Response to antimicrobial resistance in South-East Asia Region

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Summary

Antimicrobial resistance (AMR) inflicts significant mortality, morbidity and economic loss in the 11 countries in the WHO South-East Asia Region (SEAR). With technical assistance and advocacy from WHO, all countries have developed their respective National Action Plans on AMR that are aligned with the Global Action Plan. Historically, the WHO Regional Office has been proactive in advocacy at the highest political level. The past decade has seen an enhancement of the country's capacity to combat AMR through national efforts catalyzed and supported through several WHO initiatives at all levels—global, regional and country levels. Several countries including Bangladesh, India, Indonesia, Nepal, Sri Lanka and Thailand have observed a worrying trend of increasing drug resistance, despite heightened awareness and actions. Recent AMR data generated by the countries are indicative of fragmented progress. Lack of technical capacity, financial resources, weak regulatory apparatus, slow behavioural changes at all levels of the antimicrobial stewardship landscape and the COVID-19 pandemic have prevented the effective application of several interventions to minimize the impact of AMR.

Keywords: AMR Global Action Plan; AMR National Action Plan; AMR surveillance; Advocacy; One Health; Antimicrobial Stewardship

Introduction

Antimicrobial resistance (AMR) is a significant growing global concern since it results in close to 1.27 million deaths annually, and importantly this trend continues to rise globally.[1] If no remedial action is taken, it is estimated the mortality attributable to AMR could rise to 10 million globally and this would mean a cumulative loss of US$100 trillion to the global economy by 2050.[2] AMR poses a major hurdle to achieving Universal Health Coverage and health-related goals in the Sustainable Development Goals (SDG) framework. Beyond Goal 3, AMR is central to several other SDGs, for example, SDG 1 (no poverty), SDG 2 (zero hunger) and SDG 8 (decent work and economic growth).[3] AMR is now being recognized as a global health security threat. We have witnessed in this interconnected world that resistant superbugs could easily spread across borders and make many treatable infections untreatable.

The adverse impacts of AMR go beyond the health sector and the well-being of people, it has serious ramifications also for economic well-being. According to a World Bank report, AMR shall be responsible for a decrease of up to 3.8% in global exports, with a diminishing of livestock production by 7.5% per cent per year. It will also result in an increase in healthcare-related costs of US$1 trillion by 2050.[4]

The threat of mortality, morbidity and economic loss associated with AMR poses an additional burden on countries already grappling with challenges associated with infectious disease prevention and treatment.[5] Countries in the WHO South-East Asia Region fall in this category. WHO risk assessment surveys have projected 389,000 deaths attributed to AMR in South Asia.[1]

The SEA Region has taken pioneering steps to identify the threat and develop cogent response strategies to address AMR. As early as 2011, health ministers of countries in the Region adopted the Jaipur Declaration for Prevention and Control of Antimicrobial Resistance which called for a concerted action against AMR.[6] It indicated an early realization of the challenge even though the Region at that time was not fully equipped to address it. In 2014, the regional response to AMR got a boost when it was identified as one of the Flagship Priority areas for the WHO SEARO Region.[7] Since then, WHO has been providing guidance to Member States on improved implementation of AMR national action plans (NAPs). This has resulted in a multisectoral 'One Health' approach covering human health, animal health, plant and food chains, food safety and the environment. At the 2015 regional committee meeting in Timor-Leste, member

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states passed a key resolution for steadfast political commitment and multisectoral coordination to tackle AMR.[8] Next, a regional strategy to support the development and implementation of AMR National Action Plans was finalized to guide countries in strengthening their national AMR prevention and containment programmes.[9]

The SEARO is implementing activities to contain AMR in line with the following five strategic objectives derived from the Global Action Plan launched in 2015 by WHO in collaboration with Food and Agriculture Organization and World Organization for Animal Health (founded as OIE).[10] These objectives are:

- To improve awareness and understanding of antimicrobial resistance through effective communication, education and training;
- To strengthen the knowledge and evidence base through surveillance and research;
- To reduce the incidence of infection through effective sanitation, hygiene and infection prevention measures;
- To optimize the use of antimicrobial medicines in human and animal health; and
- To develop the economic case for sustainable investment that takes account of the needs of all countries and to increase investment in new medicines, diagnostic tools, vaccines and other interventions.

This article focuses on progress made by the Member States of the WHO South-East Asia Region in containing AMR and WHO's strategic support in taking the AMR agenda forward. The article also states the present and future challenges and efforts needed to move forward in achieving the 2030 goal.

Disease burden

Globally, more people die due to reasons related to AMR than HIV/AIDS or malaria. In the SEA Region, 4 million people died in 2019 due to sepsis as an immediate or intermediate cause of death.[11] Of these deaths attributed to sepsis, 62% were caused by bacterial infections.[11] The remaining 38% were caused by other pathogens such as viruses, fungi, and parasites. Out of the deaths due to bacterial infections, between 0.39 and 1.41 million people died because of bacterial AMR.[11] Table 1 shows the composition of infection-related deaths, including AMR, in the Member States of the WHO South-East Asia Region.

In 2020, two AMR indicators were included in the monitoring framework of the SDGs. These indicators monitor the proportion of bloodstream infections (BSIs) due to *Escherichia coli* which is resistant to third-generation cephalosporins and methicillin-resistant *Staphylococcus aureus* (MRSA).[12] Data availability for these indicators has improved over 2017–2020. Table 2 shows the progress in the SDG indicators in the region. The available data shows a persisting level of AMR in the Region with varying trends across countries.[12] Importantly, the available data clearly shows an increasing trend in hospital-associated infections.[13,14] However, the data is not nationally representative as most samples were drawn from tertiary care hospitals.

