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A REVIEW ON HIDDEN THREAT BEHIND ANTIMICROBIAL RESISTANCE OF COVID-19 PANDEMIC

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ABSTRACT

A novel corona virus had hit the world in 2019 resulting in major shutdown which was later declared as Pandemic killing more than a million people worldwide. It was estimated that AMR alone could kill 10 million people per year by 2050. Antimicrobial resistance (AMR) has been cited as the most significant trouble to the global health and global frugality in recent years, however is currently possible to be transcended by COVID-19 for some time. The fear of COVID-19 infection together with lack of sufficient knowledge of the value of antibiotics infection, particularly in low- and middle-income countries with poor antibiotic control actions and restricted access to health settings has directly impacted the increased access to the over-the-counter antibiotics. Antibiotic resistance, in particular, has accelerated the spread of bacteria known as "superbugs," which place an immense strain on health systems and economies, and result in increased hospitalizations and deaths. Globally, India tops the list of countries with the highest antibiotic consumption, and highest AMR. Review on studies published on hospitalized COVID-19 patients identified that majority of patients received antibiotics, only fewdemonstrated superimposed bacterial or fungal co-infections. An individual's inappropriate attitude about the use of antibiotics has been found to be a major global risk factor for antibiotic resistance. Increased risk of infection potentially leading to an overuse of antimicrobials can occur due to vaccine services disruption. To mitigate further harm implementation of antimicrobial stewardship principles in COVID-19 patients is urgently needed. There is a need to look into the post-COVID-19 era when antimicrobial resistance will remain a challenge to be overcome.

KEYWORDS: Antibiotic resistance, Antimicrobial resistance (AMR), COVID-19, Antibiotic stewardship.

INTRODUCTION

Antimicrobial resistance (AMR) is a worldwide public health concern.[1] A novel corona virus had hit the world in 2019 resulting in major shutdown which was later declared as Pandemic killing more than a million people world wide. Antimicrobial resistance (AMR) has received increased international attention since 2015, had already been named a priority for global public health for the year 2020.[2] It was estimated that AMR alone could kill 10 million people per year by 2050.[3] This was estimated before covid19 pandemic forecasting higher death rate in the near future. It's been more than 75 years discovering first antibiotic but notion regarding use of antibiotic still continues. According to a study performed by the WHO, a veritably common misconception amongst the public is that antibiotics can be used for viral infections (i.e., the common cold).[4] Antimicrobial resistance(AMR) has been cited as the most significant trouble to the global health and global frugality in recent years, however is currently possible to be transcended by COVID-19 for some time.[4] In a massive multicentre Chinese study, 58% of patients admitted to hospital received IV antibiotics.[5]

Epidemic which led to increased/advanced hygiene practices may reduce the spread of AMR, which is a very is a veritably positive outcome. Still, there is also a potential negative impact that could arise from increased use of similar products, as numerous of them contain biocides.[4] Biocides are antimicrobials found in surface disinfectants and menage cleaners which will conjointly lead to the emergence of AMR.[6] Climate change is a "throuble multiplier" for spread of contagious diseases and antibiotic resistance.[7]

The known declines in routine pediatric vaccine during covid19 epidemic exaggerated risks for outbreaks of vaccine-preventable conditions.[8] National and international ways for the management of antibiotic resistance advocate education for health-care professionals and therefore the public to promote prudent use of antibiotic.[9]

Antibiotic Resistance and Covid 19

Since the start of the COVID-19 pandemic, there has been growing concern for a implicit rise in AMR secondary to increased antibiotic prescription for COVID- 19 patients.[10] AMR is a leading reason behind death around the world, with the loftiest burdens in low-resource settings. As per the study performed by Murray, their predictive statistical model estimated

4·95 million (3·62–6·57) deaths associated with bacterial AMR in 2019, including 1·27 million (95% UI 0·911–1·71) deaths attributable to bacterial AMR.[11] Lower respiratory infections reckoned for further than 1·5 million deaths associated with resistance in 2019, making it the most burdensome infectious disease.[11] Public has easy access to the internet regarding information on the use of antibiotics to treat COVID-19 infection.[12]

The fear of COVID-19 infection together withlack of sufficient knowledge of the value of antibiotics infection, particularly in low- and middle-income countries with poor antibiotic control actions and restricted access to health settings has directly impacted the increased access to the over-the-counter antibiotics.[13] Compared with January–June 2019, higher consumption of antibiotics, including β- lactam/ β-lactamase inhibitor combinations, carbapenems, quinolones, colistin, tigecycline, fosfomycin, glycopeptides, linezolid and daptomycin, was observed during January–June 2020.[14]

