

Prevalence of Multidrug-Resistant *Salmonella* spp. in Asia: A Mini-Review

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ABSTRACT

Salmonella is a known causative agent for food poisoning across the world with thousands of cases reported annually. The surging multidrug-resistant *Salmonella* was also evident throughout the decade, worsening the situation and making it an even more crucial public health burden. This paper aims to raise public health awareness on the rapid progression of *Salmonella* infection resulting from proliferating antimicrobial resistance in different Asian regions. A total of 50 articles extracted from Google Scholar, PubMed, NCBI, and ScienceDirect were included in this review. The prevalent *Salmonella* serotype and antibiotic that most isolates have built resistance to were identified per Asian region. Overall, *Salmonella* Typhi is identified as the most isolated typhoidal *Salmonella* strain while *Salmonella* Typhimurium is the prevalent NTS strain in Asia. Tetracycline is revealed to have the highest percentage of resistance among all isolated *Salmonella* spp. in conducted Asian studies. Alarming tetracycline resistance was observed in 11 out of 38 countries incorporated in this mini-review, this is due to chromosomal mutation and ribosomal binding site mutation. Most *Salmonella* isolates have inherited genetic elements with tetracycline-specific resistant genes, increasing the intrinsic mechanism for antimicrobial resistance. Following tetracycline, significant resistance against nalidixic acid and ampicillin was also observed. Thus, it is highly suggested for public health officials focus on improving the sanitary conditions in food production and processing together with water management safety to address the problem with *Salmonella*.

Keywords: Asia, Antibiotics, Multidrug-Resistant, Non-typhoidal, *Salmonella*, Typhoidal.

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INTRODUCTION

Salmonella spp., reported to have over 1 800 serovars, are facultatively anaerobic Gram-negative bacilli characterized by its definitive antigens: Vi, O, and H. It is one of the most common causative agents of microbiological food poisoning in all nations.^[1] *Salmonella* has long been recognized as a serious infection that can affect both humans and animals. As it is considered a true pathogen, ingestion of food or water containing even a trace amount of *Salmonella* colonies can immediately

result in a life-threatening infection. Isolates of this pathogenic bacteria are often obtained in most food products, including meat, seafood, eggs, vegetables, fruits, and even processed foods.^[2]

In general, the disease caused by *Salmonella* is referred to as Salmonellosis, which classified into non-typhoidal, and typhoidal depending on the serovars that caused the infection. Symptoms of Salmonellosis include upset stomach, diarrhea, fever, as well as discomfort, and cramping in the abdomen.^[3]

The inappropriate administration of antibiotics is a prevailing problem in the medical field because it contributes to the emergence of resistant strains of pathogenic bacteria. Multidrug-Resistant (MDR) *Salmonella* is designated as a 'Serious Threat Level Pathogen' by the Centers for Disease Control as it causes severe diseases and is much more unresponsive

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during treatment.^[4] In the 2019 AR Threats Reports, 4,100 cases and 212,500 cases of infection caused by MDR typhoidal and non-typhoidal strains of *Salmonella* were reported, respectively.^[5]

Since *Salmonella* spp. can be easily transmitted through ingestion, and the current numbers are expected to further increase as years go by. The objective of this mini-review is to introduce a scientific overview that assesses the prevalence of multidrug-resistant *Salmonella* spp. in Asian countries. It aims to provide public health awareness on the worsening severity of *Salmonella* infection due to increasing antibiotic resistance and to compare its state within the different regions of Asia.

MATERIALS AND METHODS

Literature Search

The literature search was conducted in four online databases: Google Scholar, PubMed, NCBI, and ScienceDirect. Articles included in the review are published from the year 2012 up to the present year 2022. The keywords used for article collection are combinations of “*Salmonella*”, “Multidrug-Resistant”, “Salmonellosis” and “Asia”.

The following are the inclusion criteria in this mini-review: [1] published articles written or translated in the English language, [2] articles with reported *Salmonella* infection in Asia, [3] published articles with *Salmonella* infection reported as either typhoidal or non-typhoidal, [4] published articles about *Salmonella* cases reported as a multidrug-resistant strain. The exclusions in this review are the following: [1] published articles that are not written nor translated in the English language, [2] published articles about *Salmonella* infection outside Asia, [3] published articles with reported cases of *Salmonella* that are not identified as multidrug-resistant strain, [4] published articles without detailed methods mentioned.