Reports from Bangladesh, Nepal and Sri Lanka indicate a high level of resistance to beta-lactams especially due to the presence of extended-spectrum beta-lactamase (ESBL) producing pathogens.[15–17] Data from India have shown an increasing trend of resistance as well[18] Imipenem susceptibility of *E. coli* has dropped steadily from 86% in 2016 to 64% in 2021 and that of *Klebsiella pneumoniae* dropped steadily from 65% in 2016 to 43% in 2021. Resistance to carbapenems in *Acinetobacter baumannii* was recorded as 87.5% in the year 2021. Methicillin-resistant *S. aureus* (MRSA) rates are increasing from 2016 to 2021 (28.4%–42.6%). In Indonesia, in accordance with the SDG indicator, the proportion of ESBL-producing *E. coli* was 57.7% among the total *E. coli*-induced bloodstream infections.[19] In children, in Myanmar, high rates of carbapenem resistance were noted for *E. coli* (48%), *K. pneumoniae* (42%), and *Acinetobacter* sp. (59%).[20] Lim et al., in 2016 estimated that 19,122 of 45,209 (43%) deaths in Thailand among patients with hospital-acquired infection were due to multidrug-resistant bacteria, representing excess mortality caused by resistant pathogens.[21]

Progress in national action plans

WHO Regional Office for the South-East Asia region has been conducting situational analysis and monitoring of AMR using the Regional Office tool to analyse AMR prevention and containment.

Three self-assessment surveys have been conducted that have taken place (2016–2017, 2017–2018, 2018–2019) to assess the progress of 31 indicators as a proxy for strategic interventions/programmes across eight focus areas.[22,23] All 11 countries in the South-East Asia Region have developed and endorsed respective National Action Plans (NAPs) in line with the Global Action Plan.[21] Eight Member States have updated their NAPs as the initial NAPs period ended in 2022. These NAPs were developed with the technical assistance of the WHO.

The implementation of NAP has been fragmented and varies from country to country as well as within-country.[20] The 2018–2019 situational analysis revealed significant progress in the implementation of NAPs across different focus areas in the SEAR Member States in the preceding three years (Figs. 1 and 2).[22] The self-assessment done by the countries in the WHO survey showed that >90% of SEAR countries had started implementing NAPs with 27% actively monitoring the implementation.[22] The progress in the implementation of NAPs, as expressed by the median values of the percentage of indicators with an implementation status phase of 3 and above, found in the third situational

Countries	Sepsis	Bacterial infections	Resistance (associated)	Resistance (attributable)
Bangladesh	229,144	161,912	98,779	26,193
Bhutan	1138	760	464	124
DPR Korea	38,937	27,552	16,178	4131
India	2,990,000	1,790,000	1,040,000	297,036
Indonesia	444,880	302,592	133,753	34,530
Maldives	261	182	97	25
Myanmar	113,088	78,905	40,233	11,170
Nepal	55,803	37,826	23,204	6413
Sri Lanka	22,088	15,452	8815	2300
Thailand	134,738	82,573	43,885	10,775
Timor Leste	2574	1610	667	154

Source: AMR. IHME. 2019. https://www.healthdata.org/antimicrobial-resistance.

Table 1: **Composition of infection-related deaths in Member States of WHO South-East Asia Region.**

analysis in 2021 for all countries in the Region was 64%, compared to 40% in 2018 and 16% in 2016.[22] None of the countries showed any slide in the implementation status during 2021 compared with the situational analysis in 2018. The progress in the animal and agricultural sectors was found to lag compared with the human sector, while progress in the environmental sector was the least among all the sectors.[22]

Out of 11 countries in WHO South-East Asia, nine countries—Bangladesh, Bhutan, DPR Korea, India, Myanmar, Nepal, Sri Lanka, Thailand and Timor-Leste—were already functioning One Health coordination mechanism.[22] In Indonesia, presidential instruction No. 4/2019 supports the development of a fully functional cross-sectoral coordination mechanism for AMR control, which also demonstrates the strong commitment of the Indonesian government to ensure the implementation of an integrated AMR approach through a partnership of several sectors.[22]

Awareness and understanding

Improving awareness and understanding of AMR is critical not only for health professionals and veterinarians but also for the general public. Since 2015, WHO has observed World Antimicrobial Awareness Week (WAAW) from 18 to 24 November every year.[24] Every year, the WHO Regional Office and country offices organize a series of events to harness momentum around tackling AMR and fueling behaviour change the programmes feature talk shows, social media events, campaigns and community events at schools, universities, and other locations. Government agencies, health institutions, and other stakeholders, also spearheads initiatives on WAAW campaign.

In 2021 and 2022, activities during WAAW expanded across sectors and included a 'Go Blue' campaign under the theme 'Spread Awareness, Stop Resistance'.[25] As part of this campaign, important public buildings around the world chose to immerse themselves in blue

Country	The proportion of bloodstream infections due to							
	E. coli resistant to third-generation cephalosporin				Methicillin resistant *S. Aureus*			
Year	2017	2018	2019	2020	2017	2018	2019	2020
Bangladesh	*na*[a]	70	93.1	71.43	*na*	*na*	*na*	0
Bhutan	*na*	*na*	56.78	53.93	*na*	*na*	20.79	11.67
DPR Korea	*na*	*na*	*na*	*na*	*na*	*na*	*na*	*na*
India	75.11	78.83	80.81	86.81	52.5	63.1	60.61	64.66
Indonesia	*na*	71.88	70.14	75.63	*na*	52.3	39.85	36.24
Maldives	*na*	*na*	*na*	*na*	*na*	*na*	*na*	*na*
Myanmar	*na*	84.91	77.78	80.56	*na*	74.1	55.61	50.97
Nepal	*na*	65.33	77.27	72.97	*na*	55.6	*na*	79.01
Sri Lanka	*na*	67.67	63	61.92	*na*	*na*	55.99	53.29
Thailand	41.72	36.42	37.26	39.4	16.7	11.3	12.43	10.63
Timor Leste	*na*	*na*	*na*	61.54	*na*	*na*	*na*	*na*

[a]na—Not Assessed/Not available. Source: WHO 2020: SDG Target 3.d.2.

