Residual antimicrobial agents in food originating from animals

Mohammad Mahmudul Hassan [a,**], Mohamed E. El Zowalaty [b,c,***], Åke Lundkvist [c],
Josef D. Järhult [d], Md Raihan Khan Nayem [a], Abu Zubayer Tanzin [a], Md Rahim Badsha [e],
Shahneaz Ali Khan [a], Hossam M. Ashour [f,g,*]

[a] Faculty of Veterinary Medicine, Chattogram Veterinary and Animal Sciences University, Chattogram 4225, Bangladesh
[b] Department of Clinical Sciences, College of Medicine, University of Sharjah, Sharjah, 27272, United Arab Emirates
[c] Zoonosis Science Center, Department of Medical Biochemistry and Microbiology, Uppsala University, Uppsala, SE 75 123, Sweden
[d] Zoonosis Science Center, Department of Medial Sciences, Uppsala University, Sweden
[e] Faculty of Food Science and Technology, Chattogram Veterinary and Animal Sciences University, Chattogram 4225, Bangladesh
[f] Department of Integrative Biology, College of Arts and Sciences, University of South Florida, St.Petersburg, Florida, 33701, USA
[g] Department of Microbiology and Immunology, Faculty of Pharmacy, Cairo University, Cairo, 11562, Egypt

A R T I C L E   I N F O

A B S T R A C T

Background: The agricultural food products industry in Bangladesh depends on utilizing antimicrobials indiscriminately as growth promoters and for controlling infectious diseases. Thus, there is always a risk of antimicrobial agent accumulation in food sources that originate from agricultural production.
Methods: In the present study, we collected data from published articles between January, 2013 and December, 2019 on antimicrobial residues in human food sources such as meat, milk, eggs, and fishes.
Results: Liver contained the highest percentage of antimicrobial residues (74%; 95% CI: 59.66–85.37) against the *in vitro* enteric pathogen *Escherichia coli* in layer chickens. Similar results were demonstrated in liver (68%; 95% CI: 53.30–80.48) and kidney (66%, 95% CI: 51.23–78.79) of layer chickens against *Bacillus cereus* and *Bacillus subtilis*. Amongst all antibiotics, the highest concentrations of ciprofloxacin were detected in kidney (48.57%; 95% CI: 31.38–66.01), followed by liver (47.56; 95% CI: 40.88–54.30) of broiler chickens. Ciprofloxacin was also present in liver (46.15%; 95% CI: 33.70–58.96) of layer chickens. The percentage of ciprofloxacin in thigh and breast meat in broiler bird were 41.54% (95% CI: 34.54–48.79) and 37.95% (95% CI: 31.11–45.15) respectively. Enrofloxacin was the second most dominant antimicrobial agent and was present in the liver of both types of poultry (Broiler and Layer chickens: 41.54%; 95% CI: 29.44–54.4 and 437.33%; 95% CI: 30.99–44.01). The prevalence rates of enrofloxacin in thigh and breast meat of broiler chickens were 24.10% (95% CI: 18.28–30.73) and 20.51% (95% CI: 15.08–26.87), respectively. Tetracycline, a commonly used antibiotic in livestock, was present in the liver (49.23%; 95% CI: 36.60–61.93) of layer chickens. In case of aquaculture food products, the highest amount of amoxicillin (683.2 mg/kg) was detected in Tilapia fish (*Oreochromis niloticus*), followed by 584.4 mg/kg in climbing perch (*Anabas testudineus*) and 555.6 mg/kg in Rui fish (*Labeo rohita*). Among the five types of fishes, Rui fish (0.000515 mg/kg) contained the highest concentrations of chloramphenicol antibiotic residues.
Conclusions: The presence of antimicrobial residues in meat, milk, egg, and fish is a serious public health threat due to the potential induction of antimicrobial resistance. It can negatively impact the food supply chain, especially with the current strain that it is already facing with the current COVID-19 pandemic. The findings of the present study highlight the ongoing risk of residual antimicrobial agents in food of animal origin in Bangladesh and countries with similar practices. This can draw the attention of public health officials to propose plans to mitigate or stop this practice.

---

1. Introduction

Antimicrobial resistance, emerging viruses such as (SARS-CoV-1, MERS-CoV, and SARS-CoV-2), avian influenza and several other zoonotic infectious diseases pose continuous threats and challenges to human public health. Antimicrobial resistance incurs increasing costs in lives and money, and is threatening modern medicine as we know it today. Antimicrobial agents have been used globally for many years in human and veterinary practices (Prescott, 2017). However, the indiscriminate use of antimicrobial agents may lead to the development of resistance through pathways that include the accumulation of antibiotic residues in the human food chain. Hence, maximum residue limits (MRLs) have been implemented by the Food and Agricultural Organization (FAO) for public health safety (Food and Agricultrual Organization of the United Nations, 2018). Antimicrobial resistance (AMR) has become a massive public health threat in many countries including Bangladesh, in which the practice of boosting agricultural production systems with overwhelming amounts of antibiotics is prevalent.

Bangladesh is a lower middle-income overpopulated country with increasing demands for protein-based food sources; which led to the establishment of extensive dairy, poultry, and aquaculture industries across the country. These farms play a significant role in the economy of Bangladesh through the production of poultry, meat, milk, and eggs (Department of Livestock Service, 2020). Moreover, indigenous or family-reared chicken/poultry supplied a significant amount of meat and eggs throughout the years to meet the protein demands of the rural communities. This created pressure on commercial farmers to produce more meat and eggs for the growing population and triggered the unregulated use of growth promoters and probiotics to meet the high production demands. More recently, milk and meat production have increased several folds by implementing specific and outcome-oriented initiatives by the government, non-government organizations (NGOs), and farmers (Ministry of Fisheries and Livestock, 2020). Farmers are, unfortunately, not very well aware about the antibiotic withdrawal period and they seem to be more concerned about the economic impacts of the products such as milk. This has led to commercial food products with varying amounts of heavy metals (Kundu et al., 2017) and antimicrobials used to prevent diseases and thus enhance farm production (Hasan et al., 2011). More precisely, farmers frequently treat the whole flock with antibiotics and growth promoters without consulting veterinarians, physicians, or public health experts (Chowdhury et al., 2009). They also do not typically maintain the prescribed antibiotic withdrawal period before marketing their food products such as meat, milk, egg and fish (Nonga et al., 2010). In broiler chickens, antimicrobial agents are used in feed and water to prevent diseases. Hence, the meat of broiler chickens, egg, and milk may contain antimicrobial residues which increase the possibility of developing resistant bacteria (Hasan et al., 2012; Hassan et al., 2014) which represents a serious threat to public health (Sachi et al., 2019). Aquaculture such as commercial fish and prawn farming is popular in Bangladesh as a source of low-cost protein to underprivileged groups of the society (Ahmed et al., 2008; Das et al., 2018). Antimicrobial agents are also used as feed additives in fish farming triggering antimicrobial resistant bacteria in water bodies and contaminating the aquaculture and the environment (Ahaduzzaman et al., 2014; Hassan et al., 2015).

Humans consuming livestock and aquaculture-derived food products might have the chance to develop resistance against specific antimicrobials due to antimicrobial residues being introduced into the human food chain (Roess et al., 2013). To investigate the situation of antimicrobial residues in animal-derived food, we consulted previous reports (Bakar et al., 2013; Barman et al., 2018; Bristy et al., 2019; Chowdhury et al., 2015; Ferdous et al., 2019; Hossain et al., 2018; Islam et al., 2016; Khan et al., 2018; Sarker et al., 2018; Sattar et al., 2014). Some studies proposed different techniques for antimicrobial residue detection in different types of animal-derived food products. In this review, we assessed the current reported data on antimicrobial residues in order to guide future public health measures in Bangladesh and other developing countries that have similar antibiotic-residue problems.

2. Materials and methods

2.1. Review protocol

The review followed the standard systematic review procedures established by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (Liberati et al., 2009). The procedural guidelines shown in Fig. 1 were followed: (a) database search to categorize potentially relevant articles, (b) assessment of the relevance of the articles, (c) quality assessment and (d) extraction of data.

2.2. Search strategy

A structured literature search approach was used to identify published studies reporting the presence of antimicrobial residues in foods of animal origin in Bangladesh. The scientific databases Google scholar, PubMed, and Science Direct were searched for relevant studies published between 2013 and 2019. Specific Boolean words were developed based on the objectives of the study. The search terms have been categorized into outcome, population, descriptive, and area categories. The articles were downloaded using the Chattogram Veterinary and Animal Sciences University (CVASU) library network. The Boolean words of each category were combined using "AND" whereas "OR" was used to join the term within a category. Some modifications have been made based on the requirements of the search engines, and advanced search criteria have been used to search Google scholar. Duplicate entries were identified and removed before the final selection of articles. Studies that did not meet the predetermined inclusion criteria were removed. Studies outside the scope were excluded. This included antimicrobial residues, poultry/livestock/fish, detection methods such as microbial inhibition test (MIT)/thin layer chromatography (TLC)/ultra-high-performance liquid chromatography (UHPLC)/liquid chromatography-mass spectrometry (LC-MS), conducted/published before 2013, studies published in languages other than English, reviews, abstracts, and conference proceedings.

