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Review Article

Antibiotic Resistance in WHO Priority Bacteria: South-East Asia's Looming Crisis

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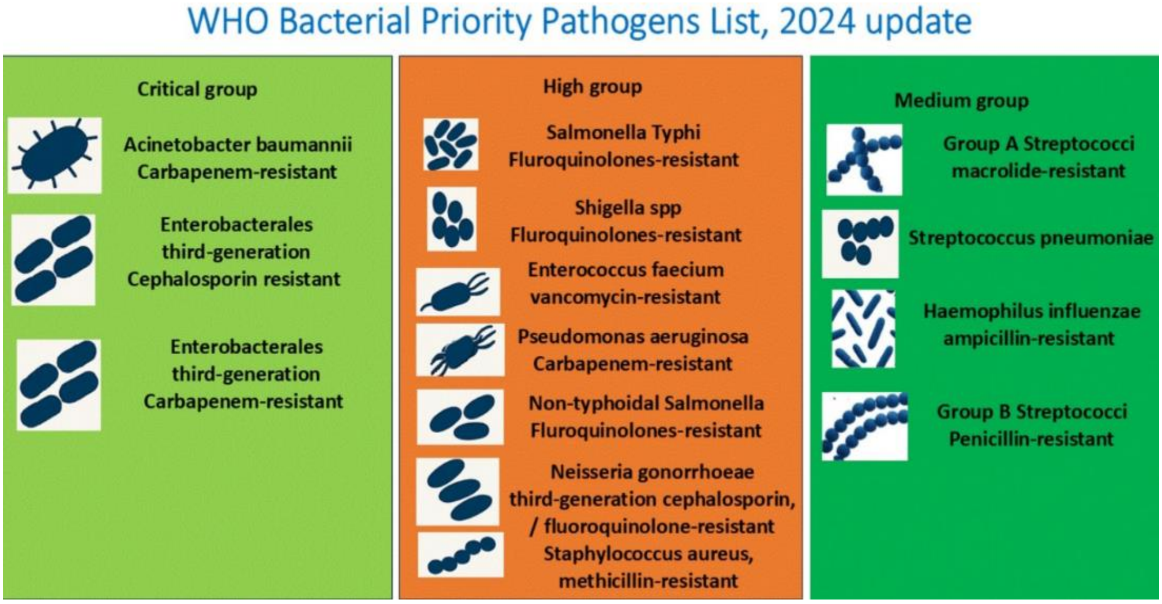

Graphical Abstract

One of the biggest concerns to world health is still antimicrobial resistance (AMR), which disproportionately affects South and Southeast Asian nations. According to latest WHO research, bacterial AMR is projected to be responsible for approximately 5 million fatalities per year by 2025. Self-medication, illogical antibiotic usage, inadequate sanitation, and unregulated antibiotic use in the poultry, aquaculture, and agricultural sectors all contribute to the acceleration of resistance in these areas. Acinetobacter baumannii, Escherichia coli, Klebsiella pneumoniae, and Gram-positive Staphylococcus aureus are among the resistant Gram-negative pathogens that represent a serious threat, according to the World Health Organization's 2024 edition of the Global Priority Pathogens List (GPP). GLASS, the World Health Organization's Global Antimicrobial Resistance and Use Surveillance System has expanded to over 130 countries by 2024, with enhanced modules to monitor antimicrobial use and resistance patterns in real time. Southeast Asia remains a high-risk zone for the appearance and dissemination of multidrug-resistant organisms, including carbapenem-resistant Enterobacteriaceae and colistin-resistant Acinetobacter species, with increasing detection of resistance genes such as blaNDM-5 and mcr variants. This review highlights the evolving resistance trends in South and Southeast Asia, focusing on high-priority pathogens and their mechanisms of resistance—such as efflux pumps, target modification, and enzymatic degradation. The abstract concludes by stressing the importance of coordinated surveillance, antimicrobial stewardship, cross-border collaboration, and One Health strategies to effectively curb the spread of resistance and safeguard future treatment efficacy.

Keywords; Antimicrobial-resistant, Acinetobacter baumannii, Escherichia coli, Klebsiella Pneumoniae, Staphylococcus aureus, South East Asia.