Table 2: **Status of SDG Indicators for AMR in countries of the South-East Asia Region (2017–2020).**

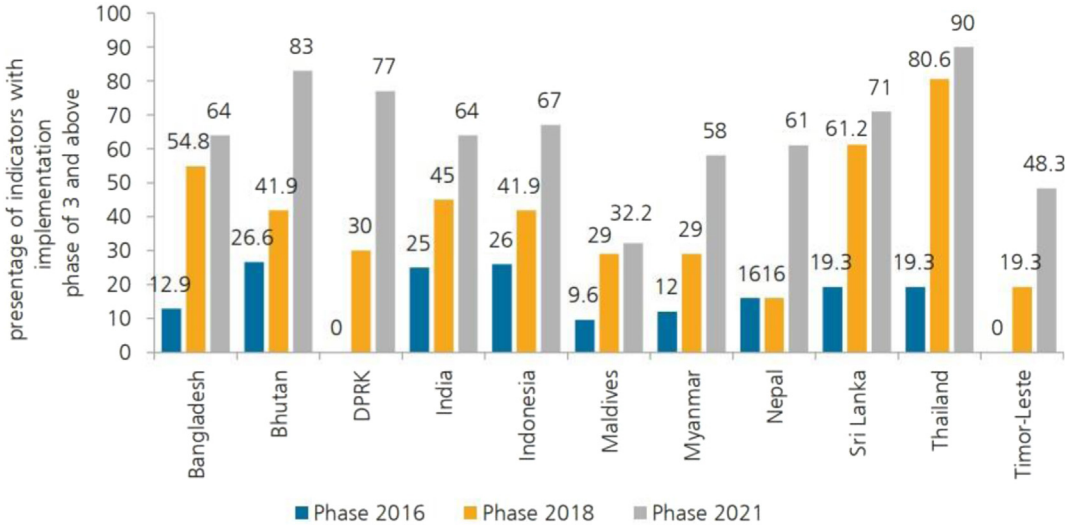


Fig. 1: **The proportion of indicators with implementation phase 3 or above in each country from 2016 to 2021.** Source: Third progress analysis of implementation of antimicrobial resistance national action plans in the WHO South-East Asia Region 2022.

colour. In all 11 countries (100%), the governments regularly led education campaigns on AMR to raise awareness in the public, this was an increase from the situation in 2018 (81%).[22]

Monitoring and surveillance

In 2022, the Regional Tripartite Coordination, embodied by participating UN agencies Food and Agricultural Organization (FAO), WOAH (World Organization for Animal Health) and WHO to reflect the multisectoral nature of AMR, was expanded to include the UN Environment Programme (UNEP). This was to facilitate additional environmental aspects of AMR in the frameworks of action. This will hence evolve into Quadripartite Coordination (FAO, WOAH, UNEP and WHO) from 2022 onwards. All Member States have

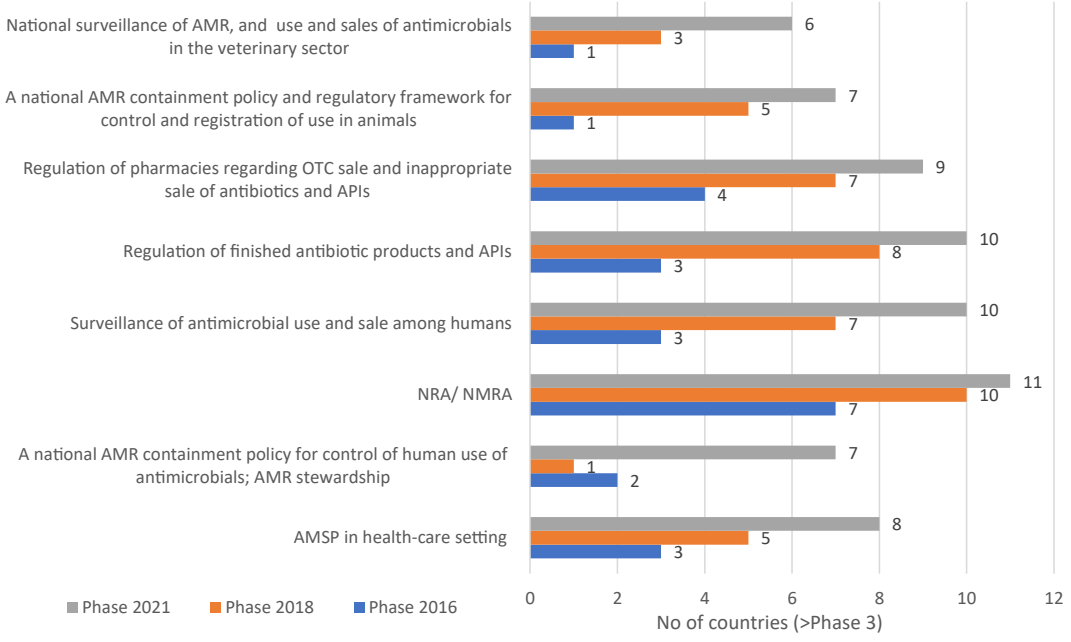


Fig. 2: **Progress in the country's response to contain AMR (2016–2021).** Source: Third progress analysis of implementation of antimicrobial resistance national action plans in the WHO South-East Asia Region 2022.

