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The antimicrobial resistance (AMR) scenario in Malaysia: A review of current trends, perspectives and strategic action

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Abstract

Fast becoming a global health crisis, antimicrobial resistance (AMR) is causing numerous deaths and having economic implications worldwide. This review paper highlights the AMR scenario in Malaysia, primarily in regard to the clinical implications of common bacterial pathogens. Other highlights of the study include the perspectives of public and private healthcare professionals, as well as consumers, on the knowledge, attitudes, and practices (KAP) associated with AMR and antibiotics usage, the aim being to identify gaps in the way AMR is addressed in Malaysia. In addition to the human factor, the agriculture and aquaculture sectors also contribute to AMR. The crucial role of the antimicrobial stewardship program (ASP) in Malaysia is also discussed here, with its implementation outlined chronologically. Furthermore, Malaysia's AMR strategic action is assessed against the policies of other Southeast Asian countries to obtain a more comprehensive understanding of various international efforts to mitigate AMR issues. Alongside government measures, many non-governmental organisations (NGOs) are also actively involved in various AMR initiatives through international workshops and meetings, the creation of task forces, and heightening AMR awareness through publications, social media, and toolkit development. These efforts and more are necessary to raise awareness of AMR and address the related issues effectively.

Keywords: Antimicrobial resistance (AMR), Antibiotics, Antimicrobial stewardship program (ASP), Healthcare professionals, Public awareness, Agriculture, Aquaculture, Non-governmental organisation (NGO)

1. Introduction

An antibiotic is an agent that destroys bacteria by inhibiting their growth through various mechanisms of action, including inhibiting the synthesis of bacterial cell walls and the synthesis of proteins and deoxyribonucleic acid (DNA) [1]. Since being discovered by Alexander Fleming in the late 1920s, penicillin has been widely considered a panacea for treating bacterial infectious diseases. This revolutionary discovery also became a historical turning point when antibiotics were used as life-saving agents during the world wars. However, Fleming himself warned that if antibiotics were readily available and people were exposed to suboptimal doses, the health consequences could one day be fatal [2].

After decades in which antibiotics have saved countless lives, antimicrobial resistance (AMR) has now become an alarming global threat [2]. The continued and indiscriminate use of antibiotics in humans and animals has led to an unbalanced increase in AMR because no new antibiotics have been discovered since the late 1980s, when medical advances began to focus on other non-communicable diseases like cancer, diabetes, cardiovascular disease, and chronic respiratory disease [3]. This worsening situation is often associated with human behaviours

and practices, such as the use of antibiotics for irrelevant conditions not caused by bacterial infections, poor patient adherence to antibiotic dosing, and the rising use of antibiotics in marine, agricultural and livestock industries [4].

The World Health Organization (WHO) assessed the risk of AMR in Southeast Asia, and it was postulated that AMR might spread globally through active tourism and travellers if not effectively addressed [5,6]. In 2011, the WHO expressed concern about the region's lack of available data on AMR [7]. With the Jaipur Declaration on Antimicrobial Resistance in 2011, immediate action in Southeast Asia was demanded [8]. In 2014, AMR was declared a growing global threat that required concerted countermeasures. The vigorous efforts to combat AMR led to the Flagship Priority in 2014, an international initiative focusing on AMR strategy at regional and national levels. In 2015, the Global Action Plan established by the WHO called on countries worldwide to implement national action plans to combat AMR at their respective national levels [9]. The surveillance of antibiotic use in Malaysia and the prevalence of AMR cases have been discussed in numerous papers [2,9]. Researchers have identified the need for an established and standardised surveillance tool for sustainable stewardship efforts in the areas of audit training; data collection, classification, storage, and retrieval; the analysis and presentation of large volumes of health data; the facilitation of data comparability and benchmarking over time; and a focus on critical key indicators in Malaysia [10].

The impact of AMR in Malaysia should be addressed seriously and swiftly. Studies have found all antibiotics tested in Malaysia to be resistant to several microbes, based on data derived from public tertiary healthcare settings and focused on the presence of AMR. Other than in human samples, AMR in chickens is another common problem in Malaysia and other developing countries where antibiotics are used as feed additives and for prophylactic treatment of infectious diseases. However, data on the rate of mortality due to AMR in Malaysia is lacking, and this limitation demands that studies be expanded to include areas like private primary healthcare settings, agriculture, and aquaculture [11].

This review article aims to identify the current scenario of AMR as an emerging threat and elaborate on the actions that have commenced to eliminate the spread of AMR among Malaysian communities. More specifically, the paper discusses the extent of AMR in Malaysia through reports of clinical patterns and the implications of AMR. The dimensions contributing to the occurrence and spread of AMR are further outlined from the perspectives of healthcare professionals, members of the public, as well as those engaged in the agriculture and aquaculture sectors. Next, the implementation of the antimicrobial stewardship program (ASP) in Malaysia is discussed and compared with similar programs implemented across Southeast Asia. Furthermore, the strategies taken by various non-governmental bodies in Malaysia to unite and create awareness of this global threat are also reviewed so that they can be better understood.

