Sri Lanka's journey through antimicrobial resistance – gaps and gains

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Introduction

The journey of Sri Lanka through antimicrobial resistance (AMR) is a "Tale of two cities". This article attempts to track the events related to the battle against AMR in Sri Lanka to guide the reader across many facets over two decades.

Development of Antimicrobial Resistance (AMR) is a natural phenomenon in microorganisms, but its amplification and spread are through an array of practices by humans which facilitate "selective pressure". Infections by microorganisms resistant to antimicrobials take longer to heal, require expensive and at times toxic antimicrobials making the infections untreatable causing high mortality, morbidity and increased healthcare cost. The depleted pipeline of novel antimicrobials on top of AMR, aggravates the problem.

Resistant organisms move across countries through travel and trade making it a global challenge. Antimicrobial resistance is now considered as a threat to global development though it was initially described as an immediate threat to human health [1]. South-East Asia is highly affected by AMR according to the World Health Organisation (WHO) risk assessment done in the year 2016 [2]. If neglected, AMR has a profound impact on the health and economy of a country. Understanding this imminent threat, certain countries have come forward to float global efforts to strengthen the resource poor countries to battle AMR. The efforts made by WHO over the last decade has paved the way to combat AMR in a global scale.

The World Health Assembly in May 2015 adopted a Global Action Plan (GAP) on antimicrobial resistance realising the grave danger humans are facing due to the threat of AMR. GAP outlines 5 strategic objectives.

1. Improve awareness and understanding of antimicrobial resistance through effective communication.
2. Strengthen the knowledge and evidence base through surveillance and research.
3. Reduce the incidence of infection through effective sanitation, hygiene, and infection prevention measures.
4. Optimise the use of antimicrobial medicines in human and animal health.
5. Develop the economic case for sustainable investment that takes account of the needs of all countries, and increase investment in new medicines, diagnostic tools, vaccines, and other interventions.

As AMR and human health is intertwined with agriculture, animal husbandry, and the environment, the next step was the adoption of the "One Health" approach.

Sri Lanka spends 12.7% of its health budget (amounting to Rs.3.3. billion) on antibiotics / antimicrobials. The top 10 pharmaceutical items that have costed the most during 2021 and 2022 includes two antibiotics co-amoxiclav and meropenem [3]. The apparent magnitude of the burden of AMR in the country is significant. Multi drug resistant strains, carbapenem resistance, 3rd-generation cephalosporine (3GC) resistance, vancomycin resistant enterococci and Methicillin-resistant *Staphylococcus aureus* (MRSA) are not uncommon among our pathogenic microbial population.

The country has taken major steps since the dawn of this century to combat AMR, converting the country's scenario from zero information status to be par with the

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international community. Initiation of AMR surveillance in 2008 was a historical milestone in AMR battle though it was limited to a few centres. Attempting to streamline rational use of antibiotics and awareness programmes on AMR were among the many activities implemented aligned with the five strategic objectives of the GAP-AMR, following the One Health approach. However, during the process the country has faced many challenges, multiple gaps have been identified and many lessons were learnt. The efforts made and lessons learnt is now turning up the way forward of the country's battle towards combating AMR.

Current situation related to AMR in Sri Lanka

The first multi-centre AMR surveillance of the country, identified as the Antibiotic Resistance Surveillance Project (ARSP) conducted by the Sri Lanka College of Microbiologists (SLCM) in 2009 in a few selected hospitals, produced data from blood culture isolates [4]. It showed significant resistant rates to the antibiotics in common use [4]. Out of the 142 *Escherichia coli* isolates 85/135 (63%) were resistant to cefotaxime (74 Extended-spectrum beta-lactamases (ESBL) positives and 11 of the non-ESBL group resistant to cefotaxime), 60/102 (58.8%) were resistant to ciprofloxacin. In *Klebsiella* spp 120/137 (87.6%) were resistant to cefotaxime, 51/104 (49%) were resistant to ciprofloxacin. The important finding was non-detection of carbapenem resistance in *E. coli* and *Klebsiella* spp. Among Acinetobacter species carbapenem resistance was seen with 40% resistance to meropenem and 30.5% and 47.5% were resistant to amikacin and gentamicin respectively.