INTRODUCTION

Southeast Asian countries are always under scrutiny for developing novel resistant pathogens(1,2), Lack of education, awareness of hygiene, poverty and Antibiotics used in poultry(3), fisheries(4), Disinfectants use in agriculture and environment (5)and irrational use of Antibiotics and irrelevant combinations of antibiotics (6)particularly in Indian market plays a crucial role in proliferation and development of some most virulent and resistant superbugs, in community as well as nosocomial infections, , it is very obvious that it the WHO In 2024 published(7) list of pathogen under classification of critical, high and moderate pathogen most critical (Table 1) are equipped with the strategy of resistant that is Binding site modification(8), Developing efflux pump(9) and Enzymes to Degrade antibiotics(10,11). There is a need to comply with the guidelines of WHO to use antibiotic. And there is an urgent need to regulate the Market of antibiotics in Asia (12). We are racing against the time and our options are getting reduced from time running by. Antimicrobial resistance is a ticking time bomb that are making our chances of survival narrower. It may lead to up "post antimicrobial era" 1.9 million peoples died annually(13) because of Failure of Antimicrobial chemotherapy(14), Common infection may lead to serious consequences, that are difficult to treat with conventional antibiotics available in the market, that needs to explore novel molecules and other methodologies to combat the infection(15,16), In the current review article, we are discussing the scenario of Asian subcontinent countries, the problem they are facing to cope with multiple drug resistance antimicrobial agents, and the options they are left with, the current available drugs with and novel methods to Counter Superbugs(17,18). Recent studies Shows that resistance to commonly used antibiotics for treating harmful bacteria related to a variety of stomach conditions as more than doubled in 20 years in European countries(19) While overall the risk of both emergence and spread of antibiotic resistance among human is highest in Southeast Asian regions (20) Poor sanitation, low income groups(21), and irrational use of antibiotics ads to the problem many fold in Indian subcontinent including Bangladesh(22), Pakistan and Shri Lanka , environmental factors ,food and probiotics resistance to drugs also responsible for a speeding up and scaling up the process of antimicrobial resistance(23),

WHO Global Priority List Pathogens

In 2024, the World Health Organization (7) (WHO) published a list of global priority pathogens. (24) (GPP) – 12 species of bacteria with critical, high, and medium antibiotic resistance (AR)

Table 1: WHO global priority pathogens list

Priority category	**Pathogens**	**Antibiotic resistance**	**Grams stain**
Critical	Acinetobacter baumannii	Carbapenem-resistant	Gram-negative
	Enterobacterales	Third generation cephalosporin, resistant	Gram-negative
	Enterobacterales	Third generation Carbapenem, resistant	Gram-negative
High	Enterococcus faecium	Vancomycin-resistant	Gram-positive
	Staphylococcus aureus	Methicillin-resistant Vancomycin intermediate and resistant	Gram-positive
	Helicobacter pylori	Clarithromycin-resistant	Gram-negative
	Campylobacter	Fluoroquinolone-resistant	Gram-negative
	Salmonella spp.	Fluoroquinolone-resistant	Gram-negative
	Neisseria gonorrhoeae	Third generation	

		cephalosporin-resistant	Gram-negative
	Pseudomonas aeruginosa	Carbapenem-resistant	Gram-negative
	Shigella spp.	Fluoroquinolone-resistant	Gram negative
Medium -	Streptococcus pneumoniae	Penicillin-non-susceptible	Gram-positive
	Haemophilus influenza	Ampicillin-resistant	Gram-negative