Eligibility Criteria

This study is limited to published data regarding the prevalence of Multidrug-Resistant *Salmonella* reported in countries of different Asian regions: Central Asia, East Asia, South Asia, Southeast Asia, and Western Asia.

Articles and journals included in this literature review were strictly written or translated into the English language and were published from 2012 to 2022; research studies published before the aforementioned year were excluded. Reported cases of Typhoidal and Non-typhoidal *Salmonella* infection caused by multidrug-resistant strains with specified methods mentioned were

preferred. *Salmonella* infections that were not directly specified as a multidrug-resistant variant were not accepted.

RESULTS

The increasing resistance of *Salmonella* spp. causing both typhoidal and non-typhoidal infections to display evident growth throughout the past decade, countries from the Asian region are suffering from MDR strains of *Salmonella* due to unsanitary conditions in the food-handling procedure and production combined with unsafe food practice and lifestyle.

Central Asia

In Central Asia, *Salmonella* isolates were mostly obtained from human samples. *S. Enteritidis* is reported to be the most non-typhoidal *Salmonella* in Kazakhstan while *S. Typhi* is the most prevalent typhoidal *Salmonella* serovar in Uzbekistan. Figure 1 shows that the isolated *Salmonella* serovar *S. Enteritidis* was most frequently resistant to ciprofloxacin (47.6%), nalidixic acid (42.9%), and enrofloxacin (35.3%) in Kazakhstan.^[6] The *S. Typhi* isolated from Uzbekistan is reported to be the most resistant to nalidixic acid (80%), followed by ampicillin (19%), chloramphenicol, and trimethoprim-sulfamethoxazole (14%), and only 13% of *S. Typhi* isolates from Uzbekistan were multidrug.^[7] This summarizes that most of the isolated *Salmonella* serovar in Central Asia were revealed to be resistant to nalidixic acid.

East Asia

Reported cases of non-typhoidal infection were greater than typhoidal infection in East Asia. Only China contains records for infection caused by *S. Typhi*.^[8] Typhoid fever remains a public health burden in highly populated countries like China as it is obtained through serovars exclusively transmitted in a human host, unlike its counterpart that has a wide range of hosts and possible modes of transmission.^[9] Non-Typhi *Salmonella* serovars were the focal point of studies from Hongkong, Japan, South Korea, and Taiwan. The serovars investigated in East Asia were summarized in Figure 2. Although no serotype prevailed as the main NTS strain in East Asia, several were consistently mentioned; namely, *S. Enteritidis* and *S. Typhimurium*. Most research studies from this Asian region were obtained through ingestion of *Salmonella* isolates from farm animals such as cattle, pigs, and chickens, which explains the high frequency of NTS serovars.

Among all five countries, China also houses the *Salmonella* isolates resistant to the most antimicrobial

agents. *Salmonella* spp. from all five countries showed high resistance against tetracycline and ampicillin. Specifically, most *Salmonella* spp. from East Asia have built resistance from is tetracycline.

Salmonella isolated from China were resistant to tetracycline (97.7%), ampicillin (97.7%), and sulfamethoxazole (100%).^[10] MDR *S. Typhimurium* from Hong Kong was recorded to be 36.2%, with the most building resistance against ampicillin (30.5%), ciprofloxacin I (42%), and nalidixic acid (56%). Although most outbreaks were due to the *S. Enteritidis* strain, *S. Typhimurium* is of equal burden in Hongkong as it is significantly more resistant.^[11] Almost half of the isolates (48.9%) in Japan were revealed to be multidrug-resistant while the remaining (98%) were resistant to at least one antibiotic, with most isolates being resistant to streptomycin-tetracycline.^[12] In South Korea, 27% of the isolates were revealed to be resistant to five to sixteen antibiotics, with nalidixic acid (59.4%), tetracycline (49.3%), and ampicillin (45%) as the most significant ones.^[13-14] Most MDR strains of *Salmonella* from Taiwan were resistant to ampicillin (94%), tetracycline (92%), and chloramphenicol (85%).^[15] General resistance against ceftazidime, cefotaxime, ceftiofur, kanamycin, streptomycin, and trimethoprim was also observed among *Salmonella* isolates from East Asia.