Another multi-centre project on AMR was established in 2011 as a collaborative project of SLCM and the Ministry of Health (MoH), identified as the National Laboratory Based Surveillance of Antimicrobial Resistance, of which the data of urine culture isolates were analysed and published in 2016 [5]. In this study, organisms were not identified to species level and the pooled data for the coliforms showed 52.9% resistance to cefotaxime and 9% resistance to meropenem.

Sri Lanka was enrolled for Global Antimicrobial Resistance and Use Surveillance System-AMR (GLASS-AMR) data submission in 2018 and since then data has been submitted annually. It is encouraging to see a downward trend of resistance for 3GC in E. coli isolated from bloodstream infections (Figure 1). This may be due to the actions taken by Sri Lankan professionals and authorities in implementing the National Strategic Plan (NSP) for combating AMR. Resistance to fluoroquinolones (levofloxacin and ciprofloxacin) and cotrimoxazole is around 60% and 3GC is 57% in 2021. Meropenem resistance in E coli in blood cultures was 10.6% which is very high compared to countries such as the UK (0%) and Switzerland (0.04%). (Figure 2) [5].

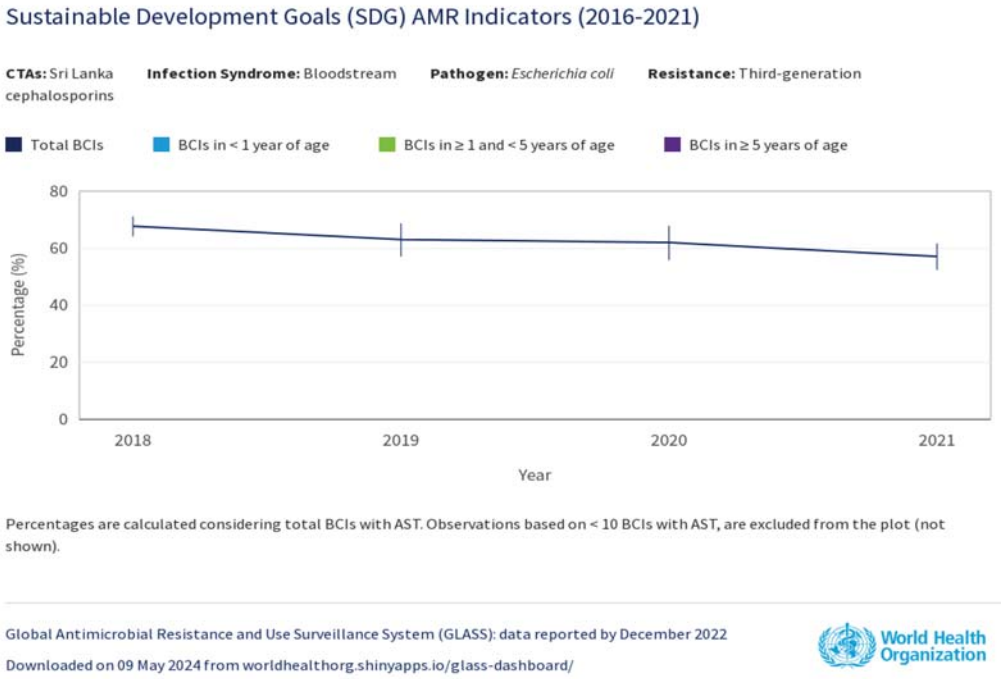

Figure 1.