A retrospective study found that the prevalence of carbapenem- resistant Enterobacteralescolonisation increased from 6.7% in 2019 to 50% in March–April 2020.[15] For instance, many individuals presenting with mild disease without pneumonia or moderate disease with pneumonia receive antibiotics.[16] A review of studies published on hospitalized COVID-19 patients identified that while 72% (1450/2010) of patients received antibiotics, only 8% (62/806) demonstrated superimposed bacterial or fungal co-infections.[17] The choice on antibiotic use was grounded on clinical presentation and less so on radiology or laboratory markers.[5] Responders considered Procalcitonin as the most important factor to influence antibiotic prescribing decision among the laboratory markers of inflammation.[5] A recent study conducted in intensive care units in 88 countries showed that 70% (10 640/15 165) of patients had received at least one antibiotic either for prophylaxis or treatment purposes although only 54% (8135/15 165) of them had suspected or proven bacterial infection.[18] As per study from Wuhan, fungi were isolated in 4% of patients and antifungals were prescribed in 15%of cases.[19]

Some of the reasons for thehigh rate of antibiotic utilisation for patients infected with SARS-CoV-2, particularly in severe COVID-19 cases are as follows: (i) as the prevalent presentations of SARS-CoV- 2 infection (cough, fever and radiological infiltrates) are also hall-marks of community-acquired bacterial pneumonia, clinicians empirically add a broad-spectrum antibiotic despite the suspicion of a viral origin; (ii) the anxiety and uncertainty regarding the COVID- 19 outbreak as well as the absence of effective anti-SARS-CoV-2

treatments are potential drivers of widespread and excessive pre-scription of antibiotics; and (iii) co-bacterial, fungal or secondary infection with COVID-19 is possible; however, it is difficult to differentiate between sole SARS-CoV-2 infection and co- or secondary infections.[14] Improper or suboptimal antimicrobial prescribing is important deleterious effect of COVID-19 on AMR.[20]

Antibiotic stewardship

Antibiotic stewardship was implemented in 2011 and focuses on five 'D's': Drug, De-escalation of therapy, Discontinuation of therapy, Dose and Diagnosis. Antibiotic stewardship has 7 core elements viz., Leadership Support, Accountability, Pharmacy Expertise (formerly Drug Expertise), Action, Tracking, Reporting and Education. Stewardship interventions are listed in three categories below: broad, pharmacy-driven; and infection and syndrome specific. Principles of antibiotic stewardship is to measure and improve how antibiotics are prescribed by clinicians and used by patients. Improving antibiotic prescribing and use is critical to effectively treat infections, protect patients from harms caused by unnecessary antibiotic use, and combat antibiotic resistance.

Antimicrobial stewardship refers to coordinated, collaborative programs and interventions designed to improve antimicrobial prescribing by promoting the selection of the optimal antimicrobial drug regimen including dosing, duration of therapy and route of administration and minimize unintended consequences.[21]

Rather than relying on existing empiric treatment guidelines for influenza patients with secondary bacterial infections growing evidence suggests, antimicrobial stewardship measures specific for COVID-19 patients should be preferentially followed.[1] To mitigate further harm implementation of antimicrobial stewardship principles in COVID-19 patients is urgently needed.[5] However, previous studies commonly reported non-adherence to or poor uptake of local and international guidelines.[22,23] With the ongoing pandemic is stretching the limits of optimal antibiotic stewardship, continuing this intervention to curb inappropriate antibiotic usage and surveying the reasons for guideline non- adherence should be conducted within hospitals.[24] Health care providers struggle to save the COVID-19 patients are assumed due to decline in adhering to stewardship programs.[25] Yet, indeed during a epidemic antibiotics should be used wisely and cautiously.[26]

The recent update of WHO's interim guidance on the clinical management of COVID-19 incorporates antibiotic stewardship principles with specific recommendations.[24] Unless signs and symptoms of a bacterial infection exist guidance does not recommend antibiotic therapy or prophylaxis for patients with mild or moderate COVID-19.[16] Leadership must be developed within local teams managing SARS-CoV-2 patients, to support the redeployment of stewardship teams, supported by the development of evidence-based guidelines for the role of diagnostic tests to inform appropriate empirical treatment.[10] Increasing rates of antimicrobial prescribing and potential breakdowns in well-established stewardship programmesmay exacerbate the propagation of AMR.[10]

Context-specific antimicrobial stewardship program will work which include education about AMR, the development of guidelines, infection prevention and control guidelines, intravenous to oral switch therapy, contributions from an infectious disease consultant at the hospital level, rules and regulations for antibiotic quality control, upgraded microbiology laboratory capacity, the development of a national action plan, and the implementation of an infection prevention control program.[27] To come out of this global pandemic to be faced by an increase in the need for effective antibiotics, Antimicrobial stewardship is important.[28] There is a need to look into the post-COVID-19 era when antimicrobial resistance will remain a challenge to be overcome.[17,29]

Factors aiding antibiotic resistance

The main drivers of antimicrobial resistance include the misuse and overuse of antimicrobials; lack of access to clean water, sanitation and hygiene (WASH) for both humans and animals; poor infection and disease prevention and control in health-care facilities and farms; poor access to quality, affordable medicines, vaccines and diagnostics; lack of awareness and knowledge; and lack of enforcement of legislation.