participated in all the self-assessment surveys conducted so far.[26]

The Third One Health Situational Analysis 2021 reported progress in all eight focus areas and indicators.[27] More countries started implementing actions under these indicators – the national AMR plan and governance, raising awareness, national AMR surveillance system, rational use of antimicrobials and surveillance of use/sale including and AMS, IPC, research and innovation, One Health engagement and overarching coordination mechanisms for One Health engagement.[28] However, no progress was observed with AMR awareness generation and education on AMR in the environmental sector, and the implementation of an AMR early warning system (EWS), wherein almost none of the countries managed to start a national programme in these areas during the situational analysis in 2021, 2018 and 2016 (Fig. 2).[27]

WHO support for strengthening surveillance is to provide technical assistance to expand sentinel sites to generate nationally representative and good-quality AMR data. By 2021, 10 of 11 countries in the Region had initiated AMR surveillance in the human sector (Table 2). By September 2022, all Member States in SEAR got themselves enrolled in the Global AMR Surveillance System (GLASS) and 6 Member States enrolled in GLASS- antimicrobial consumption (AMC). India has initiated a multi-site surveillance system for AMR based on the standard protocols[29] (Box 1).

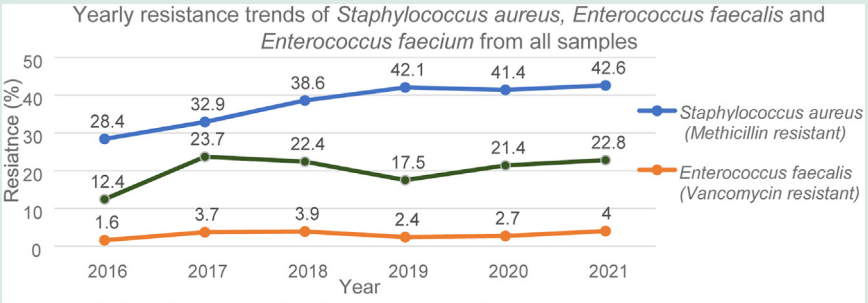
GLASS provides a standardized approach to the collection, analysis, interpretation and sharing of data by countries and seeks to actively support capacity building and monitor the status of existing and new national surveillance systems. It promotes a shift from surveillance approaches based solely on laboratory data to a system that includes epidemiological, clinical, and population-level data.

Inappropriate use of antibiotics is rampant in the Region and is a major contributor to antimicrobial resistance but data on antibiotic use and consumption are scant.[30] The median value of the overall consumption of antimicrobials is 16.6 (range, 12.3–31.2) Defined Daily Dose (DDD) per 1000 inhabitants per day while for three countries in WHO South-East Asia (Bhutan, Maldives and Nepal) it was 15.3 (range, 9.5–57.4) (Fig. 3). Countries reporting from SEA Region also showed significant variations in the usage of antimicrobial drugs.[31] India consumes a large volume of broad-spectrum antibiotics that should ideally be used sparingly. The total DDDs consumed in 2019 was 5071 million (10.4 DDD/1000/day).[32] While consumption of human antimicrobials in Thailand in 2017 was 75.68 DDD/1000 inhabitants/day.[32] Hoque et al., in 2020 observed the widespread availability of antimicrobials without prescription in Bangladesh.[33] All countries in the WHO Eastern Mediterranean Region reported a consumption 31.8 [range, 29.4–53.6] and where six European countries is 15.3 [range, 9.2–30].[34] In the United

Box 1.
A case study of AMR surveillance networks in India.

India commenced AMR surveillance in 2013 and has gradually expanded this activity under two networks: organized by the Indian Council of Medical Research (ICMR) and the National Centre for Disease Control (NCDC).

ICMR initiated Antimicrobial Resistance Surveillance and Research Network (AMRSN) in 2013 to monitor trends in the antimicrobial susceptibility profile of clinically important bacteria and fungi limited to human health. The pathogens included in surveillance align with the WHO Priority List of Pathogens (2017) and are Enterobacteriaceae causing sepsis, Gram-negative non-fermenters, enteric fever pathogens, diarrheagenic bacterial organisms, Gram positives: staphylococci and enterococci and fungal pathogens. AMRSN includes six nodal centres–one for each pathogenic group, and 16 regional centres located in tertiary care health facilities.[27]



Source: AMR Surveillance Network, Indian Council of Medical Research, 2022.

NCDC runs another AMR surveillance network in India, called NARS-Net. The network currently has 35 labs in 26 states/UTs. These labs submit AMR surveillance data on seven priority bacterial pathogens of public health importance: *Klebsiella* spp., *Escherichia coli*, *Staphylococcus aureus*, *Enterococcus* spp., *Pseudomonas* spp., *Acinetobacter* spp., *Salmonella enterica serotypes Typhi* and Paratyphi.[16]

The major drawback with both networks is data generated by their surveillance systems is not truly representative of the AMR burden in the country since data is primarily from patients who have had prior antimicrobial therapy from tertiary care hospitals and not from communities.