2.3. Data screening

The full texts of retrieved published articles were screened for inclusion. Studies were selected for evaluation if they met the following inclusion criteria.

- Any research article published between January 2013 and December 2019 that reported residual antimicrobial agents in poultry, livestock, and fish in Bangladesh.
- Any research article that reported the prevalence, investigation, incidence, occurrence, survey, characterization and identification of antimicrobial residues from Bangladesh.
- Data were extracted and recorded for study location, citation, first author, time of study, year of publication, type of specimen, sample size, number of positive specimens, presence or absence of antimicrobial residue, specific antibiotic sensitivity or resistance level percentages, methods used for detection, and antimicrobial residue level.

Eligible articles were retrieved in full text format and were assessed using the case definitions specified by the respective studies (Table 1).

2.4. Data analysis

All data extracted from different publications were sorted in Microsoft excel for statistical analysis. Data were analyzed using STATA/IC version 13.0 (StataCorp. 2013. *Stata Statistical Software: Release 13*. College Station, TX, USA) to get the prevalence and 95% confidence
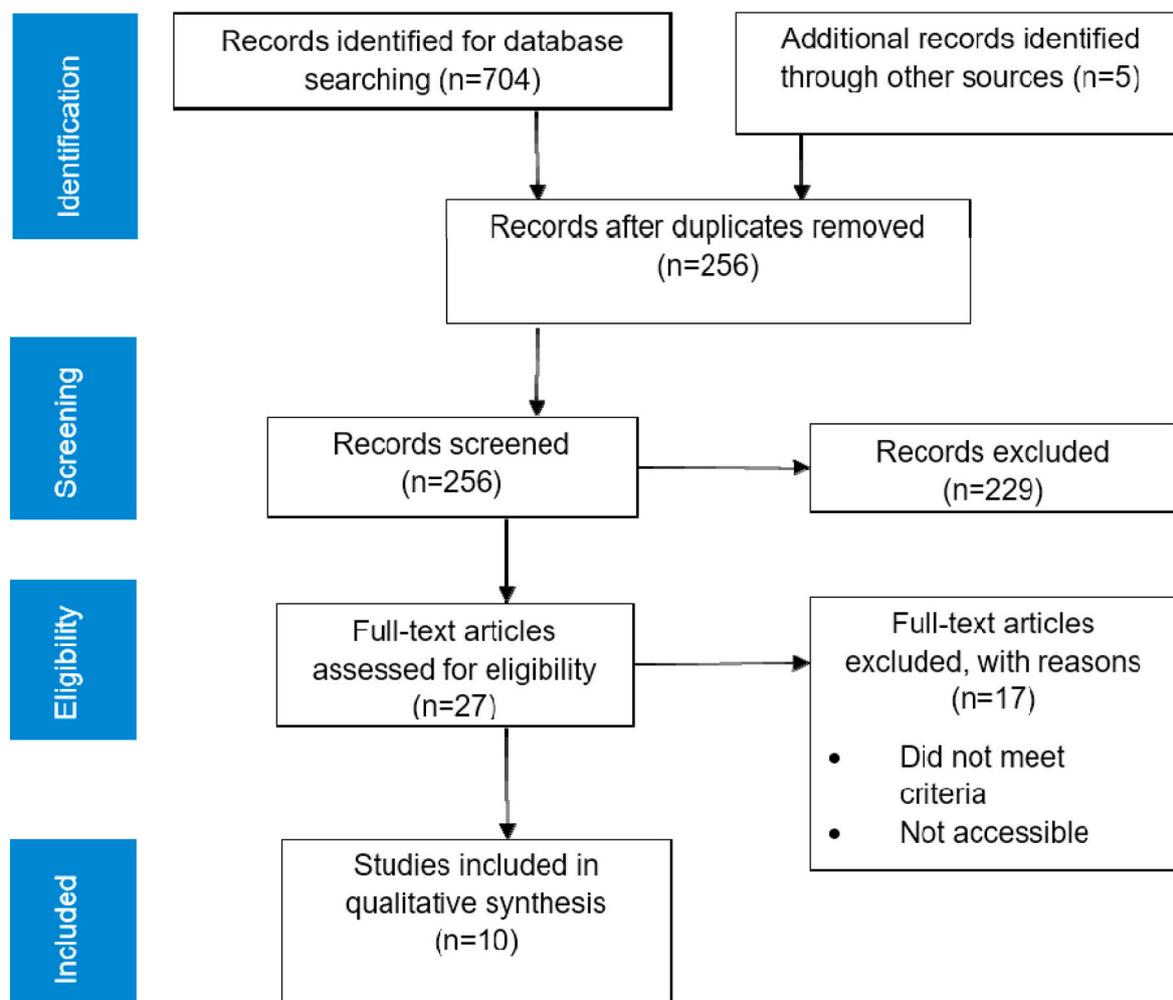
Fig. 1. Flow chart of the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) showing the search strategy and selection process for research articles published between 2013 and 2019. Based on the search criteria, a total of 704 English language published articles were identified and were further refined into 10 articles as described in the PRISMA flowchart.

interval (CI). Descriptive statistics were done to identify the numbers of articles. The study results from those articles were classified according to sample category and method of detection and were arranged in tables with the identified antimicrobials.

3. Results

3.1. Data acquisition

The preliminary search yielded 704 articles. Manual search identified five additional articles. Deduplication yielded 256 unique articles. Reports were considered duplicated if they had the same information of authors, year of publication, title of the article, volume, issue, and page number fields. After the exclusion of articles that did not meet the inclusion criteria, 10 articles were identified as eligible for data extraction and qualitative analysis (Table 1). Among the 64 districts of Bangladesh, research studies on residual antimicrobial agents were focused in only four districts (Fig. 2). Screening of residual antimicrobial agents in other districts is necessary to determine the overall situation in the country.

3.2. Residual antimicrobial agents in poultry products

Using the microbial inhibition method, qualitative detection of antimicrobial residues (Table 2) showed the highest prevalence of 68% in liver (95% CI: 53.30–80.48) followed by 60% in kidney (95% CI: 45.18–73.59), 60% in breast meat (95% CI: 45.18–73.59), 50% in thigh

meats of chicken (95% CI: 35.73–64.47), and 64% in egg (95% CI: 49.19–77.08) when tested with *B. cereus*. In case of *B. subtilis*, the highest prevalence of 66% was in kidney (95% CI: 51.23–78.79) followed by 50% in liver (95% CI: 35.73–64.47), 40% in breast meat (95% CI: 26.41–54.82), 44% in thigh meat of chicken (95% CI: 29.99–58.75), and 54% in eggs (95% CI: 39.32–68.19). In case of *E. coli*, the highest prevalence of 74% was in liver (95% CI: 59.66–85.37) followed by 72% in kidney (95% CI: 57.51–83.77), 70% in breast meat (95% CI: 55.39–82.14), 54% in thigh meat of chicken (95% CI: 39.32–68.19), and 60% in eggs (95% CI: 45.18–73.59). About 27% of ciprofloxacin (95% CI: 20.98–33.72) was detected in eggs. Amoxicillin and tetracycline have also been detected in eggs with the respective percentages of 11% (95% CI: 7.02–16.18) and 16% (95% CI: 11.21–21.83).

The published articles that used the TLC method for the qualitative detection of antimicrobial residues (Table 3) were assessed. The highest prevalence of ciprofloxacin was detected in kidney and liver of broiler chickens and were 48.57% (95% CI: 31.38–66.01) and 47.56% (95% CI: 40.88–54.30), respectively. The lowest prevalence was detected in thigh and breast meat of layer chickens and were 30.77% (95% CI: 19.91–43.44) and 29.23% (95% CI: 18.60–41.82) respectively. The highest prevalence of enrofloxacin was detected in liver of layer chickens and was 41.54% (95% CI: 29.44–54.44) while the lowest prevalence was detected in breast meat of broiler chickens and was 20.51% (95% CI: 15.08–26.87). The highest prevalence of tetracycline was detected in the liver of layer chickens and was 49.23% (95% CI: 36.60–61.93) whereas the lowest prevalence was detected in thigh meat

Table 1
Detection, sources, and prevalence of antimicrobial residues between 2013 and 2019 in Bangladesh.