2. Clinical patterns and implications of AMR

The coronavirus disease 2019 (COVID-19) struck in late 2019 and has caused millions of deaths worldwide. In addition, an estimated 4.95 million deaths were associated with bacterial AMR in 2019, including a median of 1.27 million deaths attributable to bacterial AMR that could have been prevented, ranking such deaths below COVID-19 and tuberculosis in terms of global deaths from infection [3,12]. During the pandemic, emerging cases of AMR among COVID-19 patients were reported, and the misuse of antibiotics as a cure and preventive measure for COVID-19 was prevalent. Despite the ineffectiveness of treating COVID-19 with antibiotics, protocols and existing healthcare settings suggested the use of antibiotics due to the similarities between the presentation of symptoms of COVID-19 and those of bacterial diseases or other forms of viral pneumonia. Antibiotics were also prescribed for suspected or confirmed co-infections. Support for this was provided in a review paper which stated that the difficulty of distinguishing between viral and bacterial pneumonia made it difficult to avoid the unnecessary use of antibiotics until severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) had been confirmed [13]. In Malaysia, ivermectin has been approved for veterinary use, whereas the use of ivermectin in humans has only been approved for clinical trials in appropriate settings under the strict supervision of physicians. During the COVID-19 pandemic, however, ivermectin emerged as a COVID-19 treatment option in many countries despite insufficient scientific evidence for its efficacy. Cases of ivermectin being used unregistered to treat COVID-19 in Malaysia, with or without the supervision of healthcare providers, were reported by a special combined task force comprising the Pharmaceutical Services Programme headquarters, the Ministry of Health Facilities, and the National Pharmaceutical Regulatory Agency (NPRA) [14].

Meanwhile, the extensive literature review by Murray et al. [3] presented estimates of the global burden of up to 88 pathogen-drug resistances, including that of AMR. The estimate in the paper demonstrated drug resistance to be a major global health threat for each leading pathogen. Therefore, this estimate was expected to serve as an important basis on which policymakers could make informed and site-specific policy decisions, particularly concerning infection prevention and control programs, access to key antibiotics, and research and development of new vaccines and antibiotics. A separate paper emphasised that the burden of AMR may be greater than anticipated because without effective antibiotics, modern treatment options like major transplants and chemotherapy are futile as AMR patients may die from infections [12].

The WHO recently summarised global AMR data on seven common bacterial pathogens (*Escherichia coli*, *Klebsiella*, *Staphylococcus aureus*, *Streptococcus pneumoniae*, non-typhoidal *Salmonella*, *Shigella* spp., and *Neisseria gonorrhoeae*) [15]. In Thailand, a 2010 study found that the number of deaths caused by AMR-related hospital infections had risen to 38,481 [16]. The first Malaysian case of Methicillin-resistant *Staphylococcus aureus* (MRSA) was reported in 1978; the case was then isolated from other patients in a large hospital in the capital, Kuala Lumpur. MRSA was also confirmed to be present in 10-20% of the hospitals surveyed [17]. The report provided evidence of the increasing problem of MRSA. The high prevalence of MRSA in hospitals was mainly attributed to the difficulty of maintaining adequate hygiene levels in very large and crowded tertiary hospitals. Another important factor was cross-infection due to the numerous staff who might be asymptomatic carriers of MRSA [18].

Another frequently reported AMR was the resistance of *Enterobacteriaceae* to carbapenems [19]. Colistin is the drug of last resort to treat life-threatening infections caused by carbapenem-resistant *Enterobacteriaceae*. Recently, however, resistance to Colistin has been identified in several countries and regions, so infections caused by these bacteria can no longer be treated [19].

Klebsiella pneumonia is a major cause of hospital-acquired infections such as pneumonia and bloodstream infections, including neonatal infections and those affecting intensive care unit (ICU) patients [20]. In some countries, carbapenem antibiotics are ineffective due to resistance in more than half of those treated for *Klebsiella pneumoniae* infections [20,21].

In Malaysia, surveillance of antibiotic use has been conducted in selected hospitals since 2001 [22,23]. Hospitals under the Ministry of Health (MOH), Ministry of Higher Education (MOHE), and Ministry of Defence (MINDEF), as well as private hospitals, were included in the surveillance program, which was later renamed National Surveillance of Antibiotic Use (NSAU) [23]. In July 2015, it was expanded to include MOH primary care health clinics [23]. Surveillance of carbapenem-resistant *Enterobacteriaceae* (CRE) in 2016 reported an alarming increase in the number of cases. By 2013, the Centers for Disease Control and Prevention (CDC) had reported that in 46 states in the United States, at least one *Klebsiella pneumoniae* carbapenemase (KPC)-producing *Enterobacteriaceae* had been identified [6]. Analysis showed that 95% of patients had a history of antibiotic use and 50.6% had taken antibiotics for over seven days [22]. Polymyxin resistance was also found in CRE cases, which resulted in 21.7% of deaths in 2016 [24].