South Asia

In South Asia, Typhoid fever is the most prevalent bacterial bloodstream infection. *Salmonella* serovars *Typhi* and *Paratyphi* A are responsible for their transmission. Despite success in several regions of the world in managing enteric fever, it continues to be a significant public health burden in South Asia.^[16] India was also revealed to have the most MDR *S. Typhi* among the four countries the serovar was also evidently prevalent over *S. Paratyphi*.^[17]

Figure 3 shows the antimicrobial resistance property displayed by the isolated *Salmonella* serovars in South Asia. In Bangladesh, isolates were found to be resistant to erythromycin and tetracycline in 81.82% and 80% of cases, respectively. Furthermore, *Salmonella* spp. isolated from the environment exhibited moderate resistance to both amoxicillin and azithromycin.^[18] In the country of Nepal, high antibiotic resistance was evident among *Salmonella* resulting in a nalidixic acid (71.2%), ciprofloxacin (68%), and cotrimoxazole (28%). *Salmonella* in blood samples was shown to be the most resistant to nalidixic acid (71.2%).^[19] Isolates from Pakistan, *S. Typhi* was found to be highly resistant to tetracycline (70.11%), ampicillin (38.79%), and trimethoprim (33.45%).

While serovar *S. Paratyphi* A was resistant to trimethoprim (47.19%) Oxytetracycline (25.84%), and cefuroxime (19.10%). *S. Paratyphi* B has almost identical antibiotic resistance patterns as *S. Paratyphi* A against the drugs examined.^[20] In South India isolates, all *S. Paratyphi* are resistant to nalidixic acid, ampicillin, chloramphenicol, ciprofloxacin, and trimethoprim-sulfamethoxazole and none in *S. Paratyphi* were discovered in the MDR isolates.^[17]

Southeast Asia

In Southeast Asia, it is evident that non-typhoidal serovars are more prevalent than typhoidal serovars. Among the data collected, the only country in Southeast Asia that investigated Typhoidal *Salmonella* is Indonesia, which included *S. Paratyphi* C serovar accounting for 10% of the isolates.^[21] In most studies in this region, *Salmonella* isolates were collected from raw products in retail markets, such as chicken meat which acts as a reservoir for harboring MDR *Salmonella*.^[22] The most predominant *Salmonella* serovar among the countries in this region is *S. Typhimurium* followed by *S. Weltevreden*.

Most *Salmonella* spp. isolates in the Southeast Asian region have built resistance to tetracycline and ampicillin Figure 4 summarizes the findings regarding antimicrobial resistance in each Southeast Asian country. Ten isolates (50%) in Indonesia are considered multi-drug resistant in which most of the isolates showed resistance to erythromycin (75%).^[21] In Malaysia, *S. Typhimurium* and *S. Enteritidis* displayed resistance to at least three antibiotics, with all isolates (100%) being resistant to erythromycin, penicillin, and vancomycin.^[22] For Myanmar, 72 isolates (52.2%) are considered multidrug-resistant. It exhibits resistance to trimethoprim-sulfamethoxazole (70.3%), followed by tetracycline with 54.3%, and streptomycin with 49.3%.^[23] In the Philippines, 67.8% are considered multi-drug resistant. All isolates (100%) are resistant to cefazolin, amikacin, gentamicin, and tobramycin.^[24] For Singapore, 80.8% of isolates were resistant to at least one of the antimicrobial agents while 59.6% are considered multidrug-resistant isolates exhibiting resistance to ampicillin (78.7%), chloramphenicol (61.5%), and tetracycline (61.5%).^[25] In Thailand, 92% are considered multi-drug resistant. All isolates in Thailand are resistant to sulfamethoxazole (100%), followed by spectinomycin (88%) and tetracyclines (84%).^[26] In Laos, 100% are considered multi-drug resistant. All isolates are highly resistant to tetracyclines and sulfamethoxazole, followed by streptomycin (87.5%) and spectinomycin (81.3%).^[26] In Vietnam, 66.85% of isolates show

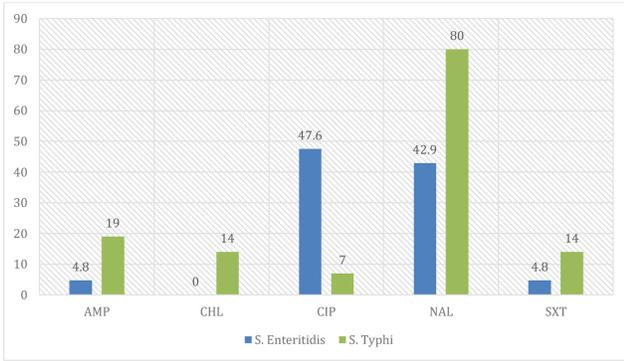


Figure 1: Antimicrobial resistance (% of resistant) of most *Salmonella* isolates in Central Asia.

