

Drug-Resistant Sexually Transmitted Infections in Southeast Asia: Regional Challenges to Control

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Abstract

Antibiotic resistance is one of the main challenges of the new century, which has limited the use and effectiveness of many first-line antibiotics. The excessive and irrational use of antibiotics has assisted the microbes to modify their genes and metabolic activities, thereby developing resistance. Addressing the situation in developing countries in the Southeast Asia region, poor hygiene, lack of sanitation, and inequalities in treatment access have further increased the infectious disease burden. In over a decade, the high prevalence rate of infections and resistance to antibacterials has appeared to be a big challenge. In addition, poor compliance with antibacterial use protocols and excessive use of antibacterials has minimized the therapeutic effectiveness of these drugs. A huge challenge in the Southeast Asian setting is the resistance among a majority of bacteria responsible for sexually transmitted diseases, which are still largely unknown. It is the paramount responsibility of local health authorities to effectively conserve the efficacy of existing antibacterials while decreasing the emergence and transmission of resistance.

Keywords: antibacterial, antibiotics, drug utilization, prescribing, resistance

BACKGROUND

A substantial number of scientific evidence have depicted the increasing importance of antibacterial agents in modern medical practice. Deadly infections back in the old days, such as tuberculosis and diphtheria that were once considered as tickets to death, have long been curable with the use of antibacterials. It is argued that antimicrobials have reduced not only the morbidity but also the mortality associated with these infectious diseases.^[1] A paradigm shift has been observed in these medical manuscripts during the last quarter of the 20th century when more researchers began to show their concerns toward the effectiveness of these antibacterial agents. By the late 1970s, the researchers started to conclude that, eventually, all antibacterials will no longer be effective against bacterial infections; the primary reason has been attributed to the rising trend in antibacterial resistance.^[2] Even more worrisome, the development pipeline of new antibacterial agents with multiple selective molecular targets poses a big challenge owing to the innate property of microbes to acquire resistance faster than the development of new drugs. The discovery of a novel antibacterial has been unsuccessful despite more than 300 potential antibacterial targets being discovered through genomic approaches since the 1990s.^[3] India and Pakistan, for instance, are facing a massive antibacterial resistance as a result of carbapenems overuse.^[2,4] Most recently, resistance to one of the last-resort antibacterials, colistin, has been identified in China and

Malaysia.^[5] This decade-long drug has been excessively used in swine production to stimulate growth. The plasmid-mediated resistance against colistin that was first noted in *Escherichia coli* has now transmitted to other species, in particular, *Klebsiella* and *Pseudomonas* spp.^[6]

CHALLENGES AND ACTIONS TAKEN

For the past three decades, countries such as Thailand, Indonesia, and Malaysia have taken the initiative to study local antibacterial resistance, joining the international solidarity in the fight against antibacterial resistance, especially through the genomic profiling of the common

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bacteria that cause antibacterial resistance^[7-11] as well as the types and distribution pattern of antibacterial resistance.^[12]

To gather further baseline data on the antibacterial resistance pattern, the Ministry of Health (MOH) in Malaysia has started a program since 2003 with the aim of investigating the resistance pattern of bacteria against the commonly prescribed antibacterials. The pattern of resistance is obtained every year for each bacterium against the same antibacterials that were tested in preceding years.^[13,14] MOH Malaysia has published its first antibacterial therapeutic guideline in 2008 and subsequently a revision in 2014. The comprehensive antibacterial guideline served to rationalize and align the clinical practice with the recent evidence-based literature, thus assisting in reducing the irrational use of antibacterials and controlling the number of antibacterials prescribed in order to reduce the chance of resistance.^[15] Contrary to the hospital setting, the number of physicians over-prescribing antibacterial in the community setting is significantly high in Malaysia. Knowing well that underprescribing or overprescribing antibacterials may ultimately increase bacterial resistance, physicians' practices in the private hospitals and clinics are not consistent with the national antibiotic guideline. In continuity with antibacterial resistance, another entity is end-users that are also contributing to the problem knowingly or unknowingly. It must be emphasized that antibacterial utilization study or audit that are conducted at private institutions is less reported. At any given time, it can be noted that at least two-thirds of Malaysians have taken antibacterial over preceded 1 year.^[16] Following non-compliance and less knowledge regarding antibacterials and their safe disposal, this population significantly contributes to increasing in resistance against antibacterials in Malaysia.^[14]

Like any other Western countries where homosexuality or similar gender sexual behaviors are a social taboo, now the Asian countries slowly come to realize that sexually transmitted disease (STI) through anal intercourse needs to be tackled. The main menace is apparently the spread of HIV-1 from unprotected anal or oral sexual contacts especially among men who have sex with men (MSM). It is a worrying sign because the phylodynamic profiles of HIV-1 subtype B and CRF01_AE circulating among the MSM population in the capital city of Malaysia have indicated that active spread of multiple subepidemic monophyletic transmission clusters could happen since 1995.^[17] Likewise, the same dire condition was observed in Thailand where an overall HIV-transmitted drug resistance of 9.2% was reported.^[18]