In 2021, according to the National Surveillance of Antimicrobial Resistance (NSAR), a total of 533,101 isolates were reported from 41 hospitals and one public health laboratory in Malaysia. The penicillin resistance of *Streptococcus pneumoniae* isolated from all samples had ranged from 0 to 3.4% in the previous five years (2017-2021), and 32.0% of isolates were resistant to Erythromycin. In addition, increased resistance rates were found in all the antibiotics tested for *Acinetobacter baumannii* isolated from all clinical samples. The antibiotics included Ampicillin/Sulbactam, Ceftazidime, Cefoperazone/Sulbactam, Imipenem, Meropenem, Gentamicin, and Amikacin. Furthermore, Cefoperazone/Sulbactam had a higher resistance rate (42.4%) than in the previous year [11], although the resistance rates of *Pseudomonas aeruginosa* to all antibiotics were still below 10%. For *Salmonella enterica* serotype Typhi, Ciprofloxacin resistance decreased from 3.0% in 2020 to 0% in 2021. However, Ciprofloxacin resistance in *Salmonella sp.* from blood samples slightly increased from 0.8% in 2020 to 1.0% in 2020. Ciprofloxacin resistance in isolates from stools showed a similar pattern. Between 2020 and 2021, resistance to Ampicillin and Ceftriaxone also increased from 14.0% and 0.8% to 16.8% and 1.1%, respectively [11].

Multidrug-resistant tuberculosis (MDR-TB), a disease caused by *Mycobacterium tuberculosis*, is resistant to the first-line antituberculosis drugs Rifampicin and Isoniazid [20,25]. According to WHO estimates, about 470,000 people contract MDR-TB annually, of which 180,000 die from it [17]. Worldwide, 105 countries with representative data reported that 20% of MDR-TB patients developed extensively drug-resistant TB (XDR-TB) [21]. The emergence of MDR-TB and XDR-TB has hampered the fight against diseases like human immunodeficiency virus (HIV) and malaria [25]. In some countries, levels of 15% or more have recently been reported among people starting HIV treatment, with rates of up to 40% among those resuming treatment [26]. This dire situation needs urgent attention. Since September 2015, the WHO has recommended that all those living with HIV start antiretroviral treatment (ART) [21,26]. However, the increased use of ART is expected to further increase ART resistance in all global regions. Therefore, resistance monitoring must continue to minimise its further occurrence and spread among HIV patients, as well as maximise the long-term effectiveness of first-line ART treatment [21,27].

Resistance to first-line treatment of the malaria parasite *Plasmodium falciparum* has been detected in five Southeast Asian countries: Thailand, Indonesia, Myanmar, Cambodia, and Vietnam. Along the border between Cambodia and Thailand, where *Plasmodium falciparum* has become resistant to virtually all available antimalarials, treatment has become more difficult and the need for close surveillance cannot be overlooked [21]. This is a tangible risk because multidrug resistance is likely to occur elsewhere in the subregion [21].

The intertwining of resistance in influenza and superbugs is not new [28]. The new coronavirus is no exception, with some studies founding that one in seven patients hospitalised with COVID-19 developed a dangerous secondary bacterial infection and 50% of death cases had such infections [28]. The challenges of AMR could

become a major factor in additional illnesses and deaths in the nation's health system as coronavirus pneumonia outstrips the capacities of ICUs [29].

3. Understanding AMR from the perspectives of healthcare professionals

Widely regarded as the custodians of medicines, health professionals have the medical knowledge to perform diagnosis and treatment, and they are expected to practise good medication ethics, especially in the use of antibiotics [30]. Despite this perception, Ab Rahman et al. [8] found that antibiotic prescribing is widespread in Malaysian primary care clinics, with at least one in five examinations involving this practice. Notably, half of all antibiotic prescriptions were for upper respiratory tract infections (URTIs), which are predominantly caused by viruses. The findings suggest that the overuse of antibiotics in Malaysian clinics and prescriptions is not based on sufficient clinical indications [31].

In various studies, many general practitioners (GPs) reported that their patients expected antibiotics to be prescribed [31,33]. About 36.7% of GPs reported that patients asked for antibiotics when they were not prescribed, although more than one-fifth of the responding GPs believed that antibiotics were not specifically needed in these cases [32]. The study concluded that education was urgently needed to address the irrational use of antibiotics and AMR among all healthcare stakeholders, including patients themselves [32].