Legend: AMP - ampicillin; CHL - chloramphenicol; CIP - ciprofloxacin; NAL - nalidixic acid; SXT - trimethoprim-sulfamethoxazole.
References: (Rychshanova *et al.*, 2021),^[6] (Rahman *et al.*, 2014)^[7]

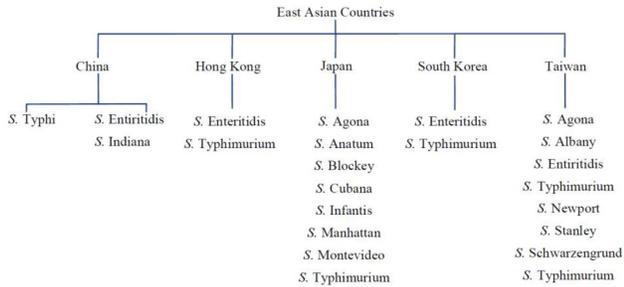


Figure 2: Identified serovars of *Salmonella* isolated from East Asia.

References: (Yan *et al.* 2016),^[8] (Lu *et al.* 2014),^[10] (Cha *et al.* 2016),^[13] (Kuo *et al.* 2014),^[15] (Woh *et al.* 2022),^[44] (Mori *et al.* 2017)^[51]

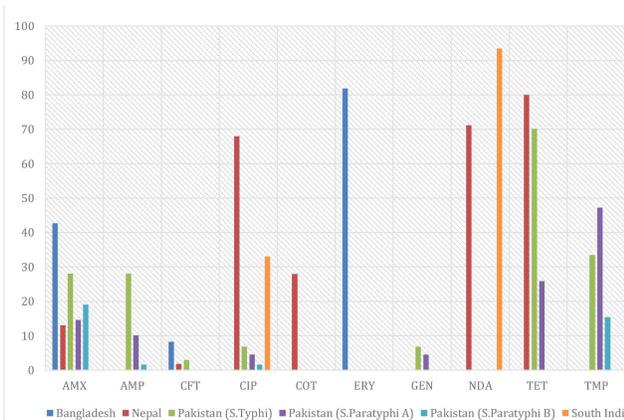


Figure 3: Antimicrobial resistance (% of resistant) of most *Salmonella* isolates in South Asia.

Legend: AMX - amoxicillin; AMP - ampicillin; CFT - cefoxitin; CIP - ciprofloxacin; COT - cotrimoxazole; ERY - erythromycin; GEN - gentamicin; NDA - nalidixic acid; TET - tetracycline; TMP - trimethoprim.
References: (Mridha *et al.*, 2020),^[18] (Bastola *et al.*, 2019),^[19] (Qamar *et al.*, 2020),^[20] (Bandyopadhyay *et al.*, 2018)^[17]

resistance to two-nine antibiotics, with isolates showing resistance to ampicillin (54.14%), tetracycline (55.80%), and chloramphenicol (62.98%).^[27]

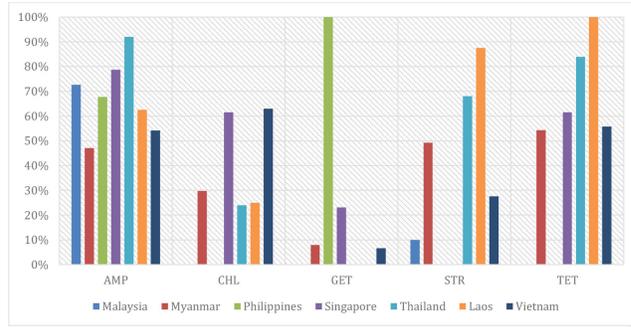


Figure 4: Antimicrobial resistance (% of resistant) of most *Salmonella* isolates in Southeast Asia.