Area	Duration	Publication year	Sample source	Sample category	Sample	Method	Antibiotics	Total samples	Outcome	References
Chattogram	2009	2016	Poultry farm	Layer chickens	Thigh Breast Liver Kidney Eggs	MIT TLC	4	100	Ciprofloxacin Enrofloxacin Tetracycline Amoxicillin	Islam et al. (2016)
Chattogram	2011–2012	2015	Poultry farm Dairy farm	Layer chickens Livestock	Eggs Milk	MIT TLC UHPLC	3	210	Ciprofloxacin Tetracycline Amoxicillin	Chowdhury et al. (2015)
Chattogram	2012	2014	Live bird market	Layer chickens Broiler chickens	Thigh Breast Liver Kidney	TLC UHPLC	4	50	Ciprofloxacin Enrofloxacin Tetracycline Amoxicillin	Sattar et al. (2014)
Chattogram	2013	2013	Live bird market Fish market	Broiler chickens Indigenous chicken Fish	Meat Liver Tilapia Pungas Anabas Trout Rui fish	LC-MS	1	80	Chloramphenicol	Bakar et al. (2013)
Chattogram	2015	2019	Live bird market Fish market	Broiler chickens Indigenous chicken Fish Shrimp	Thigh Breast Liver Climbing perch Rui fish Tilapia Bombay duck Shrimp	TLC, UHPLC	4	335	Ciprofloxacin Enrofloxacin Amoxicillin Oxytetracycline	Ferdous et al. (2019)
Sylhet	2016	2018	Fish market	Fish	Tilapia	UHPLC	1	24	Oxytetracycline	Barman et al. (2018)
Sylhet	2016	2018	Fish market	Fish	Pungas	UHPLC	1	24	Oxytetracycline	Hossain et al. (2018)
Gazipur Mymensingh	2017	2018	Live bird market and farm	Broiler chickens	Thigh Breast Liver	TLC	5	160	Ciprofloxacin Enrofloxacin Oxytetracycline Amoxicillin Doxycycline	Sarker et al. (2018)
Mymensingh	2017	2019	Poultry farm	Broiler chickens	Meat	TLC	1	108	Colistin	Bristy et al. (2019)
Mymensingh	2017	2018	Live bird market	Broiler chickens	Breast Liver	TLC	3	30	Ciprofloxacin Enrofloxacin Amoxicillin	Khan et al. (2018)

Microbial Inhibition Test (MIT); Thin Layer Chromatography (TLC); Ultra-High-Performance Liquid Chromatography (UHPLC); Liquid Chromatography-Mass Spectrometry (LC-MS).

of layer chickens and was 18.46% (95% CI: 9.92–30.03). The highest prevalence of amoxicillin was detected in indigenous chicken and was 88.24% (95% CI: 72.55–96.70) whereas the lowest prevalence was detected in eggs of indigenous chicken and was 5% (95% CI: 1.64–11.28). The highest prevalence of doxycycline was detected in liver and was 43.13% (95% CI: 35.33–51.18) whereas the lowest prevalence was detected in breast meat and was 25.63% (95% CI: 20.38–35.20). In broiler chickens, the highest prevalence of oxytetracycline was detected in the liver and was 46.25% (95% CI: 38.35–54.29) whereas the lowest prevalence was detected in breast meat and was 22.5% (95% CI: 16.28–29.76). The prevalence of colistin sulfate residue was 55.55% (95% CI: 45.68–65.12) in broiler meat. As detected by the UHPLC method, broiler meat (522.9 mg/kg) contained more amoxicillin residues than the meat of indigenous chicken (444.3 mg/kg) followed by eggs which had 29.64 mg/kg. Using the LC-MS method, meat (0.405 μg/kg) and liver (0.438 μg/kg) of indigenous chicken contained more chloramphenicol residues than meat (0.275 μg/kg) and liver (0.403 μg/kg) of broiler chickens (Table 4).

3.3. Residual antimicrobial agents in livestock products

Using MIT, the prevalence rates of amoxicillin, ciprofloxacin, and

tetracycline in milk were 26% (95% CI: 20.07–32.66), 12.5% (95% CI: 8.26–17.90), and 17.5% (95% CI: 12.50–23.49), respectively. Using TLC, the prevalence rates of ciprofloxacin and tetracycline residues in cow's milk were 11% (95% CI: 7.02–16.18) and 16.5% (95% CI: 11.64–22.38), respectively. From the published literature, the UHPLC method for the quantitative detection of amoxicillin residues in milk detected 33 mg/L (Table 4).

3.4. Residual antimicrobial agents in aquaculture products

Using the TLC method, the highest prevalence was detected in shrimp (*Macrobrachium rosenbergii*) and was 33.33% (95% CI: 17.29–52.82) whereas the lowest prevalence was detected in Tilapia fish and was 3.03% (95% CI: 0.07–15.76). Using the UHPLC method, the highest concentration of amoxicillin was detected in Tilapia fish (683.2 mg/kg). However, Climbing perch, Rui fish, Shrimp, and Bombay duck fish (*Harpadon nehereus*) contained amoxicillin residues of 584.4 mg/kg, 555.6 mg/kg, 419.5 mg/kg, and 14.8 mg/kg, respectively. Oxytetracycline residues were detected in Tilapia (0.0388 mg/kg) and Pungas fish (*Pangasius pangasius*) (0.0351 mg/kg). Using the LC-MS method, the quantitative detection of chloramphenicol residues (Table 4) indicated the highest concentration in Rui fish (0.000515 mg/kg) followed by
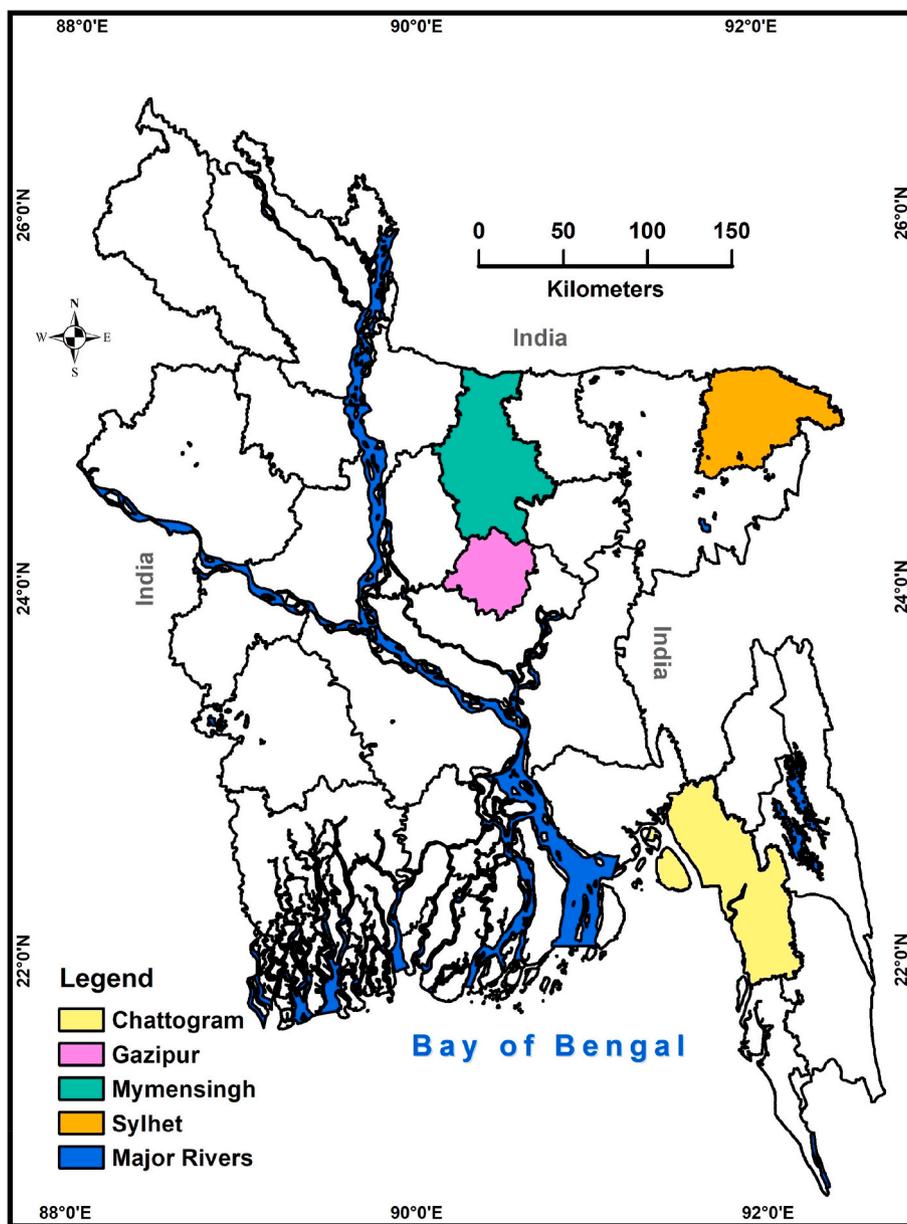
Fig. 2. A map of Bangladesh showing the study areas and the spatial distribution of residual antimicrobial agents (4 districts in different colors; Chattogram, Sylhet, Gazipur and Mymensingh). The map was plotted using ArcMap, version 10.2, Environmental Systems Research Institute, Redlands, California, USA. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

Table 2
Qualitative detection of antimicrobial residues in foods of animal origin using the Microbial inhibition test (MIT).