Lack of knowledge

Prudent use of available antibiotics plays a crucial role in view of a decline in the development of novel antibiotics.[30] Self medication and irrational use of antibiotics are the some of reasons of lack of knowledge regarding use of antibiotics. Targeted face-to-face educational intervention method effectively improved respondents' antibiotic resistance knowledge and antibiotic use knowledge and perception. Both in developed and developing countries insufficient knowledge and misconceptions about antibiotics were reported.[31] An individual's inappropriate attitude about the use of antibiotics has been found to be a major

global risk factor for antibiotic resistance.[32] Many articles reported individuals misuse antibiotics irrespective of their education level.[33] There is a need for strong enactment of strategies like continuous community awareness campaigns to regulate misuse of antibiotics through irrational use.[34]

Immunization

To prevent infections vaccines are a key tool, and hence antibiotic use and associated resistance.[35] Increased risk of infection potentially leading to an overuse of antimicrobials can occur due to vaccine services disruption.[2] 90% of 105 countries reported at least some disruptions to essential health services, with routine immunisation services among the most frequently disrupted according to a WHO report published in August, 2020.[36] A survey released in Maywhich covered more than half of the 129 countries reported complete suspensions or substantial disruptions to immunization services in March and April, putting in increased risk of contracting vaccine preventable diseases in an estimated 80 million children under 1 year old.[37]

In a recent data released by WHO and UNICEF reported, through routine immunization services 25 million children missed out on one or more doses of DTP in 2021 alone.[38] As a result of indirect impact of covid19 there will be a surge in vaccine-preventable diseases and their associated complications, leading to increased antibiotic use and risk of resistance.[2]

Climate change

Climate change on itself is a huge threat to the mankind. Although there was no significant relationship in between in the past, climate change has become unavoidable major driving factor for resistance. It is well established that multiplication of an array of infectious disease agents are augmented by increase in environmental temperatures.[39] It is estimated that a 1 C increase in environmental temperatures (above 5 C) could lead to 5%–10% increases in cases of salmonellosis, a disease that is estimated to cause annual more than one million episodes of foodborne illness in the United States (27.2% hospitalization rate).[40]

“Climate change perhaps will not create new diseases, but it will broadly increase the human populations at risk, and thereby make the imperative for effective vaccines and protective guidance more urgent” as stated by Lemery and Auerbach.[41] While treatments for the vast majority of bacterial infections heavily rely on the use of antibiotics, with 18 pathogens currently listed as “urgent”, “serious” and, or “concerning” public health threats in the United

States for developing antibiotic resistance the efficacy of these treatments is diminishing. All regions of the World Health Organization have also reported similar concern.[39]

Factors behind antimicrobial resistance in covid-19 pandemic

Two factors of the COVID-19 response have driven increased antibiotic usage: an increase in standard antibiotic usage and several forms of misguided antibiotic usage. Before widespread testing and diagnosis of COVID-19, patients presenting symptoms of respiratory infections were often given antibiotics that might treat bacterial or fungal lung infections in the absence of or prior to a diagnosis. Even though diagnosis of COVID-19 is now more efficient, antibiotic treatment is often initiated as a precaution prior to receiving a test result.

Early and precautionary antibiotic treatment is a standard of care that is often beneficial in the case of true bacterial or fungal infections. However, during the COVID-19 pandemic, the number of patients presenting with these symptoms and thus receiving this standard antibiotic therapy has drastically increased.

Initially due to absence of well-defined treatments for COVID, treatment initiated with drugs that were already clinically approved, example, azithromycin, its mechanism of action against bacteria and potential anti-inflammatory effects suggested it could have some impact on replication of SARS-CoV-2 and inflammatory symptoms, but azithromycin and closely related drugs have no effect on COVID-19 but it had increased resistance to these drugs due to use in early pandemic. The increase in telehealth appointments during the pandemic has also increased antibiotic prescriptions. The higher frequency of antibiotic prescriptions during virtual healthcare was well-documented prior to the pandemic. Antibiotics are prescribed for a broader set of symptoms in the absence of physical examinations or laboratory tests to determine whether antibiotics are truly necessary.

CONCLUSION

The global issue of AMR will persist beyond the COVID-19 outbreak, posing a major challenge to the health care system. Antibiotic stewardship remains cornerstone in tackling AMR, educational intervention remains only the solution among the public to combat AMR. Media's like television, radio and internet can be used to deliver awareness programmes the Statergies should be developed at the each level of health care system for appropriate use of antibiotics and must be implemented immediately. It takes certain period of time to include practices in a daily habits, so education should be continuous among the public.

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