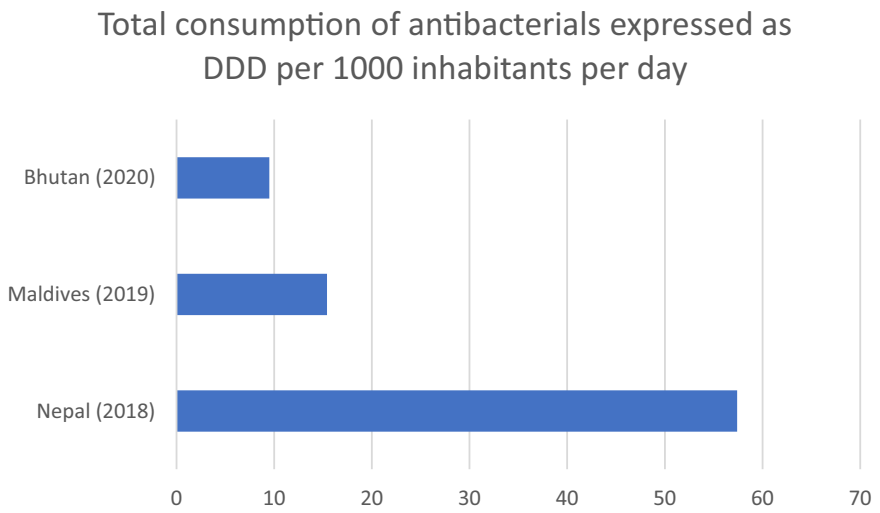


***Fig. 3*: Total consumption by antimicrobial classes in three countries of WHO SEA Region in 2020, expressed as DDD per 1000 inhabitants per day.** Source: WHO. Global antimicrobial resistance and use surveillance system (GLASS) report: 2022. WHO Geneva, 2022.

Kingdom, there were 18.2 DDD per 1000 inhabitants in 2019.[35] In a comprehensive study showed that high rates of antibiotic consumption were seen in North America, Europe and the Middle East. Total antibiotic consumption rates showed a nearly ten-fold variation between countries, ranging from as low as 5.0 DDD to 45.9 DDD per 1000 population per day. Between 2000 and 2018, global antibiotic consumption rates increased by 46% (from 9.8 to 14.3 DDD per 1000 population per day). While in the high-income countries, consumption rates remained stable between 2000 and 2018, in low- and middle-income countries, there was a 76% increase observed between 2000 and 2018.[36] They also found a rise in the irrational use of antibiotics across sectors and consequent contamination of the environment and spread of resistance. Procurement of antibiotics through over-the-counter (OTC) sale is widespread in Myanmar. More than half of the participants (58.5%) purchased antibiotics without a prescription, mainly from medical stores or pharmacies (87.9%). A disproportionately higher use of broad-spectrum and Watch category antibacterial was observed in the private sector in Sri Lanka.[32] About 97% of retailers dispensed unnecessary antimicrobials in diarrhoea, and only 3% suggested evaluation by a physician in Nepal.[37] Self-medication with antibiotics was found to be widespread in Bangladesh (45.7%). Inappropriate antibiotic use is a pertinent problem in LMICs where regulatory frame works are weak. Inappropriate antibiotic use in LMICs is a multifaceted problem that cuts across clinical and veterinary medicine and agriculture.[38] Globally, over 50% of antibiotics are sold without a medical prescription. Although over the counter sale of antibiotics is common in the developed world, this practice is more noticeable in developing countries like Ethiopia, where regulation strategies are too weak.[39,40] Despite the rise in antibiotic consumption, access to antibiotics continues to be a concern, and delays in access to antibiotics cause more fatalities than antibiotic resistance.[41] Across the developing countries, antibiotic overuse exists side-by-side with lack of access. There are millions of people in low- and middle-income countries who remain deprived of antibiotics contributing heavily to the majority of world's annual 5.7 million antibiotic-preventable deaths. The dilemma between excess of antibiotics leading to AMR and access to needy needs to be balanced out.[2,42]

The South-East Asia Regulatory Network (SEARN) responsible for supporting the regulation of medical products, including medicines, vaccines, medical devices and diagnostics across the Region, is now poised to play a more active role in surveillance, detection and regulatory action on substandard and falsified antimicrobials, and hence help to address AMR. Comprehensive strengthening of NRAs through direct WHO support and SEARN is likely to yield productive results.

Infection prevention and control

There is a strong need to reduce the overall burden of bacterial infections including in high risk settings vis health facilities or animal farms. All efforts including effective IPC in health settings, personal hygiene, vaccination and hand washing have profound impact on reducing infectious diseases.[43] Safer hospitals mean fewer infections and every infection prevented is an antibiotic avoided. The pooled prevalence of HAIs was estimated to be 9.0% in the WHO South-East Asia Region, according to a systematic review published in 2015.[44]

In 2015, responding to the need for attention to patient safety in the Member States of the South-East Asia Region, the WHO Regional Office launched the Regional Patient Safety Strategy 2016–2025.[45] It included IPC as one of the six strategic objectives, i.e., improve the structural systems to support quality and efficiency of health care and place; patient safety at the core of all levels of health care; assess the nature and scale of harm to patients and establish a system of reporting and learning at the national level; ensure a competent and capable workforce that is aware and sensitive to patient safety; prevent and control health care-associated infection; improve implementation of global patient safety campaigns and strengthen patient safety in all health programmes; and strengthen capacity for and promote patient safety research. Since then, countries are implementing the strategy with some particularly focusing on IPC. Consequent to the formulation of National Action Plans, a national infection prevention and control (IPC) programme or operational plan is available in all countries of the WHO South-East Asia Region. However, four of the countries in the Region are not fully implementing it.[46] Only three of the countries had an IPC programme supported by plans and guidelines implemented nationwide. 50.0% of the countries had a dedicated budget for IPC. In six of the countries, there was a mandate to produce IPC national guidelines.[45]

WHO initiated policy dialogue and technical assistance on improving infection prevention and control (IPC) which continued even during the COVID-19 pandemic. Adopting IPC guidelines, including WASH, was a key feature of the technical support provided by WHO to strengthen IPC in the Member States. WHO supported the development of fit-for-service dashboards to strengthen policy advocacy. In addition, training packages and guidance documents were made available to Member States for capacity building on IPC and to deal with associated challenges like the emergence of new variants of concern.