Sample category	Sample	Ciprofloxacin N, p, %, 95%CI	Tetracycline N, p, %, 95%CI	Amoxicillin N, p, %, 95%CI	*B. cereus* N, p, %, 95%CI	*B. subtilis* N, p, %, 95%CI	*E. coli* N, p, %, 95%CI	References
Layer chickens	Liver				50, 34, 68, 53.30–80.48	50, 25, 50, 35.73–64.47	50, 37, 74, 59.66–85.37	(Chowdhury et al., 2015; Islam et al., 2016)
	Kidney				50, 30, 60, 45.18–73.59	50, 33, 66, 51.23–78.79	50, 36, 72, 57.51–83.77	
	Breast				50, 30, 60, 45.18–73.59	50, 20, 40, 26.41–54.82	50, 35, 70, 55.39–82.14	
	Thigh				50, 25, 50, 35.73–64.47	50, 22, 44, 29.99–58.75	50, 27, 54, 39.32–68.19	
	Eggs	200, 54, 27, 20.98–33.72	200, 32, 16, 11.21–21.83	200, 22, 11, 7.02–16.18	50, 32, 64, 49.19–77.08	50, 27, 54, 39.32–68.19	50, 30, 60, 45.18–73.59	
Livestock	Milk	200, 25, 12.5, 8.26–17.90	200, 35, 17.5, 12.50–23.49	200, 52, 26, 20.07–32.66				

Table 3

Qualitative detection of antimicrobials residues in foods of animal origin using the thin-layer chromatography (TLC).

Sample category	Sample	Ciprofloxacin (N, p, %, 95% CI)	Enrofloxacin (N, p, %, 95%CI)	Tetracycline (N, p, %, 95%CI)	Amoxicillin (N, p, %, 95%CI)	Doxycycline (N, p, %, 95%CI)	Oxytetracycline (N, p, %, 95% CI)	Colistin (N, p, %, 95%CI)	References
Layer chickens	Thigh	65, 20, 30.77, 19.91–43.44	65, 15, 23.08, 13.53–35.19	65, 12, 18.46, 09.92–30.03	65, 17, 26.15, 16.03–38.54				(Chowdhury et al., 2015; Islam et al., 2016; Sattar et al., 2014)
	Breast	65, 19, 29.23, 18.60–41.82	65, 12, 18.46, 09.91–30.03	65, 16, 24.62, 14.77–36.87	65, 14, 21.54, 12.31–33.49				
	Liver	65, 30, 46.15, 33.70–58.96	65, 27, 41.54, 29.44–54.44	65, 32, 49.23, 36.60–61.93	65, 31, 47.69, 11.10–31.77				
	Kidney	65, 25, 38.46, 26.65–51.36	65, 24, 36.92, 25.28–49.80	65, 15, 23.07, 13.53–35.19	65, 25, 38.46, 26.53–51.36				
	Eggs	150, 60, 40.00, 32.09–48.31	50, 13, 26.00, 14.63–40.34	150, 43, 28.67, 21.59–36.61	150, 29, 19.33, 13.35–26.57				
Broiler chickens	Thigh	195, 81, 41.54, 34.54–48.79	195, 47, 24.10, 18.28–30.73	35, 8, 22.86, 10.42–40.13	195, 52, 26.67, 20.60–33.45	160, 45, 28.13, 21.31–35.77	160, 47, 29.38, 22.45–37.08		(Bristy et al., 2019; Chowdhury et al., 2015; Ferdous et al., 2019; Khan et al., 2018; Sarker et al., 2018; Sattar et al., 2014)
	Breast	195, 74, 37.95, 31.11–45.15	195, 40, 20.51, 15.08–26.87	35, 9, 25.71, 12.49–43.26	195, 47, 24.10, 18.28–30.73	150, 41, 25.63, 20.38–35.20	160, 36, 22.50, 16.28–29.76		
	Liver	225, 107, 47.56, 40.88–54.30	225, 84, 37.33, 30.99–44.01	65, 23, 35.38, 23.92–48.23	195, 81, 41.54, 34.54–48.79	160, 69, 43.13, 35.33–51.18	160, 74, 46.25, 38.35–54.29		
	Kidney	35, 17, 48.57, 31.38–66.01	35, 11, 31.43, 16.85–49.29	35, 9, 25.71, 12.49–43.26	35, 25, 71.43, 53.69–85.36				
	Meat				148, 129, 87.16, 80.68–92.09			108, 60, 55.55, 45.68–65.12	
Indigenous chicken	Meat				34, 30, 88.24, 72.55–96.70				(Chowdhury et al., 2015; Ferdous et al., 2019)
	Egg	100, 9, 09.00, 04.20–16.40		100, 7, 07.00, 02.86–13.89	100, 5, 05.00, 01.64–11.28				
Livestock	Milk	200, 22, 11.00, 07.02–16.18		200, 33, 16.50, 11.64–22.38	200, 48, 24.00, 18.26–30.53				Chowdhury et al. (2015)
Fish	Climbing perch				24, 16, 66.67, 44.67–84.37		24, 2, 08.33, 01.02–27.00		Ferdous et al. (2019)
	Rui fish				33, 21, 63.63, 45.12–79.60		33, 10, 30.30, 15.59–48.71		
	Tilapia				33, 18, 54.54, 36.35–71.89		33, 1, 03.03, 00.07–15.76		
	Bombay duck				33, 4, 12.12, 03.40–28.20		33, 0,		
	Shrimp				30, 15, 50.00, 31.30–68.70		30, 10, 33.33, 17.29–52.82		

Tilapia (0.0003535 mg/kg), Trout (0.000328 mg/kg), Climbing perch (0.000188 mg/kg) and Pungas (0.000133 mg/kg).

4. Discussion

4.1. Agricultural production systems heavily depend on antimicrobial as growth promoter and probiotics

Antibiotics have been used in agricultural production systems, especially in animals since the mid-1940s, shortly after they became available for the treatment of human diseases (Gustafson & Bowen, 1997; McEwen, 2006). Antibiotics are now widely used for therapeutic, prophylactic, and growth promoting purposes within agricultural production systems including livestock and fish industries. A significant number of antibiotics used in human medicine either belongs to the same class or have the same mode of action as those used in agricultural

systems. Several antibiotics used to treat bacterial infections in humans also have veterinary applications (Landers et al., 2012). In fact, the use of animal antibiotics for the treatment or prevention of disease closely followed their use in humans. Each year, a huge number of drugs, including antibiotics are administered to livestock to produce increased amounts of animal-derived food (meat, eggs, and dairy products) for human consumption around the globe (Vázquez-Moreno et al., 1990; Roura et al., 1992; Rassow & Schaper, 1996). In 2010, China, the United States, Brazil, India, and Germany were the five countries with the largest amount of antibiotics consumed by food-producing animals (van Bijnen et al., 2011). In that same year, the estimated global amount of antibiotics used for food-producing animals was 63,151 (±1560) tons (Boeckel et al., 2015). Antimicrobials are prescription-only medications and their indiscriminate use can lead to the development of bacterial resistance, which is a major public health concern (Ferech et al., 2006; Liu et al., 1999; van Bijnen et al., 2011; Buke et al., 2003; Ahiabu et al.,

Table 4

Quantitative detection of antimicrobial residues in foods of animal origin using Ultra-High-Performance Liquid Chromatography (UHPLC) and Liquid Chromatography-Mass Spectrometry (LC-MS).

Sample category	Sample (n)	Amoxicillin (mg/kg)	Oxytetracycline (mg/kg)	Chloramphenicol (mg/kg)	Test methods
Broiler chickens	Breast (10)	0.479			UHPLC
	Liver (10)	0.0847			
	Liver (10)			0.000403	LC-MS
	Meat (145)	522.90			UHPLC
	Meat (10)			0.000275	LC-MS
Indigenous chickens	Meat (33)	444.30			UHPLC
	Meat (10)			0.000405	LC-MS
	Liver (10)			0.000438	
	Eggs (10)	29.64			UHPLC
Livestock	Milk (10)	33.00			
Fish	Climbing perch (5)	584.40			
	Climbing perch (10)			0.000188	LC-MS
	Rui fish (8)	555.60			UHPLC
	Rui fish (10)			0.000515	LC-MS
	Trout (10)			0.000328	
	Bombay duck (2)	14.80			UHPLC
	Shrimp (7)	419.50			
	Tilapia (6)	683.20			
	Tilapia (24)		0.0388		
	Tilapia (10)			0.0003535	LC-MS
	Pungas (10)			0.000133	
	Pungas (24)		0.0351		UHPLC

Antibiotic concentrations are based on the following references (Bakar et al., 2013; Barman et al., 2018; Chowdhury et al., 2015; Ferdous et al., 2019; Hossain et al., 2018; Sattar et al., 2014).