Meanwhile, HIV that is spread through the sexual contact of HIV carriers that have been infected by contaminated blood was also monitored. Li et al. reported that the majority of the subtype B strains belong to Thailand B lineage confirming that the former blood donor or receiver with HIV had transmitted the virus via unprotected sexual relationship.^[19] Surprisingly, there is no literature about STI among some Southeast Asian countries. The most recent Indonesian study was reported in 2006 in which it was reported that the prevalence of gonorrhea infection rate was 35% among participating female sex workers in Bali, Indonesia, and

40.1% of the *Neisseria gonorrhoeae* isolated from these prostitutes were resistant to fluoroquinolone. It is really alarming considering that fluoroquinolone was first introduced to the Indonesia market just 10 years before that.^[20] It should be highlighted that the current surveillance mechanism largely focuses on high-risk populations. This may then result in the underestimation of the true prevalence of STIs.

THE UNEXPLORED GAP OF DRUG-RESISTANT SEXUALLY TRANSMITTED DISEASES

Considering the attitude of patients, the symptoms of any ailment such as angina and hypertension can determine whether or not to consult a physician. The attitude of the patient is more concerned with consulting a physician to ensure a better health-related quality of life when talking about infections because they have more prevalent symptoms such as fever or body ache. However, such a scenario is not observed when it comes to STIs. Psychological factors and the asymptomatic phase of infection appear to contribute to a higher carrier population for any given sexual infection. The situation in Malaysia is even worrisome and Malaysian youth may experience more of this problem in particular.^[21]

Countries in Southeast Asia region have legally restricted homosexuality and transsexuality; similarly, pre-marital or extra-marital sexual behaviors are socially and religiously culpable.^[22] For example, Lee et al., when focusing on Young Risk Surveillance Behavior, excluded the items that correspond to the sexual behavior of youth as stated: "modified to suit the local context."^[23] Although the Malaysian Ministry of Health provided guidelines to treat STIs, currently there is no record on the prevalent bacterial STIs in the society.^[24] Moreover, the National Surveillance of Antibacterial Resistance of Malaysia provides the resistance pattern of the common bacterial infections and resistance against specific antibacterials; the resistance among the majority of bacteria responsible for STIs is still unknown. According to the Malaysian STI clinical practice guideline: "the exact size of the problem is unknown, which is partly due to underreporting, underdiagnosis, and asymptomatic manifestations of the disease," yet there is no evidence to epitomize the magnitude of this problem.^[15] According to the infection pattern in 1994, slightly more than one-third of episodes were secondary to the species that may somehow be related to STI, for example, *Klebsiella*, *Acinetobacter*, *Pseudomonas*, and *Neisseria* spp. However, the report does not mention the type of infections associated with these microbes. It is worrisome that if one wants to compare the baseline antibacterial resistance findings of the aforementioned bacterial isolates with the resistance pattern of 2014, it is surprising to know that either these agents were not tested or reported for resistance.^[15] Practices of physicians to treat an STI depict mixed results and are somewhat considered inconsistent with national STI guidelines.^[25] Of the second

notion, utilizing available data from Malaysia that encompass antibacterial resistance and STI, it can easily be hypothesized that antibacterial resistance in the most prevalent Malaysian STI, that is, *N. gonorrhoea*, is increasing because it is not treated according to guidelines or vice versa.^[25]

To curb the spread of STI and antibacterial resistance, there shall be interventions from MOH, health care professionals in public and private sectors as well as non-governmental bodies to address this problem via two approaches: general approach, the awareness of transmittable infectious diseases, and specific approach, the strict and accountable control of antibacterials for their use in hospital and community levels. In this context, much progress has been made in the provision of such services by non-governmental organizations such as the pink triangle foundation^[26] and the Federation of Reproductive Health Associations of Malaysia.^[27] These community-based organizations actively provide sexual health and empowerment education, counseling, and support programs for vulnerable communities such as drug users, sex workers, transsexuals, and people living with human immunodeficiency virus/acquired immune deficiency syndrome.

In Western countries, the STI clinic that offers screening, education, and treatment for chlamydia, gonorrhoea, HIV, or other types of STI has been proven effective in the containment of STI as well as unplanned pregnancy. For example, community pharmacists and general practitioners in the UK, Amsterdam, or the US could undergo a short course to be a certified provider of STI treatment, which includes screening and counseling too. Meanwhile, condom and emergency contraceptive pills are subsidized and could also be obtained from the STI clinics or pharmacies. However, it is foreseen that it takes a radical paradigm shift for the community in Southeast Asia to embrace the implementation of the STI clinic. The main critics would include easy access to this service that could promote pre-marital sex or promiscuity.

COMMENT

On the basis of the spread of STIs in several Southeast Asian countries, on one hand, the younger generation is getting more liberal toward their lives, and on the other hand, the fear of getting condemned socially, on religious or cultural grounds make them avoid any medical checkup. It is the responsibility of health authorities to close the gap of cultural acceptance on STI treatment. Meanwhile, another challenge in the Southeast Asian setting is the antimicrobial resistance responsible for STIs. The efficacy of the existing antibacterials needs to be conserved while decreasing the emergence and transmission of resistance.

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Conflicts of interest

There are no conflicts of interest.

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