Legend: AMP - ampicillin; CHL - chloramphenicol; GET - gentamicin; STR - streptomycin; TET - tetracycline.
References: (Kusumaningrum *et al.*, 2012),^[21] (Thung *et al.*, 2016),^[22] (Moe *et al.*, 2017),^[23] (Calayag *et al.*, 2017),^[24] (Zwe *et al.*, 2018),^[25] (Sinwat *et al.*, 2016),^[26] (Sinwat *et al.*, 2016),^[26] (Nguyen *et al.*, 2021)^[27]

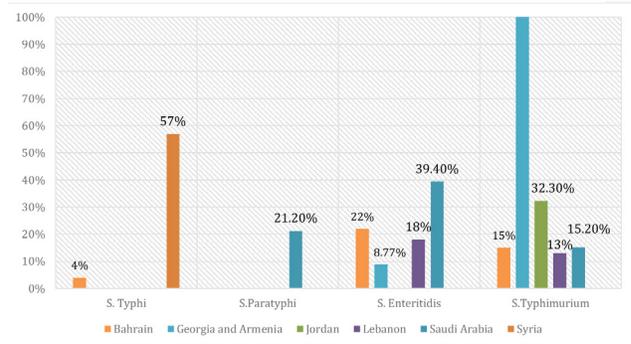


Figure 5: Isolated *Salmonella* serovars from West Asian countries.

References: (Sedrakyan *et al.*, 2020),^[28] (Khamis *et al.*, 2019),^[30] 34 Burjaq *et al.*, 2020)^[34], Malaeb *et al.*, 2016,^[36] El-Tayeb *et al.*, 2017,^[40] Al-Khafaji *et al.*, 2022^[41]

West Asia

Food and water contamination with non-typhoidal *Salmonella* (NTS) has a more widespread infection than typhoidal *Salmonella* in Western Asia. Reported cases of *S. Typhi* infections were seen in Bahrain and Syria while *S. Paratyphi* were only seen in Saudi Arabia, one of the most populous countries in the region. Of all cases, non-typhoidal *Salmonella* serovars contributed a large percentage of the incidence rate. Prevalence of serovars in each country, with *S. Enteritidis* and *S. Typhimurium* being the most predominant and most common serovars, were identified. All data explained that infections from NTS serovars typically have an animal reservoir and are acquired through the ingestion of contaminated agricultural products such as poultry or eggs, and in undercooked and raw meat.

Among all the 18 countries in West Asia, Georgia and Armenia have the most multidrug-resistant isolates. In the data shown in Figure 5, tetracycline and ampicillin are the most predominant MDRs, however, other

antibiotics have a higher resistance rate depending on which region. *Salmonella* spp. in Georgia and Armenia showed high resistance to nalidixic acid (89.47%), ampicillin (87.72%), and ceftriaxone (71.93%).^[28] MDR *Salmonella* in Azerbaijan showed resistance to ceftriaxone and tetracycline with 62.5% respectively.^[29] In Bahrain, MDR *Salmonella* is separated into typhoidal and non-typhoidal. Nalidixic acid recorded a high resistance (100%) in typhoidal infection while ampicillin recorded 33%, low resistance in non-typhoidal infection.^[30] Almost all of the isolates in Cyprus showed high resistance to sulfamethoxazole (85%) and some are resistant to streptomycin and tetracycline.^[31] In Iraq, a 100% resistance rate is recorded against *Salmonella* spp. in amoxicillin, amoxicillin-clavulanic acid, erythromycin, and lincomycin.^[32] MDR *Salmonella* isolates in Israel revealed resistance to nalidixic acid, nitrofurantoin, tetracycline, and trimethoprim-sulfamethoxazole.^[33] In Jordan, it only shows resistance to tetracycline.^[34] For both Kuwait and UAE, Kuwait isolates (9.8%) showed a higher multidrug-resistance versus UAE isolates (4.1%). However, ampicillin has the highest resistance with 26.5% and 17.1%, followed by chloramphenicol (5.6% and 5.7%), and cefotaxime with both 1.6% resistance.^[35] For Lebanon, *S. Typhi* antimicrobial resistance is still uncommon in Lebanon, although the cases differs for non-Typhi isolates of *Salmonella*. Wherein ampicillin (65-100%), trimethoprim (43-100%) for the resistance in *S. Typhi* while for non-Typhi, cefotaxime (88-100%), ciprofloxacin (91-100%), and nalidixic acid (25-57%).^[36] In Oman, both *Salmonella* spp. and *Shigella flexneri* showed high resistance toward amikacin (91.9%), gentamicin (89.2%), and cefuroxime (86.5%).^[37] In Palestine, 93 isolates (72.7%) were resistant to 16 microbial agents showing that most *Salmonella* isolates have high resistance to tetracycline (79.7%), then trimethoprim-sulfamethoxazole (48.4%), and ampicillin (17.1%).^[38] In Qatar, high resistance with tetracycline (23.9%), ampicillin (21.1%), AMC (18.7%), and sulfamethoxazole-trimethoprim (13%) were recorded. Furthermore, 22.4% of the isolates were multidrug-resistant (MDR), with 4.1% being ESBL producers.^[39] In Saudi Arabia, first-line antibiotics such as ampicillin, trimethoprim-sulfamethoxazole, chloramphenicol, and cephalosporin were now found to be resistant in enterica isolates.^[40] In Syria, *Salmonella* Typhi samples are resistant to ceftriaxone, co-trimoxazole, and ciprofloxacin.^[41] In Turkey, resistance to nalidixic acid, streptomycin, tetracycline, and vancomycin was discovered to be extremely high (89.28%). Resistance to trimethoprim-sulfamethoxazole was found in 32.14% of the samples. Resistance to ampicillin, ceftriaxone, chloramphenicol,