2016; Al-Tawfiq et al., 2010; Costelloe et al., 2010; Vaananen et al., 2006; You et al., 2008; Mather et al., 2012). Using antibiotics in agricultural systems is a major contributing factor for resistance development in bacteria that may cause infections in humans (Molbak, 2004; Wassenaar, 2005). In Bangladesh, antimicrobial agents are used regularly for the treatment and control of diseases in the agricultural system, especially of food-producing animals, and are usually used as a feed additive for growth promotion. Antibiotics are used at suboptimal concentrations for the treatment of infections; a potentially dangerous recipe for developing resistant bacteria. In addition, this enhances

potential allergic reactions and technological problems of fermented meat products. Interestingly, 80% of all food-producing animals receive medication in their entire productive period (Center for Veterinary Medicine, US Food and Drug Adminstration et al., 2017). In case of poultry, antibiotic usage has facilitated their efficient production, and also improved their health and well-being by reducing the incidence of infections (Tollefson & Miller, 2000). In Bangladesh, farmers frequently use antibiotics for therapeutic purposes and regularly add them in the feed and water at sub-therapeutic concentrations for prophylaxis and growth promotion. This unregulated administration of antimicrobial
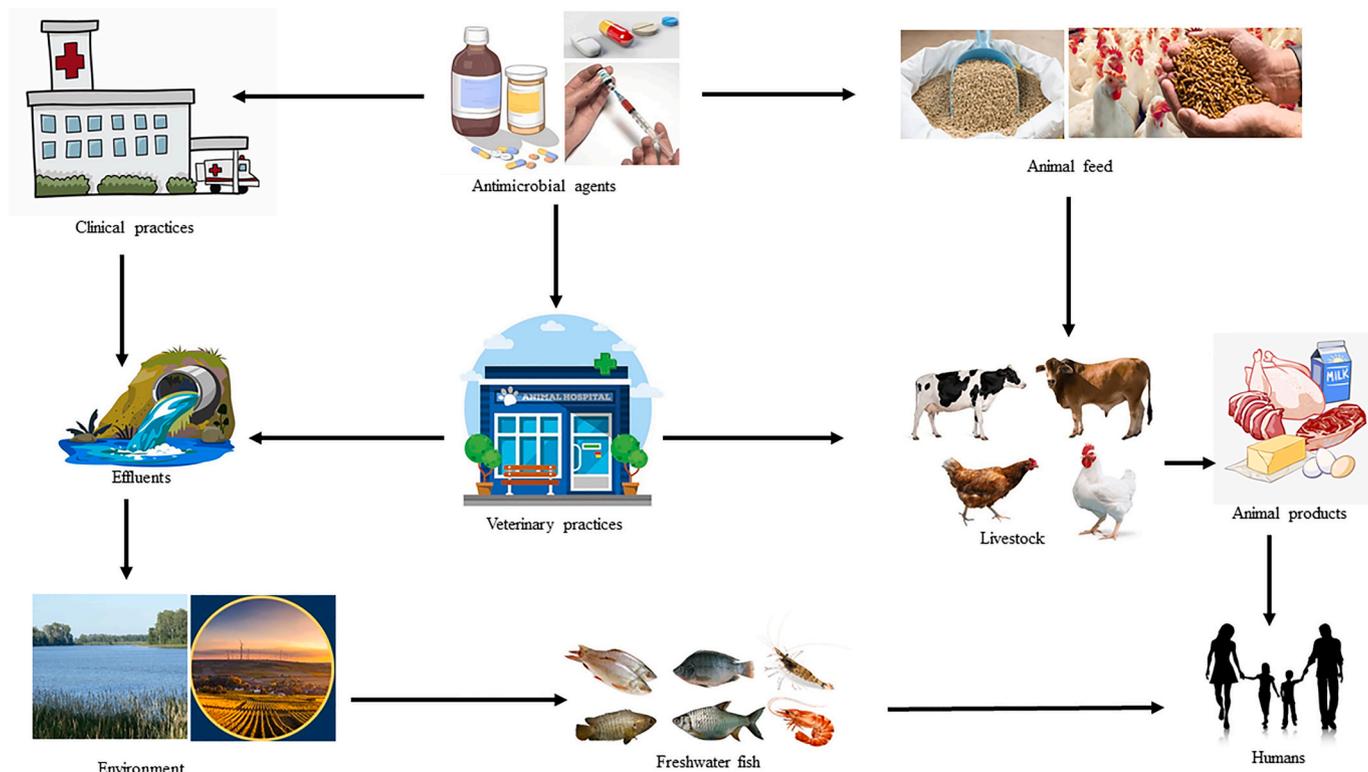
Fig. 3. Flowchart showing the presence of antimicrobial residues arising from the use of antimicrobial agents in Bangladesh.

agents in livestock and aquaculture industry for treatment, prophylaxis, and growth promotion resulted in a huge risk of their deposition to the human food chain at levels exceeding the MRL (Food and Agricultrual Organization of the United Nations, 2018). The presence of antimicrobial residues in food of animal origin as a possible point of entry into the human food chain is shown in Fig. 3. The presence of antimicrobial residues in meat, meat products, fish, and aquaculture products has been negatively impacting their international trade for the last few years (Mathews et al., 2003). The antimicrobials used as feed additive can suppress gut bacteria (Parker & Armstrong, 1987). Generally, the use of growth promoters in poultry promotes faster growth and plays a beneficial role in controlling some chronic disease conditions. Withdrawal of growth promoters can lead to reduced profitability of farming enterprises through increased capital and operational costs. However, studies from Nordic countries suggested that negative effects of removing growth promoters can be offset by improved animal husbandry (Krauβ et al., 1996). Antibiotics commonly used for treatment, prophylaxis, and growth promotion of food animals include doxycycline, colistin sulfate, neomycin, tetracycline, enrofloxacin, ciprofloxacin, and amikacin (Apata, 2009; Roess et al., 2013). There is always a possibility for these antibiotic residues to gain access to the consumers' food products and the human food chain. Poor record keeping can exacerbate the problem, when farmers sell their animals and products of animal origin without having records indicating the completion of the specified withdrawal periods.

4.2. Non-judicial use of antibiotics in the poultry, livestock, and fish production systems can exacerbate the antibiotic residue accumulation problem

The unregulated accessibility of farmers to antimicrobial agents poses a serious risk for the development of antimicrobial resistance. This is especially problematic in areas where there is scarcity of authorized veterinarians, such as in remote and rural areas. In addition, antibiotics are readily available to the farmers in retail drug stores in Bangladesh without prescription by registered veterinarians or authorized personnel. Such practice is prevalent throughout the country and has led to the misuse of antibiotics with the associated high prevalence of antibiotic resistance in bacteria from animal and food sources. Commercial poultry farmers in Bangladesh use antibiotics indiscriminately without any prescription or veterinary consultation. Several factors including the lack of knowledge among local farmers, lack of proper veterinary services in rural and remote areas, and the lure of higher profits collectively contribute to the problem (Redding et al., 2013). Antibiotics in the growth promoting category are, in some cases, the same antibiotics used in the therapeutic category. The decision to use growth-promoting antibiotics in commercial poultry is mainly an economic decision that is made by the farmers (Al Masud et al., 2020). Farmers depend on antibiotics and believe that using different types of antibiotics will keep their farm animals healthier and more productive. Farmers are not well-informed about the risks associated with the abuse of antibiotics and the potential deleterious impacts of this practice on public health. Medical representatives of pharmaceutical companies also share some responsibility for this problem as they have to fulfill their monthly target of selling a certain amount of their products (Guha, 2004; Masood et al., 2009), and it was observed that they try to convince farmers to directly use antimicrobial agents in regular schedules in order to prevent diseases, especially in poultry farms (personal communications).

Medical representatives of human medicines frequently do the same with physicians in the country, trying to convince them to prescribe more antibiotics (Habib & Alam, 2011; D'Arcy & Moynihan, 2009).

In Bangladesh, only a few companies indicate the withdrawal period of their product on their drug labels and inserts, which can increase the residue accumulation risk. Finally, there is a lack of serious enforcement of rules that prevent the abuse of antibiotics and the consumption of foods that have antimicrobial residues (Apata, 2009). Altogether, these factors all contribute to the problem in Bangladesh and other countries.