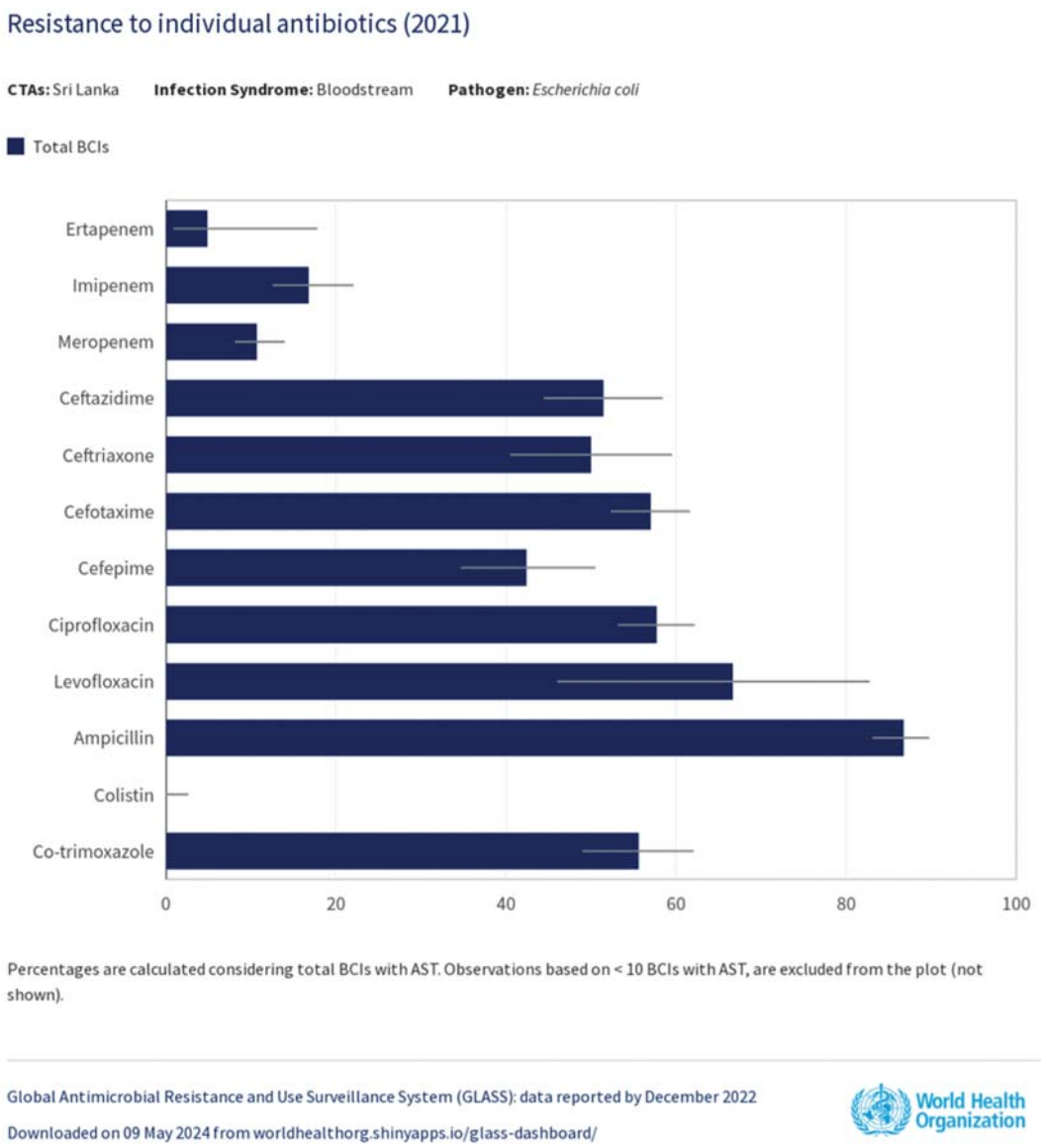

Figure 2.

In *Klebsiella pneumoniae* isolates from blood cultures, 72%, 77%, and 48% were resistant to ciprofloxacin, cefotaxime, and meropenem respectively.

Additionally, ESBL, AmpC β-lactamase and carbapenemases such as NDM and OXA genes are reported in isolates of Enterobacteriaceae from Sri Lanka [6].

Salmonella spp. isolated from blood cultures over the years have shown susceptibility to ceftriaxone up to now (indicated by cefotaxime sensitivity) [5]. Among *Neisseria gonorrhoeae*, penicillin, and ciprofloxacin resistance is 42.3%, and 62% respectively, and ceftriaxone resistance has not been detected up to now. There were no *Shigella* isolates reported by national reference laboratory or surveillance centres for 2 consecutive years.

According to GLASS data, the percentage of methicillin resistance in *Staphylococcus aureus* bacteraemia is also slowly reducing over the years. In 2021 the Methicillin Resistant *S. aureus* (MRSA) was 47.3%. (Figure 3) The prevalence of MRSA colonisation was 13.78% in the population of Colombo District in a study carried out from December 2018 to April 2019 [7].