and gentamicin was shown to be less common (8.33%).^[42] In Yemen, all 33 *Salmonella* Typhi isolates showed high resistance (100%) to lincomycin and tetracycline. Whereas rifampicin and nalidixic acid recorded an 87.5% resistance rate. Among 33 *S. Typhi*, only 14(43.9%) and 4(12.5%) were resistant to erythromycin and norfloxacin. *Salmonella* Paratyphi was (100%) resistant to lincomycin and tetracycline whereas 11 (84.6%), 10 (76.9%), 7 (53.9%) were resistant to streptomycin, nalidixic acid, and erythromycin, respectively. *S. Paratyphi* also showed the same resistance percentage of 2 (15.4%) to ciprofloxacin and norfloxacin.^[43]

DISCUSSION

Prevalence of Typhoidal and Non-typhoidal *Salmonella* serotypes in Asia

Salmonella spp. remains as the leading causative agents of bacterial diseases. *Salmonella* can be readily transmitted to humans through the consumption of everyday food such as poultry and meat products.^[44] Salmonellosis can be identified as typhoidal or non-typhoidal depending on the serotype that caused the infection. Among the data collected, NTS strains are more prevalent than typhoidal strains. Existing data revealed that the most frequently isolated typhoid *Salmonella* serotype in Asia is *S. Typhi* while *S. Typhimurium* for the non-typhoidal *Salmonella*.

Salmonella Typhi is attributed to several endemic Salmonellosis in third-world countries in Asia due to factors such as increasing poverty, social service deterioration, and employment insecurity. *S. Typhi* can be passed over from source to host by consumption of untreated water during the hot, humid season which is common for most Asian countries as identified by Srikantiah.^[45]

In congruence to the study conducted by Xiang *et al.* (2020), the non-typhoidal infection caused by *Salmonella* Typhimurium is due to the transmission characteristic of the mentioned serovar.^[46] *S. Typhimurium* is linked to acute *Salmonella* infections that can occur throughout the entire year with only 8 to 24 hr incubation time; thus, the reason for the haste transmission of the serovar. East Asians, especially Hong Kong residents, are of higher probability of acquiring infection from *S. Typhimurium* due to the high consumption of meat products associated with the serovar.^[11]

Growing Antimicrobial Resistance of Isolated *Salmonella* in Asia

Another burden in the Asian region is the growing resistance of microorganisms due to the overuse of

antibiotics for patients and the widespread usage of antibiotic agents during food processing from animal sources.^[10] Among the data collected, *Salmonella* isolates in Asia had shown increasing antibiotic resistance throughout the years. More than half of the percentage of isolated *Salmonella* in all Asian countries was revealed to be multidrug-resistant. A study conducted by Sinwat^[26] showed that 98.9% of the *Salmonella* spp. isolated are MDR. This is especially problematic for Salmonellosis since its first line of treatment is antimicrobial therapy.^[47] Awareness of the resistance characteristics of *Salmonella* isolates is essential to serve as a guide for the physicians in arranging suitable clinical treatment for the patients to avoid mortality.^[46]