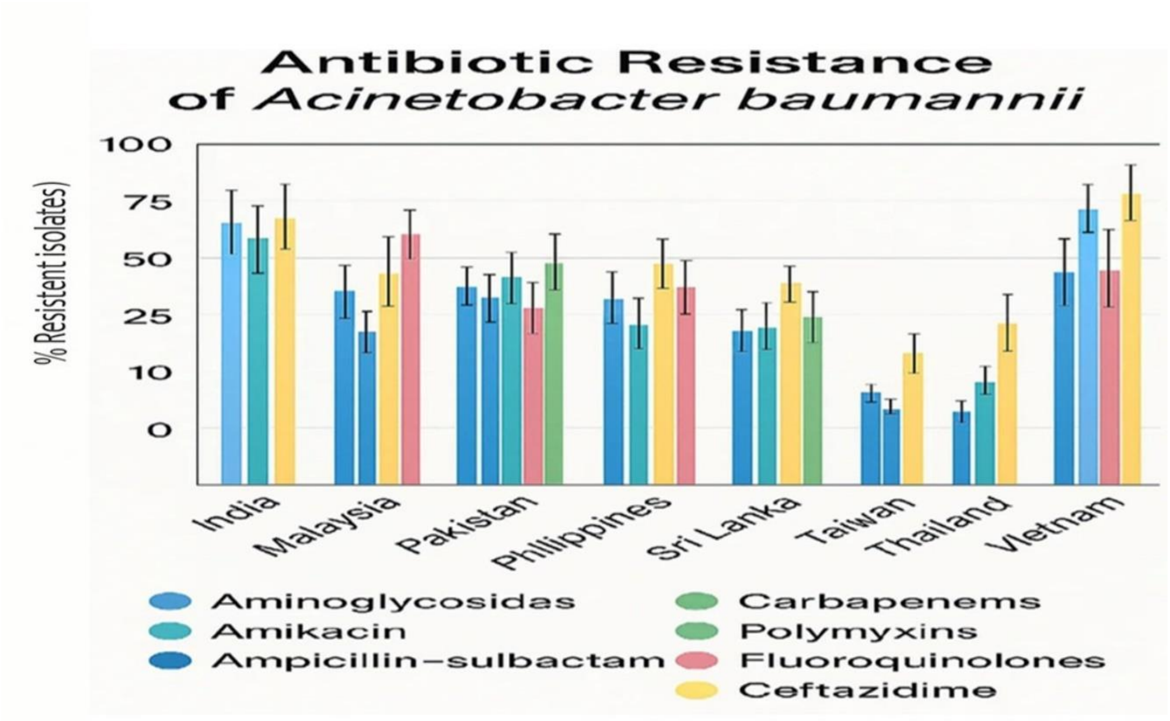

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Figure 1. The graph illustrates antibiotic resistance of *Acinetobacter baumannii* across eight countries in Asia (India, Malaysia, Pakistan, Philippines, Sri Lanka, Taiwan, Thailand, and Vietnam). The y-axis shows the percentage of resistant isolates (% resistant), while the x-axis lists the countries. Each color-coded bar represents resistance to a different antibiotic or antibiotic class.

Acinetobacter baumannii

This bacterium is on priority list of WHO and of various healthcare agency (12). It causes serious infection in lungs, blood, and brain, it also causes urinary tract and sepsis. It is an important opportunistic pathogen that can spread by direct contact and may be found in on the skin or in food, water for soil, it is a and Multiple drug resistant, has emerged as most problematic nosocomial pathogen(25). That maintains with virulence after long time starvation (26) Carbapenems Resistant Acinetobacter species Uses three main mechanisms to resist carbapenems, Production of enzyme carbapenemase (27) that hydrolysed Carbapenems (28). Change the function of membrane associated protein such as porins and activation of drug efflux pump(29) Polymyxin antibiotics are termed as last line of defence, but recently it had been reported that certain strains of *Acinetobacter baumannii* developed resistant against colistin and had been reported in clinical infection sample and faecal survey samples(30) Colistin resistance now increasingly associated with *mcr* gene variants in Asia-Pacific hospitals(31) Immunocompromised individuals are more Likely to be infected with acinetobacter baumannii, A zinc efflux system that are likely to aid environmental persistence and host colonization, A.baumannii poses broad range of zinc efflux system. that helps the bacteria to survive in a toxic level of zinc concentration(32) Certain studies shows that 32 mcg/ ml chlorhexidine is sufficient enough to kill Colony forming unit (CFU) of Multiple drug resistant of strains A. baumannii on inanimate objects(33) (Figure 1). India and Vietnam show the highest levels of resistance across most antibiotics like aminoglycosides with resistance often exceeding 70%. and >50% to Carbapenem(34) and Fluroquinolones(35), Thailand and Taiwan exhibit significantly lower resistance, generally below 30% for most antibiotics

Resistance levels are highly variable between countries, indicating possible differences in antibiotic usage, infection control policies, or diagnostic standards