Other studies examining healthcare students' knowledge of antibiotics and resistance found that more than 50% of those surveyed had little knowledge of antibiotic use, with some holding outdated health beliefs [32]. Another cross-sectional study by Sivanandy and Loh [33] involving 113 medical students found that most knew that antibiotics can only be used to kill bacteria and treat bacterial infections and that they are not meant for viral infections. Surprisingly, 50% of the participants thought that antibiotics could be used to treat sore throats, suggesting that some prescribers were not sufficiently well-informed about the proper prescribing of antibiotics [34]. Another study found a discrepancy between theoretical input and clinical practice [34]. The authors also noted that clinical competence in antibiotic prescribing during student internships resulted largely from learning by imitating senior colleagues; it was suggested that this method be corrected [34]. Another study conducted among final-year pharmacy students found they had moderate knowledge of antibiotics and AMR use but lacked constructive attitudes towards reducing AMR [35]. The latter study concluded that an improved education program through curriculum change could promote AMR control initiatives among health professionals, especially doctors and pharmacists [36]. The study also advocated building appropriate professionalism to promote the prudent use of antibiotics [36].

A study involving final-year pharmacy students from a public university found a good understanding of AMR, but most respondents did not have positive attitudes towards AMR control and prevention [35]. Another study involving 72 medical and 51 pharmacy students from the International Islamic University of Malaysia found the participants were knowledgeable about antibiotic usage, AMR, AMR development mechanisms, and awareness of the need to minimise AMR [37]. Comparatively, the pharmacy students exhibited better comprehension skills than the medical students [37]. However, the results cannot be generalised as this was a single-centre study. Two studies suggested improved training programs for all health professionals, especially physicians and pharmacists [36,37].

The WHO, as well as several national guidelines and protocols, strongly discourage patients from discontinuing treatment with antibiotics even if symptoms improve, due to fears that premature termination could result in the growth of resistant bacteria. Therefore, health professionals must have a sound knowledge of antibiotic use so that patients receive optimal benefits from their treatment [30].

4. Directing awareness among the public on the use of antibiotics

In Malaysia, several small-scale studies have been conducted to discover the views of the population on the use of antibiotics [38-42]. One study found critical gaps between the attitudes and practices of the population of Cheras (a district in the capital Kuala Lumpur) regarding the use of antibiotics. The study reported that up to 55% of respondents who had been prescribed antibiotics in clinics stopped taking them once their symptoms improved [38]. Another study conducted among patients in a hospital outpatient department found that some (22.3%) stopped taking their antibiotics as soon as their symptoms disappeared. The same study found that respondents generally lacked knowledge and awareness of the use and purpose of antibiotics; this was deemed to be significantly related to poor adherence to antibiotic therapy. In relation to antibiotic treatment, the study highlighted important knowledge and attitude gaps and at-risk individuals [42]. Interventions to improve public knowledge and attitudes towards antibiotic use, as well as appropriate measures to regulate the availability of antibiotics and the development of targeted antibiotic education and patient counselling campaigns, will play important roles in promoting effective antibiotic use among the population [38-42]. The results of antibiotic consumption studies conducted in Malaysia generally demonstrate that consumer awareness patterns depend on socioeconomic backgrounds [38,40-41]. Qamar et al. [41] conducted a self-administered cross-sectional survey

among 380 respondents using a pre-validated questionnaire in public places in Shah Alam, Malaysia. The survey analysis showed that 43% of the respondents had good knowledge about antibiotics. Most knew that antibiotics are used for bacterial infections. However, 40% held the incorrect idea that antibiotics are used for viral infections. Although the population's knowledge of antibiotics was generally acceptable, greater awareness of the importance of correct antibiotic use should be promoted, as should a change in attitude towards antibiotic use [41].

As revealed in the findings of a cross-sectional public survey of 408 respondents at the Penang State Hospital Outpatient Pharmacy department, almost 55% of the respondents had a moderate level of antibiotics knowledge. Of the respondents, 59.1% were aware of the phenomenon of AMR related to the overuse of antibiotics. As for attitudes, 38% believed that taking antibiotics for cold symptoms could accelerate their recovery, while 47.3% expected antibiotics to be prescribed for cold symptoms [39].

A study was conducted by Kong et al. [40] with respondents aged 60 years and above, the results of which revealed low levels of knowledge in more than half of them; meanwhile, more than one-third of the respondents mistakenly self-medicated with antibiotics after a cold. This signalled the importance of educational interventions to promote the prudent use of antibiotics among the public. Prospective outreach efforts should deliver important messages about the role of antibiotics and the prominence of antibiotic adherence in this community [40].

4.1 Trends of AMR in agriculture and aquaculture

Many classes of antibiotics used for humans are also being used for livestock. Besides using antibiotics for treatment purposes, some food producers also use them for growth promotion or routine disease prevention, usually in crowded and unhygienic farming conditions [43]. The indiscriminate use of antibiotics accelerates the development of AMR bacteria, allowing them to escape and spread through communities [38]. These activities, in combination with domestic and clinical uses of antibiotics, are having a profound impact on microbial ecology, as evidenced by the rising prevalence and diversity of AMR genes in urban and agricultural sites, as well as seemingly undisturbed environments [4]. The findings of a recent study by Ibrahim et al. [44] indicated a high prevalence of multi-drug resistant *Salmonella* spp. and *E. coli* in poultry farms in the East Coast region of Peninsular Malaysia, which could be attributed to excessive antibiotic use by poultry farm owners [44]. Meanwhile, an investigation conducted from January 2000 to December 2015 by the Regional Veterinary Laboratory in Bukit Tengah, Penang, Malaysia, isolated a total of 2,345 *E. coli* cases from the AMR clinical cases received by the laboratory [45]. The significant rising trend of resistance to antibiotics, namely the Aminopenicillin, Fluoroquinolone, Aminoglycoside, and Tetracycline classes found mainly in poultry and pigs, may have derived from the usage of antibiotics as feed additives [46]. This cause for concern prompted the Malaysian Department of Veterinary Services to issue the Malaysian Veterinary Antimicrobial Guidelines (MVAG) in 2021, which highlighted seven principles of the prudent use of antibiotics in livestock, as illustrated in Figure 1 [46].