Though 13 isolates of *Streptococcus pneumoniae* were submitted to GLASS, AST was not reported for any of the antibiotics for more than 10 isolates and therefore the percentages were not analysed. In a study conducted in a leading children's hospital on patients admitted from January 2005 to March 2007, 24 S. pneumoniae isolates from blood cultures and cerebrospinal fluid (CSF) cultures were analysed [8]. More than 90% (91.3%) of the isolates were resistant to penicillin (MIC >1.0 mg/ml) and 47.8% were resistant to cefotaxime.

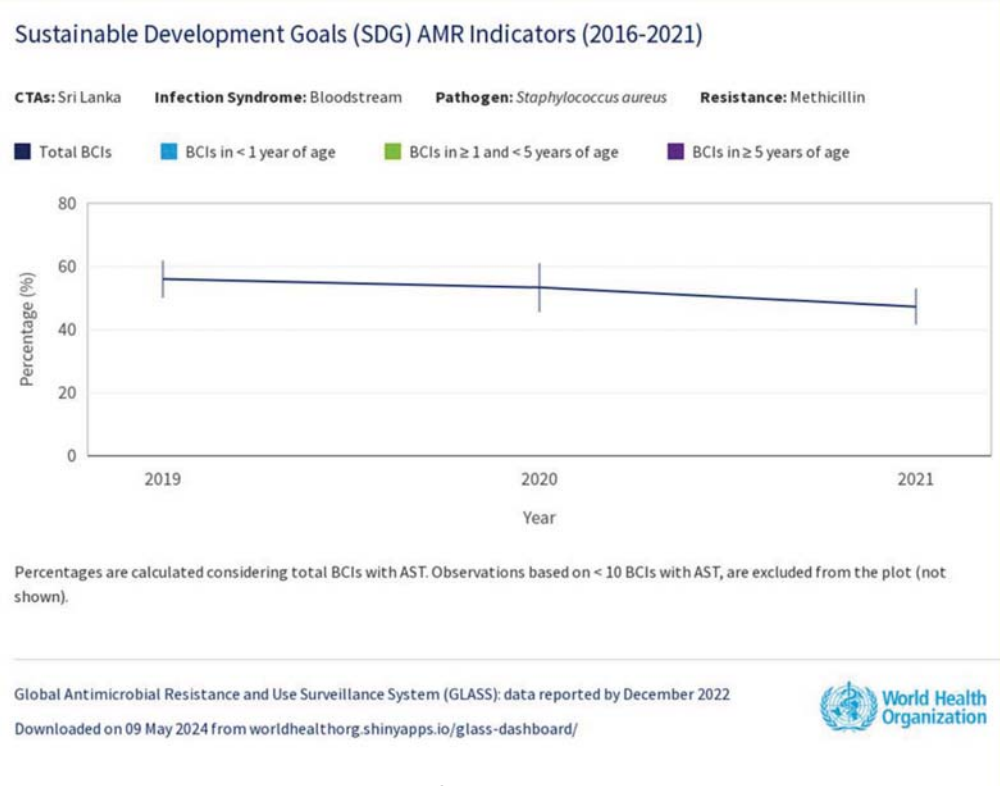

Figure 3.

A survey on consumption of antibacterial agents listed under antibacterials for systemic use (J01) in the Anatomical Therapeutic Chemical (ATC) classification system was carried out for 2017 retrospectively. Of the total antibacterials consumed, 54.19% were from the Access category while 45.57% were from the Watch group with an Access: Watch ratio of 1.18 [9]. According to Institute for Health Metrics and Evaluation, in Sri Lanka in 2019, there were 2,300 deaths attributable to AMR and 8,800 deaths associated with AMR. Sri Lanka had the 58th highest age-standardised mortality rate per 100,000 population associated with AMR across 204 countries [10].

Action taken to mitigate AMR in Sri Lanka

With the increasing awareness of the presence of AMR in the country, the need for enhancing measures to prevent and control AMR became a priority. SLCM initiated discussions among the membership as well as prescribers, and the MoH and implemented several activities pioneering the battle against AMR in the country. Multifaceted strategies for combating AMR were employed at hospital level. The Microbiology Task Force of the MoH, Sri Lanka served as the platform to facilitate laboratory services and AMR related activities at the national level. At the turn of the century, there was only one clinical microbiologist in the state sector hospitals. Microbiological diagnostics and infection prevention and control (IPC) activities of Sri Lankan hospitals improved gradually with the appointment of consultant microbiologists to hospitals of all provinces of the country. Regular training conducted by the Postgraduate Institute of Medicine helped to develop expertise in the fields of medical microbiology, virology, mycology, parasitology and immunology.