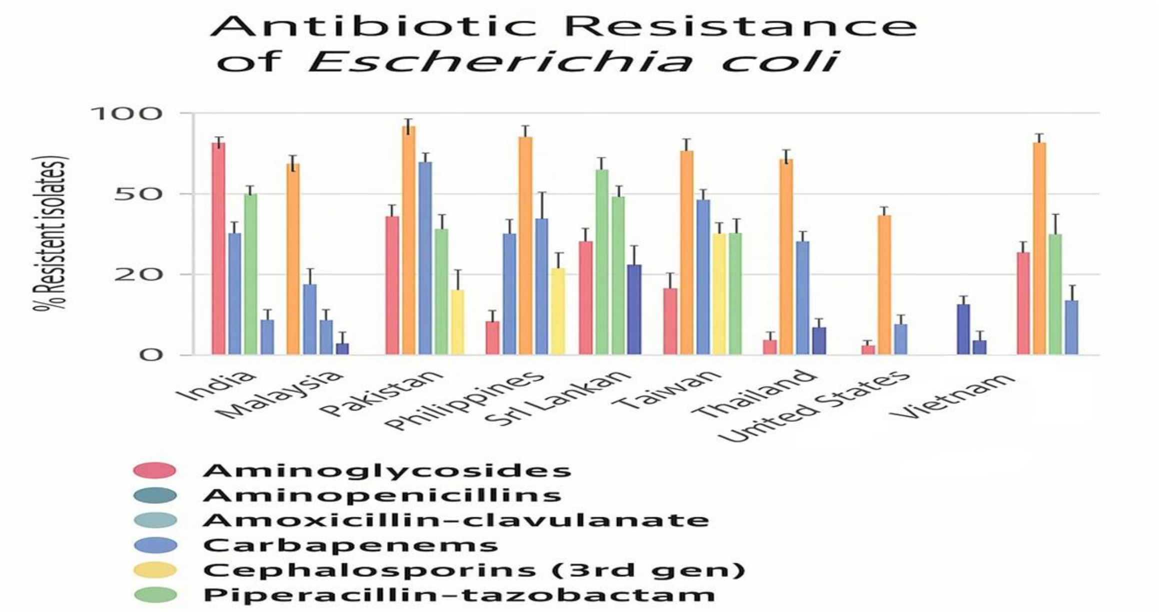

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Figure 2. The graph presents antibiotic resistance of Escherichia coli across ten countries (India, Malaysia, Pakistan, Philippines, Sri Lanka, Taiwan, Thailand, United States, and Vietnam). The y-axis represents the percentage of resistant isolates (%), while the x-axis shows the countries. Different colored bars represent resistance to different antibiotics or classes.

Escherichia coli is the most abundant enteric bacteria present in the gut of humans and some animals(36), It is one of the predominant pathogens of sepsis and septic shock and an important cause of urinary tract infections (UTIs)(37), enteric infections, and systemic infections. The most serious concern with Escherichia coli is its ability to retain resistant genes via horizontal gene exchange (38). E coli emerged as a superbug, with variety of multiple resistance genes, that is extended-spectrum beta-lactamases (ESBL) (39), carbapenemase, aminoglycoside modified enzymes (40) (AME) and Quinolone resistant (41). A single, locally dominant subclone of Escherichia coli ST131 has expanded, leading to a higher prevalence of extended range beta-lactamases across Southeast Asia. Escherichia coli that produces the NDM-1 gene (blaNDM-1) is said to be one of the most important multidrug-resistant bacteria that cause nosocomial infections in hospital and clinic settings.(42) Among most Problematic Multiple drug resistance organism Polymyxin antibiotics are last line of defence and active against Carbapenem-Resistant Enterobacteriaceae CRE(43) South East Asian countries are often been particularly pointed out to be locus of emerging infections without a proper data in support or may be Inability of these country to collect required data(44) (Figure 2). High resistance to aminopenicillins and 3rd gen cephalosporins in South and Southeast Asia indicates widespread antibiotic misuse (45), possibly due to over-the-counter availability and empirical prescriptions. Carbapenems remain largely effective (46), but signs of emerging resistance (especially in India and Pakistan) are concerning. Aminoglycosides and piperacillin-tazobactam show variable resistance, suggesting regional selection pressure and differential clinical usage. Thailand and the U.S. show comparatively effective resistance control, likely due to better antibiotic stewardship and healthcare infrastructure. Highlights the urgency for global and regional AMR (antimicrobial resistance) monitoring, policy reinforcement, and public health interventions