The trend of the worldwide emergence of MDR *Salmonella* spp. in Asia is observed in all types of antimicrobial agents. In particular, resistance against Tetracycline is of great prevalence among isolated *Salmonella* spp. in the studies, which is followed by Nalidixic acid and Ampicillin. Resistance against tetracycline is the most prominent in 11 out of 38 countries included in this mini-review. These three antibiotics shared a common property which may explain the increased resistance of *Salmonella* against them, Tetracycline, Nalidixic acid/Quinolones, and Ampicillin are all used as a treatment for both human and animal infection.^[6] Thus, resistance might have developed during the exposure of animal reservoirs of *Salmonella* during food processing, passing down the antimicrobial resistance to the human host via horizontal transfer.

In addition, Grossman (2016) associated Tetracycline resistance with three main reasons: inheritance or acquiring genetic elements with tetracycline-specific resistant genes, increased intrinsic mechanism for antimicrobial resistance as a result of chromosomal mutation, and ribosomal binding sites mutation.^[48] TET (ten-eleven-translocation) genes, located in transposon Tn1721, were commonly observed in tetracycline-resistant non-Typhi *Salmonella* serotypes such as Typhimurium and Enteritidis. Encoding of resistance against old antibiotic cases is linked with *tet* genes.

Comparison of Results among Asian Regions

As the largest continent in the world, Asia consists of countries that greatly vary in terms of culture, lifestyle practices, and economic standing. Public health concerns for bacterial diseases such as Salmonellosis are being addressed by more capable countries with enough resources and are often neglected by developing countries. Among the 51 territories of Asia, 12 countries present no research records about MDR *Salmonella* serving as an obstacle in tracking its overall prevalence

in the continent. These 12 countries are the Kyrgyz Republic, Tajikistan, Turkmenistan, Macau, Mongolia, North Korea, Afghanistan, Maldives, Bhutan, Sri Lanka, Timor-Leste, and Brunei. East Asia has the most number of journal articles available, with a total of 16 articles.

In addition to unsanitary conditions during food processing, the abundance of research studies regarding the prevalence of MDR *Salmonella* is attributed to the culture of eating raw meats and seafood of individuals from this Asian region, making the people more susceptible to acquiring foodborne diseases. Consumption of sushi and sashimi poses a high probability of being infected with highly resistant *Salmonella* as 65.6% of the test sample was positive for MDR.^[49]

Only two countries from Central Asia conducted research studies about *Salmonella*, in which non-Typhi and Typhi *Salmonella* persisted in Kazakhstan and Uzbekistan, respectively. Isolates from this Asian region are still susceptible to several antibiotics and MDR *Salmonella* is not yet prevalent. Five out of twelve (41.67%) isolates are MDR in Kazakhstan while only 13% are MDR in Uzbekistan.^[6-7] Nalidixic acid resistance is the most common in Central Asia.

China and its dependencies are the countries in East Asia that draw the most concern regarding *Salmonella* infection. Typhoidal and non-typhoidal serovars of *Salmonella* showed an increasing number of cases over the years but non-Typhi *Salmonella* is more prevalent in East Asian countries. Only China contains records for infection caused by *S. Typhi*.^[8] Among East Asian countries, China also houses the *Salmonella* isolates resistant to the greatest number of antimicrobial agents. *Salmonella* spp. from all five countries showed resistance against tetracycline and ampicillin. The data gathered showed that the antibiotic that most *Salmonella* isolates from East Asia have built resistance from is Tetracycline. Typhoidal *Salmonella* is the only observed serovars among the data collated from South Asia, with *Salmonella Typhi* as the leading strain. The current percentage of MDR strains among the isolates is 80.91%.^[18] In particular, the resistance of *Salmonella* isolates against Nalidixic acid is already common in South Asia while there is an evident surge of Tetracycline resistance over the past decade.^[17] Only Indonesia investigated Typhoidal *Salmonella* in Southeast Asia. Except for Timor-Leste and Brunei, the remaining South Asian countries highlighted the disease-causing ability of uncommon nontyphoidal serovars. *S. Weltevreden*, *S. Enteritidis*, *S. Albany*, and *S. Saintpaul* are the most common *Salmonella* strains isolated in Indonesia, Malaysia, Myanmar, and Singapore,

respectively. More than half of the isolates were revealed to be MDR strains, with the majority being resistant to up to nine antibiotics.^[27] Resistance against specific antibiotics greatly varies, the most commonly identified antimicrobial agents *Salmonella* strains have built resistance in fall under beta-lactams.

