities of the City

The comparative evaluation of the pattern of drug resistance and sensitive cases, observed isolatedly in each clinical set up is laid out in Fig. 3. The sequence is as follows, the name of the clinical set up followed by the number of resitant and sensitive cases: Aashirvad (3 resistant and 1 sensitive); Amruta hospitals (2 resistant and 1 sensitive); Aapan (3 resistant and 2 senstive); Century hospital (1 resistant and 3 sensitive); Genesis hospital (2 each of both resistant and sensitive); Giriraj hospital (3 resistant and 4 sensitive); Lotus hospital (2 resistant and 3 sensitive); Medisburg hospital (4 resistant and 1sensitive); Salus hospital (1 resistant and no sensitive) and Newgen laboratory (2 resistant and no sensitive). As mentioned, no sensitive isolates, altogether were reported from the last two helathcare set up in the list.

Discussion

Antimicrobial resistance (AMR) is one of the major health emergencies, threatening mankind in the present time [1, 7, 9, 15, 16]. Particularly, if the infection caused by the AMR strain is communicable, it can quickly spread in the community at large, with the implication of ultimately turning into an epidemic or even pandemic.

Concerted work has already begun to contain this explosion, generally in the form of AMR stewardship, and specifically in terms of searching for innovative diagnostics and therapeutics to combat the menace [8, 17].

India is also not untouched by the effects of the rising AMR. In the last decade, the problem of AMR has become common and been reported from various parts of the country [3]. It has reached almost an alarming level [1, 7] which has prompted the Government of India, as like other nations, to take serious note and devise strategies to check its spread, in consultation with various stakeholders. Many governmental (both central and state level) agencies, physicians, private organizations, NGOs, civil societies and district administrations are working collaboratively to resolve the crisis [18, 19]. Towards this end, various kinds of data and reports, acquired from the community, administrative and clinical set-ups, provide a proper framework to plan and prepare a roadmap for future action and precise strategy implementation [8].

Against this backdrop, the present study was designed to evaluate the extent of the prevalence of AMR among pathogens, isolated from clinical samples such as urine, stool, blood etc., collected from patients visiting various diagnostic labs and hospitals for diagnosis and treatment, in the city of Rajkot, in Saurashtra region, Gujarat, India. The data generated from the study, interestingly pointed towards a considerable high incidence of resistance among the pathogens, against the routinely used and important antibiotics such as ampicillin, piperacillin, levofloxacin, aztreonam and ciprofloxacin. Similar reports of resistance to ciprofloxacin, among *E. coli* and *K. pneumoniae* as highlighted in the study, has also been observed in countries under Global Antimicrobial Resistance and Use Surveillance System (GLASS) [20, 21]. Other isolated reports, available from various sources including WHO, also corroborate the findings of the study. E.g. *E. coli* was found to be resistant to most of the beta-lactam antibiotics, including penicillin, third generation cephalosporins and fluoroquinolones etc., the resistance particularly being conferred by enzymes such as extended spectrum beta-lactamases (ESBLs). Similarly, *Klebsiella pneumoniae* is found to be resistant to

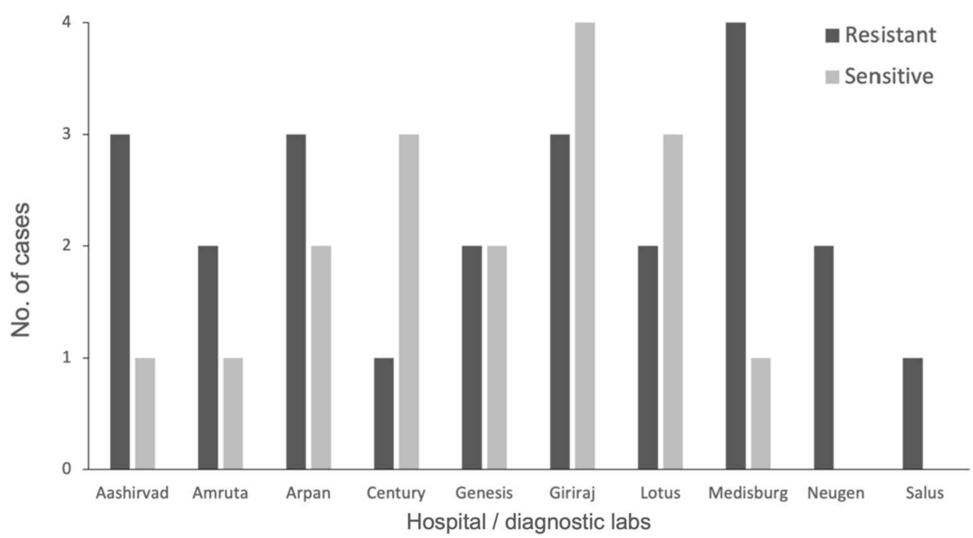

Fig. 3 Comparative evaluation of the number of drug resistant and sensitive bacterial species reported from different hospital casing infections