4.3. The antimicrobial residues in food sources (milk, meat, eggs, fish) can lead to the evolution of resistant pathogens

The possible effects of widespread use of antibiotics in poultry, livestock, and aquaculture production have been reported elsewhere (Marshall & Levy, 2011). The use of antibiotics can lead to the entry of such drugs into the human food chain in the form of drug residues in animal source foods including meat, milk, eggs and fishes. This can occur when withdrawal periods are not maintained before selling animal products for human consumption. This practice may lead to lowering the efficacy of antibiotics when used for treatment of human diseases. Moreover, extensive antibiotic usage can also lead to the emergence of antibiotic-resistant bacterial strains with the possibility of transfer of resistant genes to other pathogenic and nonpathogenic bacteria (Peterson & Kaur, 2018) or to the human food chain (Smith, 1969). Humans can thus acquire antibiotic resistant bacteria following consumption of poultry, livestock, and fish products. Antibiotic resistance against human pathogens is now a major global public health issue (Martínez-Martínez & Calvo, 2010). There is an evident association between antibiotic use in animals and the development of resistance in human pathogens as was previously reported (Hoelzer et al., 2017; Landers et al., 2012; Wegener, 2012). Evidently, the use of antibiotics in livestock production has been associated with the development of antibiotic resistance in humans. The development of resistance in several microorganisms due to the use of sub-therapeutic concentrations of penicillin, tetracyclines, and sulfa drugs in the agricultural industry has been highlighted as a problem by the World Health Organization (Landers et al., 2012; Prajwal et al., 2017). The ability of tetracycline resistance to persist for a long period of time after the withdrawal period was previously reported (Grossman, 2016).

4.4. Practices that promote the spread of resistant bacteria to different components of the agricultural production system

Herds and flocks that have been treated with tetracycline and aminoglycosides might show widespread transmission of resistance genes or resistant pathogens. In case of the aquaculture industry, resistant pathogens have evolved via antibiotic use in feed additives, poultry offal, and litter which had an impact on fish in different water bodies. The contamination of water with antibiotic-contaminated waste and effluents from both veterinary practices and human hospitals may lead to antimicrobial residue deposition in water, which can subsequently transmit resistant bacteria to different components of the agricultural production system (Manyi-Loh et al., 2018). Vancomycin-resistant enterococci readily detected in healthy human fecal material is the ultimate result of the use of avoparcin in pig industry (Van den Bogaard et al., 2002). Avoparcin withdrawal has been successful in reducing vancomycin-resistant enterococci contamination in pork (Nilsson, 2012). Antibiotic resistance genes may be transferred from animal pathogens or commensals to human pathogens (Argudín et al., 2017; Blake et al., 2003; von Wintersdorff et al., 2016). Resistant bacteria with similar resistance genes and patterns in both animals and of humans were previously reported (Ahmed et al., 2019; Marshall & Levy, 2011; Wegener, 2012). It is evident that resistant bacteria with the same resistance patterns and/or of the same genotype in food are also increasing. There are possible *One Health* components that might contribute to the spread of resistant genes or bacteria through the human food chain (Ashour, 2014; Asante et al., 2019 Khan et al., 2020). Interestingly, the antimicrobial residues deposited into the fish bodies can also be transferred to the human food chain, an observation that was previously made for ampicillin and olaquindox (Smith, 1969). The MRLs of oxytetracycline for poultry liver, eggs, and milk were 0.06 mg/kg, 0.04 mg/kg, and 0.01 mg/L, respectively, whereas the MRLs for colistin sulfate were 0.015 mg/kg and 0.03 mg/kg for poultry liver and eggs, respectively (Food and Agricultrual Organization of the United Nations, 2018; Health Canada Government of Canada, 2017). The current study

identified antimicrobial residue concentrations that are higher than the MRL for most of the antimicrobial agents. Existence of chloramphenicol residues in food of animal origin is an indication of a public health problem (Davies & Wales, 2019). The dynamics of the flow of antimicrobial residues to humans is summarized in Fig. 3.

Food-producing animals may receive antimicrobial agents directly as a treatment or in the feed as growth promoters. Some antimicrobial residues can remain in the food products if the withdrawal period of a specific antimicrobial agent was not maintained during human consumption of the animal-derived food products.

On the other hand, the effluents from medical hospitals and veterinary practices can indirectly contaminate water bodies in which fish is raised leading to the presence of antimicrobial residues in fish, which can then be consumed by humans.

5. Interventions and suggestions

Based on this study, we recommend the judicial use of antimicrobials in food-producing animals and to only administer antimicrobials to the food-producing animals when prescribed by registered health professionals. In addition, it is important to maintain withdrawal periods after antibiotic treatments and to discard the products for human consumption before the end of the withdrawal period. Furthermore, the use of antimicrobials as food additives in food-producing animals including fish should be restricted. We recommend against the use of poultry offal, litters, and livestock waste in aquacultures. Human and veterinary hospital effluents should be stopped from reaching aquatic environments without proper sewage treatment. Finally, there should be investment in improved animal husbandry to reduce the antimicrobial growth promoter use without losing revenue.

It is noteworthy that there is limited data on antimicrobial residue concentrations in foods originating from livestock and aquaculture. Some studies tested only a few antimicrobial agents or included a few animal species such as domestic poultry, broiler and layer chickens, fish, and shrimp.

6. Conclusions

In summary, residual antimicrobial agents in food products from animal sources including but not limited to meat, milk, egg, fish and shrimp pose the risk of inducing the development of antimicrobial resistance. The high residue concentrations might be the result of the indiscriminate use of antimicrobials in the agricultural production systems or an inappropriate withdrawal period. The residual antimicrobial agents can then be transferred to the human food chain causing further enhancement of resistance genes in human pathogens, and the potential development of antimicrobial resistance. Farmers need to adhere to the guidelines from health professionals, including guidelines on the prudent use of antimicrobials and observing the withdrawal periods. We recommend the removal (banning) of poultry offal and other livestock waste from the aquaculture industry. Following the appropriate guidelines and protocols will eventually limit the presence of antimicrobial residues in animal-derived food products and the development of antimicrobial resistance which will reduce the risk to the public. This will also support the food supply chain, which has been severely affected by the ongoing COVID-19 pandemic.

Declaration of competing interest

No conflict of interest.

Acknowledgment

Disclaimer

Any opinions, findings, conclusions or recommendations expressed in this manuscript are those of the authors and do not necessarily reflect the views of the funding agencies.

References

Ahaduzzaman, M., Hassan, M. M., Alam, M., Islam, S., & Uddin, I. (2014). Antimicrobial resistance pattern against Staphylococcus aureus in environmental effluents. *Research Journal for Veterinary Practitioners, 2*, 13–16.

Ahiabu, M. A., Tersbol, B. P., Biritwum, R., Bygbjerg, I. C., & Magnussen, P. (2016). A retrospective audit of antibiotic prescriptions in primary health-care facilities in Eastern Region, Ghana. *Health Policy and Planning, 31*, 250–258. https://doi.org/10.1093/heapol/czv048

Ahmed, N., Demaine, H., & Muir, J. F. (2008). Freshwater prawn farming in Bangladesh: History, present status and future prospects. *Aquaculture Research, 39*, 806–819.

Ahmed, I., Rabbi, M. B., & Sultana, S. (2019). Antibiotic resistance in Bangladesh: A systematic review. *International Journal of Infectious Diseases, 80*, 54–61.

Al Masud, A., Rousham, E. K., Islam, M. A., Alam, M.-U., Rahman, M., Al Mamun, A., Sarker, S., Asaduzzaman, M., & Unicomb, L. (2020). Drivers of antibiotic use in poultry production in Bangladesh: Dependencies and dynamics of a patron-client relationship. *Frontiers in Veterinary Science, 7*.

Al-Tawfiq, J. A., Stephens, G., & Memish, Z. A. (2010). Inappropriate antimicrobial use and potential solutions: A middle eastern perspective. *Expert Rev Anti Infect Ther, 8*, 765–774. https://doi.org/10.1586/eri.10.56

Apata, D. (2009). Antibiotic resistance in poultry. *International Journal of Poultry Science, 8*, 404–408.

Argudín, M. A., Deplano, A., Meghraoui, A., Dodémont, M., Heinrichs, A., Denis, O., Nonhoff, C., & Roisin, S. (2017). Bacteria from animals as a pool of antimicrobial resistance genes. *Antibiotics, 6*, 12.

Asante, J., Noreddin, A., & El Zowalaty, M. E. (2019). Systematic review of important bacterial zoonoses in Africa in the last decade in light of the "One Health" concept. *Pathogens, 8*(2). https://doi.org/10.3390/pathogens8020050. In this issue.

Ashour, H. M. (2014). One health—people, animals, and the environment. *Clinical Infectious Diseases, 59*(10), 1510-1510.

Bakar, M., Morshed, A., Islam, F., & Karim, R. (2013). Screening of chloramphenicol residues in chickens and fish in Chittagong city of Bangladesh. *Bangladesh Journal of Veterinary Medicine, 11*, 173–175.