An interesting example of improvement is the implementation of IPC tailored to the local situation in Cox's Bazar area in Bangladesh. In collaboration with WHO and relevant partners, local authorities and teams established IPC committees and IPC focal persons in 137 healthcare facilities in the Rohingya camps and all eight sub-district referral healthcare facilities, used checklists for IPC assessments, and undertook the training of trainers to create local expertise.[47]

Antimicrobial stewardship

Irrational use of antibiotics is well recognized to be one of the main drivers of AMR.[48] WHO has been strongly advocating for prescribers and users to assure optimal utilization of these agents. It has extended continuous support to strengthen antimicrobial stewardship, which encompasses interventions designed to promote the optimal use of antibiotics, including selection, dosing, route, and duration of administration and is a critical element of curbing and preventing AMR.

WHO continued to support countries in updating national Essential Medicines Lists by incorporating essentials of WHO's Access-Watch-Reserve (AWaRe) classification for antimicrobials.[48] Antimicrobials have been grouped into these three categories, with recommendations on when each category should be used. It also includes the details of 258 antibiotics along with their pharmacological classes, anatomical therapeutic chemical codes and WHO essential medicine list status. WHO recommended country-level targets of at least 60% of total antibiotic consumption being from the Access group of antibiotics.[49,50]

By 2022, Bhutan, Indonesia, Maldives, Nepal, Timor Leste and Thailand had adopted the AWaRe categorization into their national EMLs.[51] Other countries are also planning to use this strategy. To improve the affordability of medicines, all SEAR Member States employ some aspect of a policy to control the prices of medicines and devices and to contain pharmaceutical expenditure.

Antimicrobial stewardship (AMS) plans are being implemented in countries across the Region with WHO support. These aim to optimize the use of antimicrobials, improve patient outcomes, reduce AMR and healthcare-associated infections, save healthcare costs overall, and lead by example for other sectors. WHO has developed tools to assist AMS activities at the healthcare facility level in low- and middle-income countries, which have helped to advance implementation at the national level as well as within healthcare facilities and clinical practice. AMR has been included or is in the process of being included, in medical, nursing and pharmacy curricula in several countries in the SE Asia Region.[52] This has been achieved by engaging ministries of health, education, and universities. Technical support has been provided to the Region's countries to develop national antimicrobial stewardship (NAMS) policies.

Discussion

Globally, AMR would have been the third leading GBD cause of death in 2019, on the basis of the counterfactual of no infection.[53] WHO-conducted risk assessments have shown, the Region is likely the most at-risk part of the world as about 30% of AMR attributable deaths are occurring in the Region.[1,11,52] The WHO South-East Asia Region is particularly affected due to the rapid intensification of food-production systems, loosely regulated access to antimicrobials, poor awareness, widespread irrational prescribing and self-medication, and an abundance of substandard-quality or counterfeit drugs.[54,55] All these factors combined with a high prevalence of infectious diseases and weak healthcare systems drive the AMR in the Region.[56]

Much has been done in the Region to counter this increasing burden of AMR. One such intervention was WHO's advocacy for putting the right policy for AMR control. National Action Plan is a strategic tool for AMR containment with the objective to guide stakeholders for integrated responses against AMR through the identification of priority areas for work and collaboration. It is a result of political momentum facilitated by the coordinated efforts of WHO.[10] While all Member States of the WHO South-East Asia Region have developed national multisectoral action plans, implementation remains a challenge. Only a few countries report that their NAP is being implemented effectively or have allocated financing in their national budgets for AMR programmes.[22,57] By 2022, none of the countries had costed the AMR programmes so that adequate budget can be marked. Bangladesh and Bhutan have effectively implemented training on the National Action Plan Budgeting and Costing Tool to increase country capacity on the use of the tool to help build and cost an operational plan for their NAP.[57] In addition, an e-learning course is being developed to complement the virtual/face-to-face trainings and to ensure greater dissemination and use at country level. Limited technical capacity within different programmes of MOH and related sectors hinders the efficient implementation of NAP despite political commitment at the highest level.[57] The Member States have a dependency on WHO and donor partners to move forward in areas like manpower, technical expertise, and funding support. Advocacy efforts in the field of Antimicrobial Resistance (AMR) have indeed faced challenges in achieving optimal political and financial responses. Several factors contribute to this situation are lack of Awareness on AMR in the general public compared to other health issues, lack of robust AMR data locally, as a "silent pandemic" nature of AMR makes it harder to rally urgent responses, competing with global health priorities (pandemics, non-communicable diseases, and poverty) and stakeholder fragmentation.

AMR solutions can result in considerable economic benefits with long-term effects, both in terms of addressing AMR and broader health priorities.[58] For instance, a modelling study done in Japan has shown that 18 new antimicrobials can be developed over next the 10 years with a collective investment of $78 billion by G7 countries.[59] Such an investment will have a return on-investment ratio of 6:1 for Japan's share of investment. The ROI shall increase to 28:1 if the timeframe is extended to 30 years. The global ROI could be much higher, at 27:1 over 10 years and 125:1 over 30 years. The number of lives saved across the world shall be 518,000 at the end of 10 years and 9.9 million by the end of 30 years.[59] However, such modelling studies have not yet been done in the regional context.