third-generation cephalosporins, again aided by ESBLs, and also to carbapenems [22]. *S. aureus* has also been reported to exhibit resistance to many antibiotics, including significantly to methicillin. Such strains being particularly known as 'Methicillin resistant *S. aureus*' (MRSA) [23, 24]. Infections with MRSA, are quite routinely acquired by patients admitted in clinical set-ups like hospitals etc., and then transmitted within the community. This appears particularly dangerous, because methicillin is regarded as the last-resort antibiotic, to treat the *S. aureus* infections [25]. In the same vein, resistance to penicillin has been observed, quite routinely in *Streptococcus pneumoniae*.

The study findings clearly indicate towards the evolution and spread of the acquired resistance to antibiotics, among the bacterial pathogens isolated from varied areas of the city (Fig. 1). This was clearly highlighted in many other significant findings from the study, e.g. more number of resistant infections reported from the surveyed clinical set ups, compared to the susceptible ones; non-specific resistance pattern observed across samples collected from patients for example blood, pus, urine, and across all age groups and similar resistance pattern exhibited by pathogens like *E. coli, S aureus and P. aeruginosa* against all routinely used antibiotics e.g. penicillin, ciprofloxacin and chloramphenicol. Scoping report [8] very similarly highlights the high risk of mortality to patients in India from infections caused by resistant pathogenic species like Salmonella, Shigella, Enterococcus, Vibrio. Similar studies have also indicated to the presence of MRSA among post-surgery samples obtained from patients e.g. pus, sputum, blood [26]. Along same lines, reports [25, 27] had reflected upon the source of MRSA infections in Rajkot, in which according to the authors, hospital-acquired MRSA cases were found to be significantly higher. Though, occasionally the trend has been observed in non-clinical samples also [3, 28]. This danger really calls for an urgent and concerted effort from the clinical practitioners and public health experts to deliberate on a serious note and come forward with some practical strategies and solutions to manage the crisis [29].

So far, the growing threat of AMR has been mostly overlooked in the average to small sized cities and towns of India, with most of the studies focussing on its impact only in the metros and industrial areas. To the best of our knowledge, this is the first survey-based comprehensive epidemiological report, regarding the prevalence of AMR in the Saurashtra belt of the state of Gujarat, India. Though, few isolated reports in the past have portrayed the rise in AMR infections in the region, from a particular hospital or sample [3, 25, 28]. This makes this study very significant and relevant in terms of creating awareness on the dangers of AMR, both from the regional and national perspective. Additionally, the results of this survey call for urgent and replicative studies, to be conducted in the other parts of the country as well, to assess the present level and spread of the anti-microbial and multi-drug resistance, among the various pathogenic bacterial strains.

Conclusions

Finally, we would like to draw the attention of the readers to the fact that AMR is at present a global health emergency [30]. We are in-fact rapidly heading toward the post-antibiotic era, where it would be imperative to discover, test and implement on a fast-track mode, alternative strategies to prevent and treat evolving bacterial infections, notably the ones caused by antibiotic and multi drug resistant bacteria [17, 31]. The present survey comprising the surveillance done at various clinical set ups in the Saurashtra belt of Gujarat, sends alarming signals in this direction by highlighting the rapid increase in the number of resistant infections, of late. Disturbingly, similar scenario exists in almost every part of the world at present, demanding an urgent need to check its spread [32]. Otherwise, very soon it can spiral out of control and usher in another epidemic like situation globally, even may be of higher proportions than Covid-19. The situation is made worse by the horizonal transfer of AMR genes between the pathogenic species, thus creating new superbugs along the way, capable of overcoming several antibiotics [33]. Presently, there is also a lot of focus among the scientific community to investigate the link between Covid-19 infections and aggravation of the AMR cases [7, 31, 34–37].