Aligned with the GAP- AMR Sri Lanka published the first NSP on combating AMR in 2017 [11]. This NSP included One Health approach to prevent and control AMR in human, animal and plant health sectors. The national advisory committee for implementing AMR was co-chaired by the three Director Generals representing each sector.

An end-term review of the AMR activities was conducted in 2023 followed by the development of the second NSP and a National AMR Action Plan for 2023-2028 [12]. Second NSP (NSP2) with a broader One Health concept including environmental health and food safety is being rolled out currently by the National AMR Focal Point (deputy director general of laboratory services MoH) with the support of relevant ministries and professional bodies.

AMR awareness programmes are conducted at hospital level and annual national level activities are organised by the MoH during the World Antimicrobial Resistance Awareness Week to enhance awareness among prescribers, other relevant stakeholders, and the general public. SLCM and other professional colleges regularly conduct training and awareness related to AMR.

ARSP was initiated in 2008 to study the resistance patterns of bloodstream pathogens with the participation of 7 centers and it was later expanded to include the common bacteria causing urinary tract infections [4, 5]. The same surveillance programme has now evolved into the national AMR surveillance network with 25 sentinel hospitals reporting data for the GLASS [13].

A Hospital Infection Prevention and Control (IPC) Manual was published by the SLCM in 2005 with a second edition in 2021. This has been used to improve IPC practices in the hospital settings and to train healthcare staff on prevention of healthcare associated infections and transmission of resistant bacteria. MRSA bacteraemia and hand hygiene compliance in hospital settings are monitored as national healthcare quality indicators since 2013.

Attempts on optimising antimicrobial prescribing practices led to the introduction of an authorisation system by the MoH through a circular on Red Light Antimicrobials in 2016 [14]. This was intended to ensure the appropriate use of 15 antimicrobials. A new circular has been issued in 2024 to adopt the WHO AWaRe classification in the country to facilitate the rational use and monitoring of consumption of antimicrobials [15]. The first edition of the National Guidelines on Empirical and prophylactic use of antimicrobials was published in 2016 and the second edition is ready for printing in 2024.

Many research projects on AMR related topics published in local and international journals reflect the gravity of the AMR situation in human health [4, 5, 7]. A few publications in One Health areas raise concerns on AMR in animal health and the environment [16, 17].

Challenges and gaps identified in tackling AMR in Sri Lanka

Activities to reduce the burden of AMR is likely to confront with many challenges especially in Low Middle-Income Countries such as Sri Lanka.

Poor adherence to guidelines, limited availability of antimicrobial stewardship programmes with monitoring in the community and in healthcare facilities and inadequate diagnostic stewardship are some of these. Monitoring of small-scale farms and back yard systems is a challenge. Inadequate laboratory facilities and the high cost of laboratory testing is a barrier for diagnostic stewardship.

Although the country has strong legislation on drug registration, the poor post-marketing surveillance, and the limited availability of laboratory facilities for efficacy testing, has resulted in the country receiving antimicrobials with doubtful quality. This undermines the faith of the prescribers leading to poly pharmacy and poor-quality drugs may lead to low blood levels of antimicrobials leading to development of resistance. Deficiencies in trained, experienced human resources further challenge the implementation of activities for combating AMR in the country. Brain drain which occurred especially with the economic crisis and political unrest of Sri Lanka, negatively impacted ongoing AMR activities. In addition, the lack of a dedicated team for AMR activities, inadequate infrastructure facilities, and financial constraints together with deficiencies in administrative support largely limit AMR mitigation activities.

Strengths and road map to mitigate AMR in Sri Lanka

AMR response has been implemented by the national AMR focal point with sector coordinators from human health, terrestrial and aquatic animal health and production, plant health and production, food safety, and environment sectors. The establishment of National Multisectoral Coordinating Group in 2016 which was later reformed as NAC and the National Action Plan Implementation Strengthening Team, provides a support system for AMR activities. NSP2, NAP and a costed operational plan is available for 2023-2028. This includes the process and outcome indicators for the Monitoring and Evaluation framework.