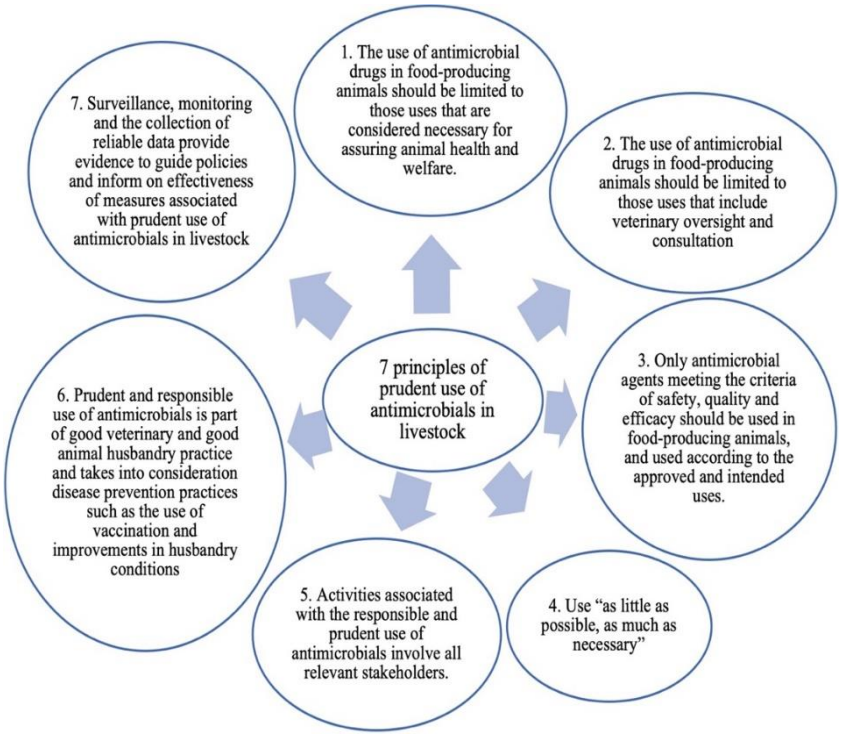

Figure 1 Principles of prudent use of antibiotics in livestock.

5. Antimicrobial stewardship program (ASP) in Malaysia

The development of AMR strains in hospitals has been exacerbated by the extensive use of antibiotics and the high volume of patients with multiple pathogens; such situations require concerted action [8]. The ASP is a coordinated, systematic approach designed to ensure the appropriate use of antimicrobial agents by promoting the selection of optimal antimicrobial drug regimens that focus primarily on improving patient outcomes through reduced morbidity and mortality from infections. Meanwhile, the regimens should optimise antimicrobial therapy by promoting the judicious use of antimicrobials, optimising selection and dosage, as well as administering and prolonging antimicrobial therapy to maximise clinical cures and prevent infections among existing and future patients [47]. Figure 2 illustrates a detailed chronology of the AMR strategic action undertaken in Malaysia and the establishment of the ASP.

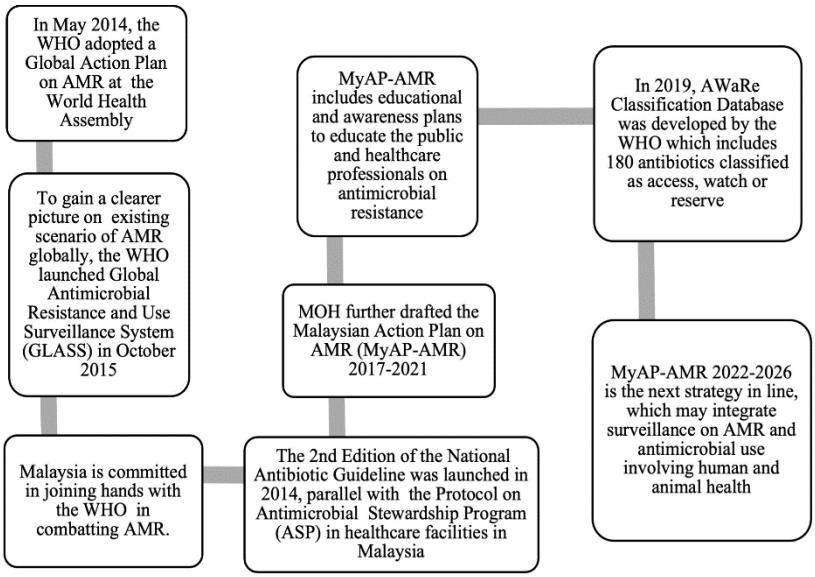

Figure 2 Chronology of the establishment of ASP in Malaysia.