Non-Typhi *Salmonella* strains are greater in numbers than Typhoidal *Salmonella* as observed in the studies conducted in West Asia. Israel, which records a consistent annual increase of 86.9 cases per 100,000 population, associates most of the Salmonellosis cases with NTS.^[33] *S. Typhimurium* is the prevalent isolated MDR NTS in West Asia. MDR strains of *Salmonella* Typhi are rare.^[36] Only 5 out of 17 West Asian countries performed research studies about Typhoidal *Salmonella*. A significant variation in antimicrobial resistance was observed among the *Salmonella* isolates in West Asia. Tetracycline, Nalidixic acid, Ampicillin, Cefotaxime, and Ciprofloxacin are the most common antibiotic agents mentioned in the studies. However, in Bahrain, the isolates were revealed to be 100% resistant to tetracycline.^[30] The high tetracycline resistance was also observed in Azerbaijan, Israel, Jordan, Palestine, Qatar, and Yemen.

The difference in the results obtained from each Asian region regarding the prevalence of Typhoidal and Non-typhoidal strains are congruent to the findings of Gal-Mor.^[9] Typhoidal *Salmonella* serovars were common and are endemic in developing countries such as Indonesia, Kazakhstan, Uzbekistan, and China due to inaccessibility to clean water and inadequate sanitation. It is not frequently isolated in food samples as humans serve as its exclusive reservoir and are of less prevalence in comparison to NTS as vaccines using attenuated *S. Typhi* are available in the market. On the other hand, Non-Typhi *Salmonella* strains are considered a threat worldwide. 93.8 million cases of NTS infection occur annually, with an estimation of 155,000 mortality.^[50] NTS strains can be easily transmitted through contaminated animal-derived products and plant produce, person-to-person contact, and even human-to-pet interaction.^[9] These isolates are also associated with short incubation time, contributing to haste transmission of infection. Although non-typhoidal *Salmonella* prevailed as the most frequent case in Asia, the cruciality of each type to be properly addressed is of equal importance as each Asian country differs in results and both types are considered a public health burden.

In this investigation, it is evident that proper food preparation and better hygienic practice during food production and processing are essential to decrease the prevalence of bacterial pathogens such as *Salmonella*.

Aside from antibiotic misuse, usage of antibiotics in the animal sector must also be taken into consideration to prevent the horizontal transfer and increased multidrug resistance of *Salmonella* serovars.

CONCLUSION

This mini-review showed that *Salmonella* spp. plays a very crucial role in public health risk. The constant increase of multi-drug resistant *Salmonella* spp. became a major concern for the general public, especially the physicians, to treat the disease. Although most reports came from developing countries in the Asian region, cases have also been found in some of the most developed countries. However, journal articles and publications are still limited in some countries due to the lack of studies and disease recognition. It is strongly recommended that public health authorities should implement stricter preventive and control in these circumstances and make better changes to improve food and water safety.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

MDR: Multidrug-Resistant; **NTS:** Non-typhoidal *Salmonella* (NTS) strains; **TET:** Ten-eleven-translocation.

SUMMARY

Salmonella spp. persist to be one of the dominant causes of bacterial diseases. In this conducted mini-review, Tetracycline has the highest percentage of resistance which is prevalent in 11 of 38 countries in Asia. Despite the high prevalence rate of reported *Salmonella* cases in Asia, there are still territories in Asia with little to

no available data due to a lack of research about MDR *Salmonella* spp. It is concerning that *Salmonella* is one of the most common causes of food poisoning and is a well-recognized multi-drug resistant bacteria due to poor food handling and unhealthy lifestyle. At this point, public health authorities should administer more stringent preventive measures regarding proper water management, safe food handling, and animal-derived food production.

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