Before the coronavirus disease 2019 (COVID-19) pandemic, the World Health Organization (WHO) recognized antimicrobial resistance as one of the top 10 most urgent global health threats.[60] This led to intensified efforts to tackle AMR at global and national levels. Thereafter, the pandemic substantially hampered the progress towards containing AMR, especially the implementation of AMR national action plans. Ongoing responses for multiple health emergencies hindered the regular work on AMR particularly on strengthening the AMR surveillance system. Further, prolonged intensive care stays, high mortality rate, diagnostic and prognostic uncertainty and concern for secondary bacterial infections has led to frequent empiric antibacterial use during the pandemic, thus leading to increase AMR.[61] Nevertheless, the COVID-19 pandemic has highlighted the vulnerability of healthcare systems in controlling infectious disease threats and increased awareness of the importance of planning for emerging infections and maintaining robust infection control. The pandemic has generated opportunities that should be seized to harness positive effects on the management of antimicrobial resistance.[62]

Leadership and technical support play a crucial role in implementing action plans at global and national levels and the policymakers understand and rely on statistics and data generated and implied for local level or national levels. However, at present, most of the AMR statistics are still global, with limited AMR data at the national or subnational level.[63,64] This creates an opportunity to lobby for more research at a national level to generate data to measure AMR burden, accounts for the patient pathway within the healthcare setting, and strengthens diagnostic stewardship and laboratory practice that can be used to advocate for government buy-in and support.

There is a human behaviour component in all aspects of AMR since antibiotics are solely handled and used by human beings. Doctors prescribe and public consumes while veterinarians prescribe and administer antimicrobials to animals.[65–68] Lack of awareness campaigns and use of ineffective communication tactics in the Region which primarily comprises of countries in LMICs, warrants for increased public awareness to mitigate AMR.[57] Eliminating misconceptions about antibiotics being "magic bullets requires behavioural change among both antimicrobial prescribers and users. Further, the development of resistance is a natural process of adaptation of bacteria in reaction to antibiotics. This meant that antibiotics had a limited lifespan from the very beginning.[69,70] This should have been explicitly made known to the public, humans and doctors at the inception of antibiotics. This was the first missed opportunity towards mitigation of AMR, through communication targeting awareness and human behaviour.

The quality and consistency of AMR surveillance data are limited for the Region. Currently, there are several networks which contribute to AMR surveillance

in South-East Asia.[57] However, there is huge geographic heterogeneity in terms of data quality and availability. Surveillance in the Region is primarily driven by few healthcare facilities contributing data with a number of eligible patients not being tested and a lack of quality of laboratory services, hence it cannot be generalized for national representation. Overall, a large knowledge gap exists due to a weak surveillance. Though AMR research in the Region is focused on burden and patterns of resistance, yet nationwide surveillance is lacking. More research is needed to discover new antibiotics and develop rapid diagnostic tests. Investment in research and national surveillance of resistant pathogens must be prioritised.[71] Support for Member States in sharing AMR and AMC data with GLASS and in taking up a standardized approach for the collection and analysis of AMR data at the global and regional level as well as utilising those data for policy-informed decisions. While the need for research and development of new diagnostics is paramount, rigorous implementation of currently available, and affordable, IPC interventions in human and animal sectors can yield good results even in a short period.

As AMR, which is a complex challenge that spans across various sectors, including healthcare, agriculture, environment, and policy-making, global architecture and governance are essential in organising a multi-sectoral response to the problem. Organisations with a global mandate, such as the World Health Organization (WHO), Food and Agriculture Organisation (FAO), and World Organisation for Animal Health (OIE), offer platforms for international cooperation initiatives and augurs well for intersectoral coordination. In 2019 the World Health Organization (WHO), Food and Agriculture Organisation (FAO), and World Organisation for Animal Health (OIE) partnered up to utilize Antimicrobial Resistance Multi-Partner Trust Fund to combat AMR. The Antimicrobial Resistance MPTF, which consists of global/regional and country components, lessens the threat of AMR by sponsoring transformative and creative practises that assist national governments in putting the "One Health" concept into practise and maintaining it. Indonesia and Bangladesh received the fund for the purpose of tackling AMR at the national levels with backstopping support from WHO, FAO, WOAH and UNEP became a co-signatory of the Fund in 2021, enhancing the understanding of the critical environmental dimensions of AMR. The Quadripartite Organizations—FAO, UNEP WHO, and WOAH—developed the One Health Joint Plan of Action (2022–2026) which consist of six interdependent action tracks, including AMR to provide a framework for action and propose a set of activities the four organizations and upstream policy and legislative advice and technical assistance, to help set national targets and priorities across the sectors for the development and implementation of One Health legislation, initiatives and programmes. There is an urgent need to take this down to the Regional, national and subnational level. Advocating and promoting by WHO and other UN agencies, One Health approach has been stated in G20 Health Ministers' Meeting where G20 member nations commit to address antimicrobial resistance (AMR) comprehensively using the One Health approach. This involves enhancing coordination and governance across sectors, advancing research and development, improving infection prevention and control, ensuring clean water, sanitation, and hygiene, raising awareness about AMR, and promoting responsible use of antimicrobials. This includes preserving existing treatments through antimicrobial stewardship, increasing surveillance of AMR and antimicrobial usage, utilizing surveillance data for policy decisions, developing new antimicrobials guided by prioritization lists, and ensuring equitable access for everyone, including through community-based efforts. The third One Health situational analysis 2021 has shown that the environment sector has made less progress across different focus areas and indicators of AMR in the Region. The limited systemic capacity of the environmental sector and lack of resources can explain some of the gaps in progress. Further, the environment sector is less integrated into AMR response, and this probably reflects a lack of clarity in the collaborative frameworks that necessitate their involvement.[57] This could impact One Health's engagement and effective multisectoral collaboration. A strengthened One Health response will help in building connections and communication channels across sectors to ensure collaboration on research and development as well as the implementation of programs, policies and legislation.