Barman, A. K. A., Hossain, M. M., Rahim, M. M., Hassan, M. T., & Begum, M. (2018). Oxytetracycline residue in Tilapia. *Bangladesh Journal of Scientific & Industrial Research, 53*, 41–46. https://doi.org/10.3329/bjsir.v53i1.35909

van Bijnen, E. M., den Heijer, C. D., Paget, W. J., Stobberingh, E. E., Verheij, R. A., Bruggeman, C. A., Pringle, M., Goossens, H., & Schellevis, F. G. (2011). The appropriateness of prescribing antibiotics in the community in europe: Study design. *BMC Infectious Diseases, 11*, 293. https://doi.org/10.1186/1471-2334-11-293

Blake, D., Hillman, K., Fenlon, D., & Low, J. (2003). Transfer of antibiotic resistance between commensal and pathogenic members of the Enterobacteriaceae under ileal conditions. *Journal of Applied Microbiology, 95*, 428–436.

Boeckel, T. P. V., Brower, C., Gilbert, M., Grenfell, B. T., Levin, S. A., Robinson, T. P., … Laxminarayan, R. (2015). Global trends in antimicrobial use in food animals. *Proceedings of the National Academy of Sciences of the United States of America, 112*(18), 5649–5654. https://doi.org/10.1073/pnas.1503141112

Bristy, N. I., Das, S., Noman, Z.a., Ferdous, J., Sachi, S., Kabir, S. M. L., & Sikder, M. H. (2019). Colistin residue in broiler: Detection in different growth stages. *Asian-Australasian Journal of Food Safety and Security, 3*, 43–47.

Buke, A. C., Ermertcan, S., Hosgor-Limoncu, M., Ciceklioglu, M., & Eren, S. (2003). Rational antibiotic use and academic staff. *International Journal of Antimicrobial Agents, 21*, 63–66.

Center for Veterinary Medicine, & US Food and Drug Adminstration, MD, USA.. (2017). Summary report on antimicrobials sold or distributed for use in food-producing animals. https://www.fda.gov/media/119332/download. (Accessed 1 March 2020).

Chowdhury, M. H., Islam, K., & Khaleduzzaman, A. (2009). A review on antibiotics in an animal feed. *Bangladesh Journal of Animal Science, 38*, 22–32.

Chowdhury, S., Hassan, M. M., Alam, M., Sattar, S., Bari, M. S., Saifuddin, A. K. M., & Hoque, M. A. (2015). Antibiotic residues in milk and eggs of commercial and local farms at Chittagong, Bangladesh. *Veterinary World, 8*, 467–471. https://doi.org/10.14202/vetworld.2015.467-471

Costelloe, C., Metcalfe, C., Lovering, A., Mant, D., & Hay, A. D. (2010). Effect of antibiotic prescribing in primary care on antimicrobial resistance in individual patients: Systematic review and meta-analysis. *BMJ, 340*, c2096. https://doi.org/10.1136/bmj.c2096

D'Arcy, E., & Moynihan, R. (2009). Can the relationship between doctors and drug companies ever be a healthy one? *The International Journal of Risk and Safety in Medicine, 21*, 185–191.

Das, M., Islam, M., Akter, T., Kawser, A., & Mondal, M. (2018). Present status, problems and prospect of fish farming at Gazipur Sadar upazila in Bangladesh. *Progressive Agriculture, 29*, 53–63.

Davies, R., & Wales, A. (2019). Antimicrobial resistance on farms: A review including biosecurity and the potential role of disinfectants in resistance selection. *Comprehensive Reviews in Food Science and Food Safety, 18*, 753–774.

Department of Livestock Service. Bangladesh. Livestock economy at a glance. http://dls.portal.gov.bd/sites/default/files/files/dls.portal.gov.bd/page/ee5f4621_fa3a_40ac_8bd9_898fb8ee4700/Livestock%20Economy%20at%20a%20glance%20%20%282017-2018%29.pdf. (Accessed 19 February 2020).

Ferdous, J., Bradshaw, A., Islam, S. A., Zamil, S., Islam, A., Ahad, A., Fournie, G., Anwer, M. S., & Hoque, M. A. (2019). Antimicrobial residues in chicken and fish, chittagong, Bangladesh. *EcoHealth, 16*, 429–440.

Ferech, M., Coenen, S., Malhotra-Kumar, S., Dvorakova, K., Hendrickx, E., Suetens, C., Goossens, H., & Group, E. P. (2006). European surveillance of antimicrobial consumption (ESAC): Outpatient antibiotic use in europe. *Journal of Antimicrobial Chemotherapy, 58*, 401–407. https://doi.org/10.1093/jac/dkl188

Food and Agricultrual Organization of the United Nations. (2018). Maximum residue limits (MRLs) and risk management recommendations (RMRs) for residues of veterinary drugs in foods. http://www.fao.org/fao-who-codexalimentarius/sh-proxy/en/?lnk=1&url=https%3A%252F%252Fworkspace.fao.org%252Fsites%252Fcodex%252FStandards%252FCXM%2B2%252FMRL2e.pdf, 8.

Grossman, T. H. (2016). Tetracycline antibiotics and resistance. *Cold Spring Harbor perspectives in medicine, 6*(4), a025387. https://doi.org/10.1101/cshperspect.a025387

Guha, A. (2004). A comparison of codes of pharmaceutical marketing practices. *Indian journal of medical ethics, 1*, 19–21.

Gustafson, R., & Bowen, R. (1997). Antibiotic use in animal agriculture. *Journal of Applied Microbiology, 83*, 531–541.

Habib, M. A., & Alam, M. Z. (2011). Business analysis of pharmaceutical firms in Bangladesh: Problems and prospects. *Journal of Business and Technology (Dhaka), 6*, 61–77.

Hasan, B., Faruque, R., Drobni, M., Waldenström, J., Sadique, A., Ahmed, K. U., … Alam, M. (2011). High prevalence of antibiotic resistance in pathogenic *Escherichia coli* from large-and small-scale poultry farms in Bangladesh. *Avian Diseases, 55*, 689–692.

Hasan, B., Sandegren, L., Melhus, Å., Drobni, M., Hernandez, J., Waldenström, J., … Olsen, B. (2012). Antimicrobial drug–resistant *Escherichia coli* in wild birds and free-range poultry, Bangladesh. *Emerging Infectious Diseases, 18*, 2055.

Hassan, M., Ahaduzzaman, M., Alam, M., Bari, M., Amin, K., & Faruq, A. (2015). Antimicrobial resistance pattern against *E. coli* and *Salmonella* spp. in environmental effluents. *International Journal of Natural Sciences, 5*, 52–58.

Hassan, M., Amin, K. B., Ahaduzzaman, M., Alam, M., Faruk, M. S., & Uddin, I. (2014). Antimicrobial resistance pattern against *E. coli* and *Salmonella* in layer poultry. *Research Journal for Veterinary Practitioners, 2*, 30–35.

Health Canada Government of Canada. (2017). *List of maximum residue limits (MRLs) for veterinary drugs in foods*. Ontario, Canada: Health Canada Ottawa. https://www.canada.ca/content/dam/hc-sc/migration/hc-sc/dhp-mps/alt_formats/pdf/vet/mrl-lmr/mrl-lmr_versus_new-nouveau-20170802-eng.pdf.

Hoelzer, K., Wong, N., Thomas, J., Talkington, K., Jungman, E., & Coukell, A. (2017). Antimicrobial drug use in food-producing animals and associated human health risks: What, and how strong, is the evidence? *BMC Veterinary Research, 13*, 211.

Hossain, M. M., Barman, A. A., Rahim, M. M., Hassan, M. T., Begum, M., & Bhattacharjee, D. (2018). Oxytetracycline residues in Thai pangas *Pangasianodon hypophthalmus* sampled from Sylhet sadar upazila, Bangladesh. *Bangladesh Journal of Zoology, 46*, 81–90.

Islam, A., Saifuddin, A., Al Faruq, A., Islam, S., Shano, S., Alam, M., & Hassan, M. M. (2016). Antimicrobial residues in tissues and eggs of laying hens at Chittagong, Bangladesh. *International Journal One Health, 2*, 75–80.

Khan, M., Ferdous, J., Ferdous, M., Islam, M., Rafiq, K., & Rima, U. (2018). Study on indiscriminate use of antibiotics in poultry feed and residues in broilers of Mymensingh city in Bangladesh. *Progressive Agriculture, 29*, 345–352.

Khan, S. A., Shawn, A. I., Syeed, A., Shaikat, A. H., & Hassan, M. M. (2020). Antimicrobial Resistance Pattern in Domestic Animal- Wildlife- Environmental niche via the food chain to humans with a Bangladesh perspective; A systematic review. *BMC Veterinary Research, 16*(1), 302.

Krauß, J., van der Linden, M., Grebe, T., & Hakenbeck, R. (1996). Penicillin-binding proteins 2x and 2b as primary PBP targets in Streptococcus pneumoniae. *Microbial Drug Resistance, 2*, 183–186.