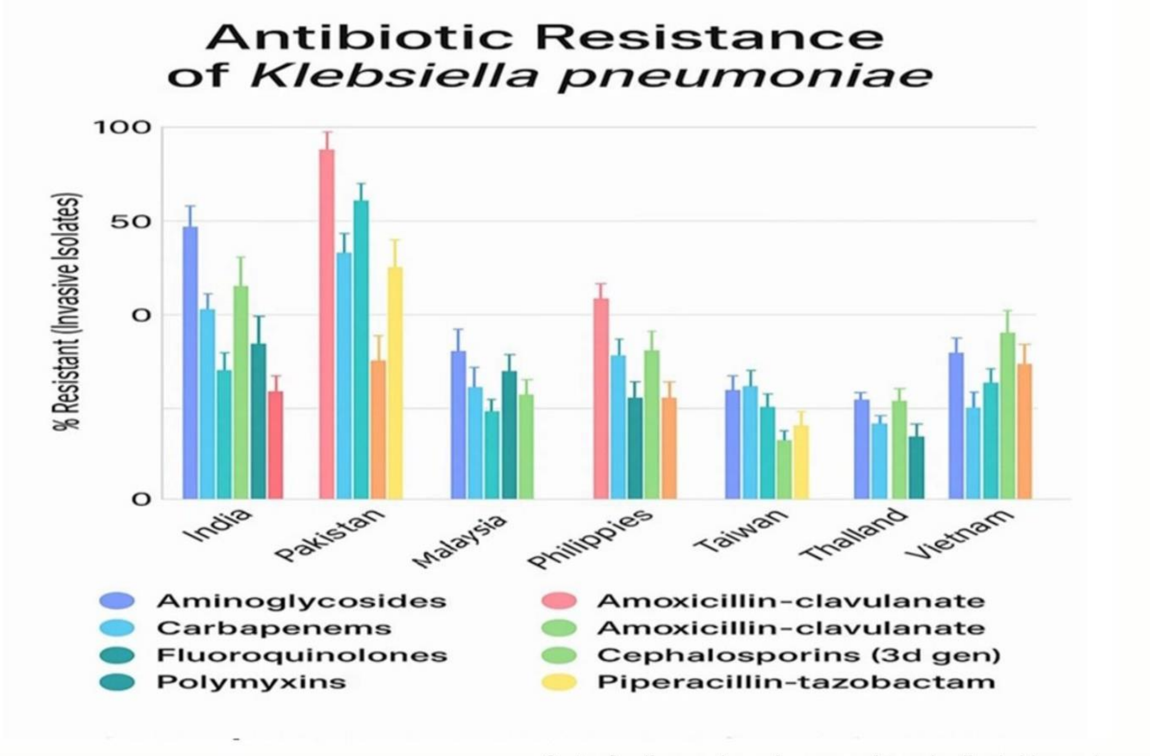

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Figure 3. The graph illustrates the percentage of resistant invasive isolates of Klebsiella pneumoniae to various antibiotic classes across seven Asian countries: India, Pakistan, Malaysia, Philippines, Taiwan, Thailand, and Vietnam.

Klebsiella Pneumoniae considered to be most Invasive and hypervirulent Opportunistic pathogen and is common cause of nosocomial and community acquired bacterial pneumonia infections (47), Urinary tract infection as well as septicaemia and wound infection (48). This bacterium resides in the gut of host while migrating to other parts of the body causes infection. Recently surfaced, leading to hepatic abscesses caused by pyogenic. In chronic alcoholic patients (49). These infections are caused by hypervirulent *K. pneumoniae* (hvKP) isolates. Had been primary reported in south east Asia, In most of the cases of infection found in younger Population in comparison to the old one (50). Hypervirulent strains of Klebsiella pneumoniae, which typically lack genes for antibiotic resistance, are linked to virulence plasmids. On the other hand, nosocomial isolates are rarely linked to virulence plasmids but frequently to resistance...(51) The most unique thing about this bacterium is camouflage that has been acquired during evolutionary mechanism it can escape host immune response and inhibit inflammasome that leads to bacterial dissemination(52) *K. pneumoniae* is resistant to extended spectrum beta lactamase and fluoroquinolones and Carbapenems(20)(53) Low resistance has been reported against Fosfomycin (54) (Figure 3). High carbapenem resistance in countries like Pakistan and India is a public health threat (55), given these are critical antibiotics. Widespread resistance to older drugs (e.g., cephalosporins, amoxicillin-clavulanate) suggests the bacteria have acquired diverse resistance mechanisms. Polymyxin resistance, though generally lower, signals the potential for pan-drug resistant strains. The variation among countries likely reflects differences in antibiotic use, infection control, and healthcare infrastructure (56).