This clearly emphasizes that the urgent need of the hour to avoid the looming threat of AMR in future is the 'One Health approach', which recognizes the interconnection between human, animal, and environmental health and emphasizes the need for a coordinated and holistic response to AMR. This will ensure concerted action and management at various fronts, e.g. enhanced awareness, more fund allocation for AMR research, development and administration of effective and innovative diagnostics and therapeutics, accessible to all, better prevention protocols e.g., proper sanitation and hygiene practices, strong legislative framework for fixing accountability, robust supply of essential resources, etc. This kind of 'AMR Stewardship' is required to win this war in the future [29].

SDGs and AMR

Sustainable Development Goals (SDGs) are a set of 17 global goals established by the United Nations General Assembly in 2015, with a deadline of 2030. These goals aim to address some of the world's most pressing challenges, including poverty, inequality, climate change, and peace and justice. The SDGs are an essential part of the global agenda, as they provide a framework for sustainable development that is both comprehensive and universal.

Antimicrobial resistance (AMR) is a significant public health concern globally. AMR occurs when microorganisms, such as bacteria, viruses, fungi, and parasites, evolve and develop resistance to antimicrobial drugs, such as antibiotics, antivirals, and antifungals. The emergence of AMR threatens the ability to treat infectious diseases, leading to higher morbidity and mortality rates, longer hospital stays, and increased healthcare costs.

Several SDGs are related to AMR, including Goal 3 (Good Health and Well-being) and Goal 6 (Clean Water and Sanitation). Goal 3 aims to ensure healthy lives and promote well-being for all at all ages, including reducing the incidence of infectious diseases and addressing the rise of AMR. Goal 6 focuses on ensuring the availability and sustainable management of water and sanitation for all, which is vital for preventing the spread of AMR.

Addressing AMR requires a One Health approach that involves collaboration between human, animal, and environmental health sectors. This approach recognizes the interconnectedness between human, animal, and environmental health and emphasizes the need for a coordinated and holistic response to AMR. To achieve the SDGs and address AMR, concerted efforts are required from all stakeholders, including governments, policymakers, healthcare professionals, researchers, and the general public. By working together, we can ensure a sustainable future that prioritizes the health and well-being of all individuals and the planet.

Bose & Chatterjee [38], in their article discuss the growing problem of antimicrobial resistance (AMR) and its impact on public health. They provide an overview of the causes and mechanisms of AMR and discusses the challenges in addressing the issue. The article highlights the need for a coordinated and multi-sectoral approach to addressing AMR, including the development of new antimicrobial agents, improved infection prevention and control measures, and increased awareness and education about the appropriate use of antibiotics.

Kumar and others [39] in their article discuss the One Health approach to tackling antimicrobial resistance (AMR).

Declarations

Conflict of Interest The authors declare that they have no conflict of interest, whatsoever, in any form for this study.

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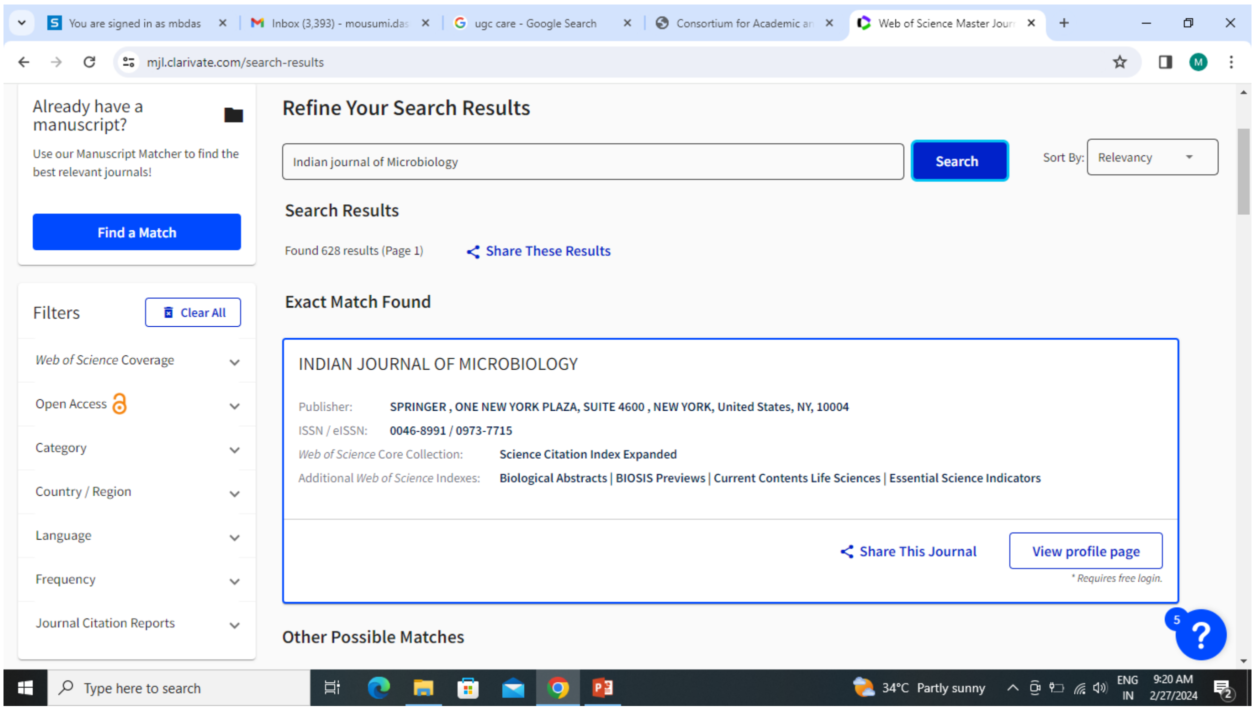
WoS INDEXING