The free healthcare delivery system of Sri Lanka is the main strength behind Sri Lanka's achievements in the field of medicine. The country has eliminated several infectious diseases such as filariasis and malaria over the last few decades with the help of a free healthcare system and dedicated human resources. Moreover, the vaccine coverage for children under five years is equal to that of high-income countries. Sri Lanka has reported success in strict enforcement of guidelines on antimicrobial use as seen in low AMR rates in tuberculosis, HIV and malaria (before elimination). Lessons learned from such pathways can be incorporated to tackle AMR in the country. The support given by the MoH and the government amid an economic crisis cannot be underestimated.

The country is in the process of further expanding surveillance of human health and planning to commence an integrated laboratory network for surveillance of AMR in animal health, agriculture, and food chain.

Developing laboratory capacity and uninterrupted supply of consumables are urgently needed to keep up with NSP-AMR.

What should be our way forward?

Sri Lanka has passed many phases in the journey of AMR. As history repeats, our way forward has to be shaped up based on the lessons learnt in the past. As a country we have many strengths in the health sector. Therefore if we pave the way to battle AMR with appropriate interventions, a success story of AMR is not a difficult task.

First and foremost, requirement in our way forward should be strengthening the governance structure for AMR. A good governance, implying the apex body for

AMR, exercising the vested authority is accountable, transparent, predictable, participative, and dynamic. Reforms to existing structure, as mentioned in the NSP2 has to be implemented.

An AMR policy supported with guidelines for public and private sector is a necessity and could be floated with a strong and dedicated apex body. In our way forward strengthening and expanding the existing surveillance system converting it to a well-supported, scientifically guided One Health system is required. A well organised system for dissemination of information and necessary action should be considered a high priority.

A sustainable and well addressed awareness programmes for public and One Health stakeholders should be available. Advocacy programmes to establish political commitment should be worked out. A communication strategy for different audiences should be planned and implemented if we are to have early results in reducing AMR.

Producing quality data for action is not possible without adequate human resources, uninterrupted supply of reagents and facilities for information technology at data generation points. Therefore, due attention should be paid to strengthen the microbiology laboratories island wide. A regular provision of quality assured antimicrobials for prescribers and receivers in both human and animal sector is a high priority.

As IPC plays a major role in preventing AMR, implementing the activities suggested in NSP2 would push our AMR rates to low levels. Obtaining support from the technical expertise on infection prevention and control from designing of hospitals to commissioning of the specific units will uplift the battle against AMR. A policy for IPC with necessary regulations imposed would be essential for our forward march. Monitoring and evaluation of IPC should go hand in hand with availability of commodities for IPC.

Consumption and utilisation of antimicrobials is an area which should carefully monitored and strictly regulated. Gaps in our system with regard to this area should be straightened without delay. Human health sector as well as all other sectors under One Health should be under this umbrella.

Some of the activities in combating AMR need good financial support. But there are many more activities listed in the activity plan of the NSP2 which are either no cost or of low cost. These low hanging fruits should be plucked without a delay. Simultaneously for the costed activities a business case should be developed for the donor agencies and those agencies have to be motivated by the governing structure for AMR to achieve success.

Prioritisation of the activities of NSP2 is a must in the way forward. Phased out implementation in collaboration with all stakeholders is a must. All these should be backed by good research. Therefore, a national scale support system prioritising One Health AMR research should be established. The future can be shaped accurately by appropriate operational research. In a nutshell adhering to NSP2 with no ad hoc activities, implementation of those with good governance and working out for supporting mechanisms will pave a smooth way ahead of us.

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Conflicts of interest

None of the authours have any conflicts of interest.

Ethical approval

Not indicted.