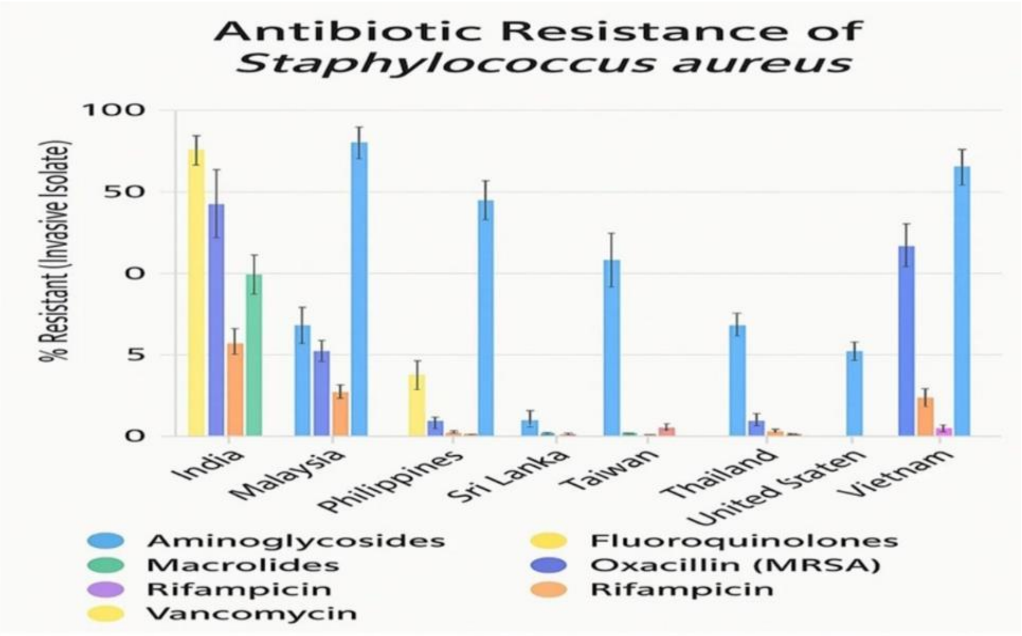

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Figure 4. The graph shows the antibiotic resistance profile of Staphylococcus aureus isolates across eight countries: India, Malaysia, Philippines, Sri Lanka, Taiwan, Thailand, United States, and Vietnam.

The y-axis represents the percentage of invasive isolates resistant to specific antibiotics or antibiotic classes

Staphylococcus aureus

MARS stands for methicillin-resistant Staphylococcus aureus. Lives commensal (57), the primary cause of soft tissue infections, systemic infection of blood (58), osteomyelitis, and endocarditis. MRSA has acquired MGEs with antibiotic resistance genes on various distinct occasions. Erythromycin (ermC) (59, 60), clindamycin (constitutively expressed ermC), penicillin (blaZ) (61), trimethoprim (dfrA and dfrK), and tetracyclines (tetK and tetL) resistance, trimethoprim (dfrA and dfrK), have all been identified (62). *Staphylococcus aureus* capsular polysaccharide is considered to be an important virulence factor under evaluation as vaccine antigen. Studies have identified many genes and pathway involved in production of *S aureus* capsule but the mechanism by which they regulate the production of capsule during infection remains a mystery,(63) Multidrug efflux pump is behind a major cause of multidrug-resistant. The multidrug efflux pump system embedded in biological membrane of the bacteria and actively removes antimicrobial agents from bacterial cell (64) Methicillin is an antibiotic that is no longer used clinically nowadays MRSA is resistant to antibiotics within same class Such as cephalosporins and carbapenems. Resistance is not due to the production of Beta lactamase enzyme but rather to the production of modified penicillin binding protein coded on the mecA gene.(65) Most of the staphylococcus aureus Infection reported worldwide one- half are reported only in Asian countries(66) (figure 4). High MRSA Prevalence: Countries like the Philippines, India, and Vietnam show very high oxacillin resistance (67), indicating widespread MRSA strains. MRSA prevalence is a major concern due to limited treatment options. Vancomycin resistance is consistently low across all countries. This reflects its role as a last-resort treatment for MRSA and its limited use, helping maintain its efficacy. Increasing resistance to fluoroquinolones and aminoglycosides in countries like India and Vietnam is troubling. Resistance to rifampicin is relatively low but rising in certain areas. Better Resistance Profiles in Developed Regions: United States and Taiwan show lower resistance across all categories, likely due to better antibiotic regulation and healthcare infrastructure

WHO's 2024 Updates on Antimicrobial Resistance Surveillance and Stewardship: GLASS Expansion and Global Policy Development?