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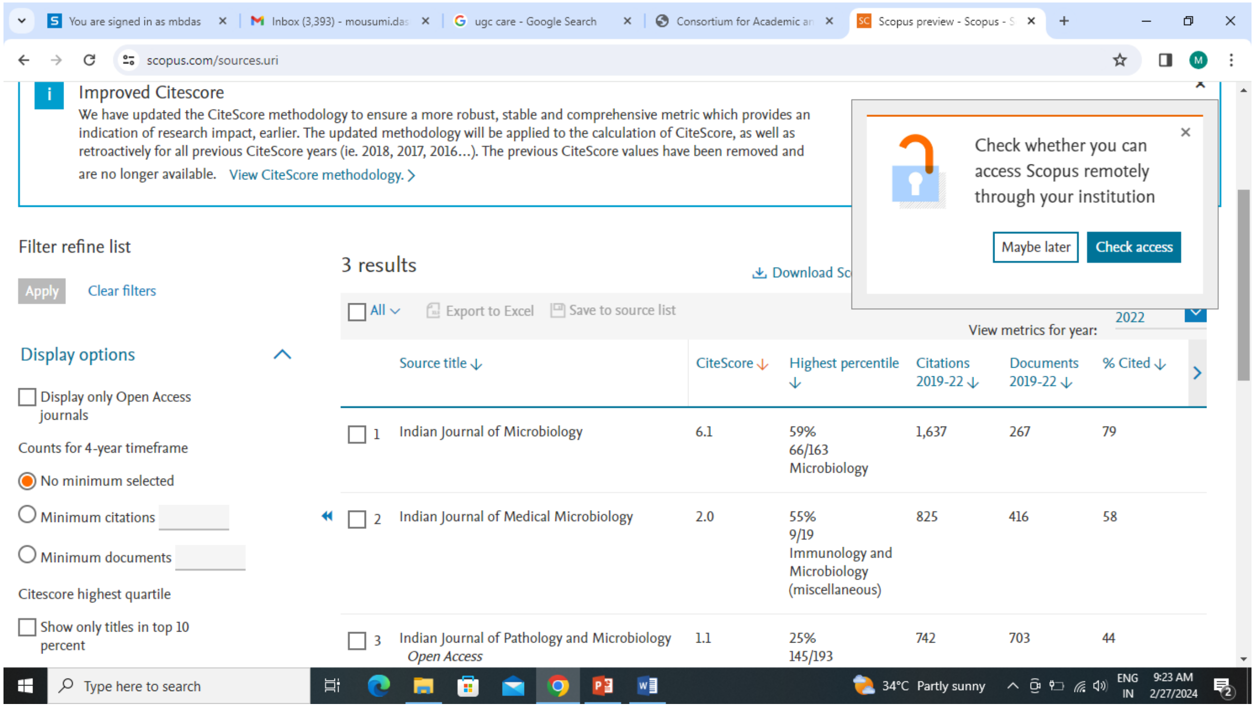

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