Patient consent

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References

1. Antimicrobial resistance; World Health Organization; https://www.who.int/news-room/fact-sheets/detail/antimicrobial-resistance (accessed on June 20, 2024)
2. O'Neill J. Tackling drug-resistant infections globally: Final report and recommendations. London, UK: Government of the United Kingdom and Wellcome Trust; 2016b. [April 8, 2021]. https: //wellcomecollection .org/works/thvwsuba.
3. Challenges and barriers for effective supply of medicines to the state sector and recommendations to the Ministry of Health, Sri Lanka. A report by the Sri Lanka Association of Clinical Pharmacology and Therapeutics (SLACPT) for the ministry of Health, Sri Lanka, August 2023; https://slacpt.lk/wp-content/uploads/2023/10/MOH-report-edited-16th-August-1.pdf (accessed on June 20, 2024)
4. Chandrasiri P, Elwitigala JP, Nanayakkara G, *et al*. A multi-center laboratory study of Gram negative bacterial bloodstream infections in Sri Lanka; *Ceylon Med J* 2013; **58**: 56-61; https://cmj.sljol.info/articles/10.4038/cmj.v58i2.5680
5. Jayatilleke SK, Patabendige G, Dassanayake M, *et al*. Analysis of urine culture isolates from seven laboratories of Sri Lanka: National Laboratory Based Surveillance of Sri Lanka College of Microbiologists in 2014; *Sri Lankan J Infect Dis* 2016; **6**(1): 17-24; http://dx.doi.org/10.4038/sljid.v6i1.8105
6. Perera PDVM, Gamage S, De Silva HSM, Jayatilleke SK, De Silva N, Alp Aydin, Virve I. Enne, Corea E M; Phenotypic and genotypic distribution of ESBL, AmpC β-

lactamase and carbapenemase-producing Enterobacteriaceae in community-acquired and hospital-acquired urinary tract infections in Sri Lanka. J. Glob. *Antimicrob. Resist.* 2022; **30**: 115-122.

7. Jayaweera AS, Karunarathne M, Kumbukgolla WW, Thushari H L. Prevalence of methicillin resistant Staphylococcus aureus (MRSA) bacteremia at Teaching Hospital Anuradhapura, Sri Lanka. *Ceylon Med J* 2017 **62**: 110-11. http://doi.org/10.4038/cmj.v62i2.8478

8. Batuwanthudawe R, Karunarathne K, Dassanayake M, *et al*. Surveillance of Invasive Pneumococcal Disease in Colombo, Sri Lanka. *Clin. Infect. Dis.* 2009; **48**: S136-40. 10.1086/596492

9. Sri Ranganathan S, Wanigatunge C, Senadheera GPSG, Beneragama BVSH. A national survey of antibacterial consumption in Sri Lanka. *PLoS ONE* 2021; **16**(9): e0257424. https://doi.org/ 10.1371/journal.pone.0257424

10. The burden of antimicrobial resistance (AMR) in Sri Lanka. World Health Organization (WHO). TrACSS 2021-2022. https://amrcountryprogress.org/download/AMR-self-assessment-survey-responses-2020-2021.xlsx

11. National Strategic Plan for Combating Antimicrobial Resistance in Sri Lanka 2017-2022. https://cdn.who.int/media/docs/default-source/antimicrobial-resistance/amr-spc-npm/nap-library/national-strategic-plan-for-combating-antimicrobial-resistance-in-sri-lanka-2017%C3%A2-2022.pdf

12. National Strategic Plan for Combating Antimicrobial Resistance in Sri Lanka 2023-2028. https://cdn.who.int/media/docs/default-source/antimicrobial-resistance/amr-spc-npm/nap-library/sri-lanka-national-strategic-plan-2023-2028.pdf?sfvrsn=d54326e0_3&download=true

13. https://worldhealthorg.shinyapps.io/glass-dashboard/_w_78f8e1da/#!/cta-profiles

14. Introduction of authorization of prescribing “Red light” antibiotics. http://www.previousmoh.health.gov.lk/CMS/cmsmoh1/viewcircular.php?cno=01-56/2016&med=english, Health circulars, MoH

15. Implementation of ‘AWaRe’ classification of Antimicrobials in Healthcare Institutions in Sri Lanka. https://www.health.gov.lk/wp-content/uploads/2024/04/01-13-2024-eng.pdf

16. Ariyawansa S, Gunawardana KN, Hapudeniya MM, *et al.* One Health Surveillance of Antimicrobial Use and Resistance: Challenges and Successes of Implementing Surveillance Programs in Sri Lanka. *Antibiotics* 2023, 12, 446. https://doi.org/10.3390/antibiotics12030446

17. Kumar M, Chaminda GGT, Honda R. Seasonality impels the antibiotic resistance in Kelani River of the emerging economy of Sri Lanka. NPJ Clean Water 2020; 3, 12. https://doi.org/10.1038/s41545-020-0058-6