Ongoing surveillance and prospective audits have revealed improved patient care and the reduction of unnecessary antimicrobial use (by between 22% and 36%), AMR, and pharmacy spending [47]. A form of governance of multidisciplinary teams from all Malaysian hospitals, the ASP incorporates various activities, including the development of local antibiotics guidelines and clinical pathways to standardise prescribers' approaches, as well as surveillance of antimicrobial prescription and consumption behaviour to aid therapy decisions [23,47]. The program assesses the public health consequences of antimicrobial misuse and evaluates the impacts of resistance containment interventions; prospective audits; and restrictions on or the pre-authorisation of certain antibiotic usage. Furthermore, an antimicrobial order tool has been designed to encourage clinicians to review basic clinical and laboratory information, as well as categorise antimicrobial use as prophylactic, empirical, or therapeutic [24,49]. As another pillar intended to optimise this program nationwide, education has been introduced in the form of newsletters, continuous medical education, and prescribing aids for healthcare practitioners [47].

Comprehensive surveillance is generally lacking in most sectors since the ASP focuses primarily on hospital settings [33,38]. A study reported that 87% of antibiotics prescriptions in Malaysia came from private primary care, reflecting the contraindicating structure of surveillance, which was biased towards public healthcare settings in Malaysia [8]. Although the ASP is still in its infancy, with time and stringent implementation, it should efficiently combat AMR in Malaysia [8,33,38].

5.1 Antimicrobial stewardship programs (ASPs) in the Southeast Asian Region

All Southeast Asian countries have adopted various ASP strategies, as listed in Table 1. Although varying in their implementation, these strategies share a common objective: to tackle AMR [9].

The WHO Global Action Plan (GAP) on AMR provides a broad framework with which countries can address AMR through five strategic objectives: improving awareness and understanding of AMR through effective communication, education, and training; strengthening the knowledge and evidence base through surveillance and

research; reducing the incidence of infection through effective sanitation, hygiene, and infection-prevention measures; optimising the use of antimicrobial medicines for human and animal health; and developing the economic case for sustainable investment that meets the needs of all countries and increases investment in new medicines, diagnostic tools, vaccines, and other interventions [21,48]. All Southeast Asian countries focus on strategically optimising the use of antimicrobials, strengthening surveillance, raising awareness of AMR, infection prevention and control, as well as developing research and participation in international cooperation through reporting, funding, dialogue, and technical support [9,49].

In Malaysia, the focus when tackling AMR has always been human health. However, due to the acknowledgement that AMR has multifactorial causes, the agenda has expanded to monitoring antimicrobial use and the usage of antibiotics in the agriculture and aquaculture sectors. Furthermore, the ASP is being actively implemented in private healthcare practices to ensure it comprehensively covers all healthcare systems in Malaysia.

5.2 Non-governmental Movement in Combating AMR

Other than the Ministry of Health Malaysia, many non-governmental organisations (NGOs) have acted cooperatively to tackle AMR among the public [24]. In 2014, Action on Antibiotic Resistance Southeast Asia (ReAct SEA), an independent organisation strongly advocating global AMR awareness, organised a meeting over three days in which scientists, doctors, researchers, health ministry officials, hospitals, and civil society representatives from a few Southeast Asia countries participated to share and learn about successful AMR interventions for adaption and adoption in their respective country settings [50].

An Asian AMR Reference Workshop was organised in 2018 by the Southern Centre and the Third World Network (TWN) to address the AMR crisis in Asian countries. This workshop included policymakers and NGOs from the participating countries and Australia. During the sessions, governments and non-governmental organisations addressed their concerns about AMR. The workshop concluded with a discussion of the factors that limited the capacity to address AMR. These included the lack of prioritisation and political interest or will; a lack of financial and human resources; insufficient equipment for diagnostic work; as well as a lack of champions and systematic stewardship programs at the national and local levels [51].

The Consumers' Association of Penang (CAP) has undertaken many initiatives to educate the public on rational antibiotic use and encourage a ban on antimicrobial feeding in livestock. Through their ongoing efforts, CAP became a signatory of the Antibiotic Resistance Coalition in 2018, along with other civil society partners, to demonstrate solidarity on initiatives to curb antibiotic use in animal feeding. This would be achieved by publishing newsletters and books to raise awareness about the overconsumption of antibiotics in food, especially from livestock, and the detrimental health effects of the drugs [52].