Worldwide Antimicrobial Resistance and Use Surveillance System (GLASS) expansion to improve global monitoring of antimicrobial resistance (AMR) and antimicrobial usage (AMU) (68), the World Health Organization (WHO) has greatly extended the Global Antimicrobial Resistance and usage Surveillance System (GLASS). 135 nations, territories, and regions have agreed to contribute data to GLASS on AMR as of December 2023.and/or AMU. In 2024, 130 countries were enrolled in GLASS, with 104 countries submitting national AMR data and 74 countries submitting AMU data at least once between 2021 and 2023.

GLASS now encompasses several modules, including:

Routine surveillance on AMR in common bacterial and fungal pathogens.

Periodic nationally representative surveys to estimate the prevalence and burden of AMR.

Surveillance of AMU in community and hospital settings

In September 2024, WHO launched an updated GLASS data visualization dashboard (69,70), providing interactive visualizations of AMR and AMU data from participating countries? The dashboard summarizes resistance rates for 23 antibiotics across 11 antibacterial classes for 8 bacterial pathogens commonly isolated from patients with bloodstream, gastrointestinal, urinary, or genital infections.

Global Reports on Antimicrobial Stewardship

WHO continues to guide countries in developing and Establishing Antimicrobial Stewardship Programs (ASPs), which are one of the most economical ways to maximize the use of antibiotics, enhance patient outcomes, and lower AMR and infections linked to healthcare.

The WHO's updated list of medically important antimicrobials (MIA List) for human medicine was released in 2024. In order to minimize the effect of antimicrobial usage in non-human sectors on AMR in humans, this list functions as a risk management tool to assist in decision-making. The MIA List offers recommendations on the proper use of necessary antibiotics in the human health sector, supplementing the WHO AWaRe (Access, Watch, and Reserve) framework and antibiotic book. Furthermore, Global leaders agreed on a number of goals and initiatives one of which was to reduce the anticipated 4.95 million human deaths from bacterial AMR by 10% by 2030, during the 79th United Nations General Assembly High-Level Meeting on AMR in September 2024. In order to help reach the goal of at least 60% of nations having funded national action plans on AMR by 2030, the declaration also calls for sustainable national financing and US~$100 million in catalytic investment.

These developments underscore the global commitment to enhancing AMR (71) surveillance and stewardship (72), providing a robust framework for countries to monitor and combat antimicrobial resistance effectively.

CONCLUSION

Antimicrobial resistance (AMR) continues to escalate as a global health emergency, especially in South and Southeast Asia, where weak regulatory frameworks, The proliferation of resistant organisms is made worse by the overuse of antibiotics and international migration of people and economic activity. As emphasized in the original conclusion, addressing AMR demands collective responsibility at local, regional, and international levels.

In 2024–2025, the World Health Organization made substantial advancements by expanding the Global Antimicrobial Resistance and Use Surveillance System (GLASS) to 130+ countries and updating the Bacterial Priority Pathogens List (BPPL). These initiatives have provided more accurate data to drive policy and clinical interventions. Furthermore, the 2024 UN General Assembly set global targets to minimize AMR-associated mortality by 10% by 2030 and emphasized national action plans with sustainable funding.

To effectively combat AMR, urgent steps are required:

- **Stricter regulation** of antibiotic distribution in human and veterinary sectors.
- **Enhancement of antimicrobial stewardship programs** in both community and hospital settings.
- **Surveillance integration** using platforms like GLASS to monitor resistance trends and antibiotic use.
- **Cross-sector collaboration**, particularly by using the One Health approach, which recognizes the interdependencies of human health, animal health, and the environment.

AMR does not recognize borders; therefore, coordination among nations is not optional but essential. Countries in Asia must align their strategies to share surveillance data, harmonize policy frameworks, and invest in public awareness campaigns, diagnostic capacities, and the development of novel antimicrobials. Without decisive action, the world risks entering a time beyond antibiotics, when common diseases can no longer be treated

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