Conclusions

The 71st session of the UN General Assembly identified AMR as a dominant global health concern, placing it high on the agenda of national policymakers, international organizations and financial institutions in developed and developing countries. Being a flagship programme in the South-East Asia Region, WHO has proactively supported countries through enhanced advocacy and augmented technical capacity. WHO is committed to support all Member States in developing and implementing National Action Plan on AMR. Using the information from monitoring and surveillance data will capture the country stage to stimulate effective and sustainable multisectoral response on AMR. It is essential to recognize that these plans entail a journey rather than an immediate fix. By acknowledging the need for phased activities over years, we are setting a realistic expectation for the time and effort required. Prioritizing interventions that can be universally adopted now is a smart approach, as their success can inspire and pave the way for others to join the fight against AMR.

Moving forward, the next decade is critical for accelerating action on AMR. The Member States of the WHO South-East Asia Region need to prioritize the AMR national action plans and allocate adequate financial resources for their implementation. The integration of these plans with primary health care and health emergencies holds the key. The first step in this direction is to cost the AMR programmes at national levels and mobilize resources—both foreign and domestic resources.

The current funding mechanisms face notable limitations when it comes to generating the necessary volume of funds and ensuring a steady flow of resources. This can impede the ambitious goals set out in the national action plans. It's crucial to explore alternative approaches such as cost-sharing and direct funding to bridge this gap. Addressing resource needs a comprehensive gap analysis to identify where the shortfalls lie and how they can be effectively covered. Methodological challenges related to costing need also be addressed, including whether to use financial units of costing. The challenges in current drug development initiatives are multifaceted and can impact the timely creation of effective treatments. Clinical trial capacities and regulatory frameworks play a pivotal role in this scenario. These challenges can result in delays, higher costs, and potential roadblocks in bringing new antimicrobials to market. Addressing these limitations requires collaborative efforts between stakeholders, including governments, pharmaceutical companies, and regulatory agencies, to streamline processes, incentivize research, and establish adaptive regulatory pathways that ensure safety while expediting drug development. Despite concerted advocacy efforts, achieving optimal political and financing responses remains a challenge. This can be attributed to a variety of factors, including competing priorities, limited awareness about the gravity of AMR, and the complex nature of policy change. Moreover, securing political commitment and sustainable funding for AMR initiatives requires ongoing dedication and engagement from a diverse range of stakeholders, including health organizations, governments, private sectors, and civil society. Building a stronger case for AMR's impact on public health, economies, and global security can enhance the likelihood of eliciting more robust political and financial responses. Rather than creating separate plans for preparedness, leveraging existing initiatives such as TB and AMR surveillance can offer a more cohesive and efficient approach. By integrating AMR surveillance efforts within broader pandemic preparedness strategies, synergies can be achieved in terms of resource utilization, expertise sharing, and overall effectiveness. This interconnected approach recognizes the interdependence of various health challenges and the need for a unified response. This not only optimizes resource allocation but also enhances the overall readiness to combat emerging health threats. Further–surveillance, detection and regulatory action on substandard and falsified antimicrobials need to be strengthened across Member States in order to check the practice of irrational and substandard use of antibiotics.[22,72,73] Irrational use of antibiotics in animal sector can be minimized through legislation. Some countries have initiated major activities on the aspect of supplementing animal feed with antibiotics. There has been significant work in minimizing irrational use of antibiotics in animal feed in Bangladesh as one of the drivers of AMR. India has also issued government orders to discontinue use of antibiotic supplemented animal feed. These should be used as foundations for development and implementation of effective legislations. Strengthening infection prevention and control (IPC) measures and antimicrobial stewardship is of paramount importance in the Member States workplan to mitigate the growing threat of antibiotic resistance and ensure the continued effectiveness of our antibiotics.[74] The adoption of AWaRe categorization by the Member States is also critical for the proper implementation of NAP. As the Region faces multiple threats to AMR, multisectoral, multidisciplinary and multi-institutional efforts are needed to address AMR holistically. Therefore, the 'One Health' approach that connects the human, animal and environmental sectors is considered vital to addressing AMR, particularly for the Region. The Quadripartite Organizations—FAO, UNEP WHO, and WOAH—developed the One Health Joint Plan of Action (2022–2026) which consist of six interdependent action tracks, including AMR to provide a framework for action and propose a set of activities the four organizations and upstream policy and legislative advice and technical assistance, to help set national targets and priorities across the sectors for the development and implementation of One Health legislation, initiatives and programmes.[75] This has been voiced in the G20 Lombok Policy Brief which emphasized support to low- and middle income countries to strengthen One Health approaches to pandemic prevention, preparedness and response including AMR as a silent pandemic.[76]

In the coming time, to make AMR interventions more effective, a more comprehensive and programmatic approach is needed, putting people and their needs at the centre of the AMR response.

Contributors

BS: reviewing, data validation, editing the draft.
RB: developed the methodology, writing the original draft, editing.
TYA: reviewing and editing.
RL: reviewing and editing.
SR: supervision, reviewing.
RS: reviewing, editing.

Declaration of interests

The views expressed in the submitted article are of the authors and not an official position of the institution to which they are affiliated. The authors except RL and SR are affiliated with WHO SEARO. The author declares no conflict of interest.

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