The Malaysian Pharmaceutical Society (MPS) has also actively expressed its views on the use of antibiotics, highlighting the importance of affordable access to antibiotics and proper systems to promote innovations that generate new antibiotics, including marketing practices to promote antibiotics and the need for their regulation. In September 2020, the MPS launched the International Pharmaceutical Federation (FIP) Commission on Antimicrobial Resistance to emphasise the role of pharmacists in achieving the United Nations Sustainable Development Goals (SDP). The Commission aims to develop pharmacists' roles in tackling AMR and explore ways to strengthen its own influence in all settings and practice areas. The MPS plans to diversify its measures against AMR with the new FIP Pharmacy Roadmap to Combat Antimicrobial Resistance, which will drive action globally, maintain momentum, as well as track and assess progress on this global health priority for pharmacy departments [53].

Malaysia is also a member of the World Alliance Against Antibiotic Resistance (WAAAR), which was founded in France in 2011. The WAAAR is a group of 700 people from 55 countries that represents all major stakeholders, including physicians, veterinarians, microbiologists, surgeons, pharmacists, nurses, evolutionary biologists, ecologists, environmentalists, and patient advocates [54]. The Alliance is supported by over 140 professional associations or groups worldwide that advocate action against AMR. In June 2014, the WAAAR initiated the Paris Declaration, which calls for a holistic policy response and contains ten proposals for action, including improved awareness and education, better diagnostics, new models for drug development, and better infectious disease control measures [54].

Lastly, the Malaysia National Poison Centre, which was a WHO Collaborating Centre for Drug Information, strongly advocates the rational use of antibiotics. The Centre's Education and Prevent Program has elevated public awareness of AMR through efforts such as public seminars, the development of AMR teaching-learning toolkits, short video clips on social media, and providing consultation on demand [55].

However, the responsibility for addressing AMR issues in Malaysia should not fall solely on the government sector. In many ways, NGOs directly impact the fight against AMR through their roles in and dedication to the struggle, as manifested in their successful communication with policymakers and decisionmakers in the health sector to draw their attention to the AMR problem and urge improvements to the current policies and systems. In

addition, NGOs actively raise awareness at all levels, including among stakeholders, health professionals, and the general public. This ensures easy access to education and awareness among target groups, which directly bridges their knowledge gaps [56]. Furthermore, NGOs undertake active efforts to publish informative newsletters and annual bulletins, organise campaigns, as well as contribute to funding specific research [54,56]. Therefore, the parallel involvement of NGOs and the government ensures a more impactful approach to combat AMR from various policy and educational perspectives. NGOs in Malaysia must also take an active role in supporting additional collaboration to produce a more holistic approach to addressing AMR issues in the country.

Table 1 Strategies and implementation methods of ASPs in Southeast Asian countries.

Country	Strategies of Antimicrobial Stewardship Programs (ASPs)	Implementation	References
Brunei	- Antimicrobial Resistance National Action Plan 2019-2023 - National Antibiotic Guidelines - National Guidelines for Prudent Use of Antimicrobials in Livestock - National Standard Drug List	- Data collection on antimicrobial usage from human and animal sectors - Establishment of ASPs in selected facilities - Prescribed medication classification for all antimicrobials	[57]
Cambodia	- Multi-Sectoral Action Plan on Antimicrobial Resistance in Cambodia 2019-2023	- Increased laboratory capacity and continuous surveillance on antimicrobial usage	[58]
Indonesia	- National Action Plan on Antimicrobial Resistance Indonesia 2017-2019	- Introduction of national AMR surveillance for humans, animals, food and aquaculture, covering district hospitals and rural hospitals in public and private sentinel hospitals/ hospital chains. - Development of regulations on antimicrobials (veterinary, human and aquaculture) and their importation, manufacture, quality, distribution, marketing authorisation, promotion and inspection, tracking and reporting. - Active planning of human vaccination programs, animal vaccination programs and campaigns.	[59,60]
Laos	- National Strategic Plan on Antimicrobial Resistance in Lao PDR 2019-2023	- A centralised laboratory database for AMR surveillance data. - Development of legislation to control AMR in humans by declaring antimicrobials as controlled medicines, monitoring importation and distribution; selling antimicrobials only by qualified professionals on presentation of a prescription. - The Food and Drugs Act is enforced by the Food and Drugs Office in relation to antimicrobial use (AMU). - National strategy is actively planned for infection prevention and control (IPC) in human health facilities to improve government hospital wards, waste management systems and hygiene plans in hospitals or farms in the agricultural sector.	[61,62]
Malaysia	- Malaysian Action Plan on Antimicrobial Resistance (MyAP-AMR) 2017-2021 - National Antibiotic Guidelines	- Standardisation of laboratory reference - Continuous monitoring of antibiotic use and healthcare-associated infections (HAI) in selected hospitals since 2001. - Frequent national point-based prevalence surveillance of antibiotic use in health facilities - Surveys on knowledge, attitudes, and practices (KAP) among the public and health professionals	[23]
Myanmar	- Myanmar National Action Plan for Containment of Antimicrobial Resistance 2017-2022	- Plan evidence-based AMRs. - Develop a national policy on AMR containment and use and related legal framework to control AMU in humans and animals, including residue testing in food, a list of essential antibiotics and guidelines for standard antimicrobial treatment in human and veterinary medicine, aquaculture and food production. - Establish a national IPC program for compliance with IPC guidelines in healthcare, animal husbandry, fisheries and the food chain, IPC training for healthcare providers, veterinarians and food handlers. - Coordinate with agricultural and environmental health surveillance bodies to assess AMR hazards and risks.	[63]
Philippines	- The Philippine Action Plan to Combat Antimicrobial Resistance-One Health Approach 2015-2020 - Good Animal Husbandry Practices and Good Aquaculture Practices for Animal Health	- Mandated the 'Food Safety Act of 2013' for animal health through obligatory declaration of animal food source and the effects of feeds and other production inputs on otherwise healthy animals - Standardisation of laboratory reference - Data exchange on emerging resistant pathogens - Departments of Agriculture and Health enforce regulations on the production, promotion, commercialisation, prescription, dispensing and use of antimicrobials	[64]

Singapore	- National Strategic Action Plan on AMR 2017	- Implementation of ASPs in all public hospitals - Periodical inspection of food and feed in food establishments - Implementation of quarantine and preferential treatments for farms and livestock keepers - Classification of all antimicrobials as prescribed medication - Legislating the prohibition of antimicrobials use for growth enhancement in Singapore farms	[9,65]
Thailand	- Thailand's National Strategic Plan on AMR 2017-2021	- According to the Animal Feed Quality Control Act, veterinarians may supervise administration of registered medicines - Production, sale and use of medicated feeding items are regulated by the Ministry of Agriculture and Cooperatives - Data sharing with GLASS - Implementation of three-phase plan for reclassification of antimicrobials in human usage: Phase 1 was completed in 2019: Antituberculosis drugs and all antibiotics for injection are now prescription drugs; Phase 2 has been running since 2021: includes all oral antibiotics and affects a broad group of stakeholders such as pharmaceutical companies, pharmacies and patients; Phase 3 starts in 2023: includes antibiotics for topical use and external use. - Establish a national governance mechanism to strengthen intersectoral collaboration under the One Health concept with a policy platform. - Ban the use of antimicrobials as growth promoters in agriculture, promote the appropriate use of medicines and chemicals in aquaculture, including antibiotics. - Develop guidelines for the use of antimicrobials in companion animals through the Thai Network of Veterinary Deans, the Veterinary Council and the University Network of the One Health Approach. - Use social marketing tactics to promote public awareness, launch Thailand's first World Antimicrobial Week in 2020.	[60,66]
Vietnam	- National Action Plan for Combating Drug Resistance 2013-2020	- Establish a national AMR reference laboratory and a stronger national AMU and AMR surveillance system, surveillance system for safe and appropriate AMUs in health facilities, livestock, poultry, aquaculture and cultivation. - Treatment guidelines for health workers and the public and a list of acceptable antimicrobials in livestock, poultry, aquaculture and cultivation. - Establish rules for compliance with treatment guidelines in health facilities and for the use of antimicrobials in livestock, poultry, aquaculture and cultivation. - Investing in production to supply the market with good quality medicines at reasonable prices. - Revise legal documents, policies, national technical regulations and hospital guidelines for human health.	[68]

6. Summary

This review paper highlights gaps in the identifying factors of the AMR issues in Malaysia. Since AMR is recognised globally as an imminent health crisis, many countries, including Malaysia, have taken progressive initiatives to address the issue. The perspectives of health professionals and the public clearly demonstrate that knowledge and awareness concerning AMR and the correct use of antibiotics are imperative in ensuring proper antibiotics-handling and -consumption attitudes and practices, whether in human, agricultural, or aquacultural contexts. With suboptimal actions to tackle AMR, the clinical implications of the spread of pathogenic bacteria are threats to health and even deaths. In line with the WHO aspiration to address AMR, Malaysia has implemented the ASP with ongoing improvements to the program and AMR outcomes [23]. Malaysia is currently finalising the Malaysian Action Plan on Antimicrobial Resistance for 2022 to 2026, which involves the environmental and agricultural sectors and addresses the misuse and overuse of antibiotics in humans or the food industry, such as in poultry, livestock, and aquaculture. This effort is a continuation of Malaysia's first Antibiotic Resistance Action Plan (MyAP-AMR) 2017-2021, which focused more on human health uses of antibiotics [22]. The Malaysian Ministry of Foreign Affairs has also committed to work jointly with the UN member states, the Tripartite Plus (the WHO, FAO, OIE, and UNEP), and other relevant UN agencies to strengthen One Health and multisectoral actions to combat AMR; learn from the COVID-19 pandemic to address the growing threat of AMR; and implement the 2030 Agenda for Sustainable Development [67]. Complementing the government's efforts to confront AMR issues, many organisations, including NGOs, are actively involved in their own AMR initiatives. This concerted action by all parties is imperative to ensure a holistic and effective approach to addressing AMR concerns in Malaysia.

7. Conflicts of interest

None declared.

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