Kundu, G. K., Alauddin, M., Akter, M. S., Khan, M. S., Islam, M. M., Mondal, G., Islam, D., Mohanta, L. C., & Huque, A. (2017). Metal contamination of commercial fish feed and quality aspects of farmed tilapia (Oreochromis niloticus) in Bangladesh. *Bioresearch Communications, 3*, 345–353.

Landers, T. F., Cohen, B., Wittum, T. E., & Larson, E. L. (2012). A review of antibiotic use in food animals: Perspective, policy, and potential. *Public Health Reports, 127*, 4–22.

Liberati, A., Altman, D. G., Tetzlaff, J., Mulrow, C., Gotzsche, P. C., Ioannidis, J. P. A., … Moher, D. (2009). The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: Explanation and elaboration. *PLoS Medicine, 6*, W49–W65.

Liu, Y. C., Huang, W. K., Huang, T. S., & Kunin, C. M. (1999). Extent of antibiotic use in Taiwan shown by antimicrobial activity in urine. *Lancet, 354*, 1360. https://doi.org/10.1016/S0140-6736(99)07446-2

Manyi-Loh, C., Mamphweli, S., Meyer, E., & Okoh, A. (2018). Antibiotic use in agriculture and its consequential resistance in environmental sources: Potential public health implications. *Molecules, 23*, 795.

Marshall, B. M., & Levy, S. B. (2011). Food animals and antimicrobials: Impacts on human health. *Clinical Microbiology Reviews, 24*, 718–733.

Martínez-Martínez, L., & Calvo, J. (2010). The growing problem of antibiotic resistance in clinically relevant gram-negative bacteria: Current situation. *Enfermedades Infecciosas Y Microbiologia Clinica, 28*, 25–31.

Masood, I., Ibrahim, M., Hassali, M., & Ahmed, M. (2009). Evolution of marketing techniques, adoption in pharmaceutical industry and related issues: A review. *Journal of Clinical and Diagnostic Research, 3*, 1942–1952.

Mather, A. E., Matthews, L., Mellor, D. J., Reeve, R., Denwood, M. J., Boerlin, P., … Reid, S. W. J. (2012). An ecological approach to assessing the epidemiology of antimicrobial resistance in animal and human populations. *Proceedings of the Royal Society B: Biological Sciences, 279*, 1630–1639. https://doi.org/10.1098/rspb.2011.1975

Mathews, J., Kenneth, H., Bernstein, J., & Buzby, J. C. (2003). International trade of meat/poultry products and food safety issues. *International trade and food safety: Economic Theory and Case Studies*, 48–73.

McEwen, S. A. (2006). Antibiotic use in animal agriculture: What have we learned and where are we going? *Animal Biotechnology, 17*, 239–250.

Ministry of Fisheries and Livestock. Chapter-10: Ministry of fisheries and livestock accessed on 03-03-2020 https://mof.gov.bd/sites/default/files/files/mof.portal.gov.bd/budget_mof/d9f53c16_c377_420a_9ba4_271ef1396986/G-1_09_144_Fisheries_English.pdf.

Molbak, K. (2004). Spread of resistant bacteria and resistance genes from animals to humans–the public health consequences. *Journal Vet Medicine B Infect Dis Vet Public Health, 51*, 364–369. https://doi.org/10.1111/j.1439-0450.2004.00788.x

Nilsson, O. (2012). Vancomycin resistant Enterococci in farm animals–occurrence and importance. *Infection Ecology & Epidemiology, 2*, 16959.

Nonga, H. E., Simon, C., Karimuribo, E. D., & Mdegela, R. H. (2010). Assessment of antimicrobial usage and residues in commercial chicken eggs from smallholder poultry keepers in Morogoro municipality, Tanzania. *Zoonoses Public Health, 57*, 339–344. https://doi.org/10.1111/j.1863-2378.2008.01226.x

Parker, D., & Armstrong, D. (1987). Antibiotic feed additives and livestock production. *Proceedings of the Nutrition Society, 46*, 415–421.

Peterson, E., & Kaur, P. (2018). Antibiotic resistance mechanisms in bacteria: Relationships between resistance determinants of antibiotic producers, environmental bacteria, and clinical pathogens. *Frontiers in Microbiology, 9*, 2928.

Prajwal, S., Vasudevan, V., Sathu, T., Irshad, A., Nayankumar, S., & Pame, K. (2017). Antibiotic residues in food animals: Causes and health effects. *The Pharma Innovation J, 6*, 1–4.

Prescott, J. F. (2017). History and current use of antimicrobial drugs in veterinary medicine. *Microbiology Spectrum, 5*. https://doi.org/10.1128/microbiolspec.ARBA-0002-2017

Rassow, D., & Schaper, H. (1996). The use of feed medications in swine and poultry facilities in the Weser-Ems region. *DTW. Deutsche tierarztliche Wochenschrift, 103*, 244–249.

Redding, L., Barg, F., Smith, G., Galligan, D., Levy, M., & Hennessy, S. (2013). The role of veterinarians and feed-store vendors in the prescription and use of antibiotics on small dairy farms in rural Peru. *Journal of Dairy Science, 96*, 7349–7354.

Roess, A. A., Winch, P. J., Ali, N. A., Akhter, A., Afroz, D., El Arifeen, S., Darmstadt, G. L., Baqui, A. H., & Group, B. P. S. (2013). Animal husbandry practices in rural Bangladesh: Potential risk factors for antimicrobial drug resistance and emerging diseases. *The American Journal of Tropical Medicine and Hygiene, 89*, 965–970.

Roura, E., Homedes, J., & Klasing, K. C. (1992). Prevention of immunologic stress contributes to the growth-permitting ability of dietary antibiotics in chicks. *Journal of Nutrition, 122*, 2383–2390.

Sachi, S., Ferdous, J., Sikder, M. H., & Hussani, S. A. K. (2019). Antibiotic residues in milk: Past, present, and future. *Journal of advanced veterinary and animal research, 6*, 315.

Sarker, Y. A., Hasan, M. M., Paul, T. K., Rashid, S. Z., Alam, M. N., & Sikder, M. H. (2018). Screening of antibiotic residues in chicken meat in Bangladesh by thin layer chromatography. *Journal of Advanced Veterinary and Animal Research, 5*, 140–145.

Sattar, S., Hassan, M. M., Islam, S., Alam, M., Al Faruk, M. S., Chowdhury, S., & Saifuddin, A. (2014). Antibiotic residues in broiler and layer meat in Chittagong district of Bangladesh. *Veterinary World, 7*.

Smith, H. W. (1969). Transfer of antibiotic resistance from animal and human strains of *Escherichia coli* to resident *E. coli* in the alimentary tract of man. *The Lancet, 293*, 1174–1176.

Tollefson, L., & Miller, M. A. (2000). Antibiotic use in food animals: Controlling the human health impact. *Journal of AOAC International, 83*, 245–254.

Vaananen, M. H., Pietila, K., & Airaksinen, M. (2006). Self-medication with antibiotics–does it really happen in Europe? *Health Policy, 77*, 166–171. https://doi.org/10.1016/j.healthpol.2005.07.001

Van den Bogaard, A., Willems, R., London, N., Top, J., & Stobberingh, E. (2002). Antibiotic resistance of faecal Enterococci in poultry, poultry farmers and poultry slaughterers. *Journal of Antimicrobial Chemotherapy, 49*, 497–505.

Vázquez-Moreno, L., Bermúdez A, M., Langure, A., Higuera-Ciapara, I., Aguayo, M., & Flores, E. (1990). Antibiotic residues and drug resistant bacteria in beef, and chicken tissues. *Journal of Food Science, 55*, 632–634.

Wassenaar, T. M. (2005). Use of antimicrobial agents in veterinary medicine and implications for human health. *Critical Reviews in Microbiology, 31*, 155–169. https://doi.org/10.1080/10408410591005110

Wegener, H. C. (2012). Antibiotic resistance—linking human and animal health. In , A15. *Institute of medicine (US). Improving food safety through a one health approach: Workshop summary* (pp. 331–349). Washington (DC): National Academies Press (US).

von Wintersdorff, C. J., Penders, J., van Niekerk, J. M., Mills, N. D., Majumder, S., van Alphen, L. B., Savelkoul, P. H., & Wolffs, P. F. (2016). Dissemination of antimicrobial resistance in microbial ecosystems through horizontal gene transfer. *Frontiers in Microbiology, 7*, 173.

You, J. H., Yau, B., Choi, K. C., Chau, C. T., Huang, Q. R., & Lee, S. S. (2008). Public knowledge, attitudes and behavior on antibiotic use: A telephone survey in Hong Kong. *Infection, 36*, 153–157. https://doi.org/10.1007/s15010-007-7214-5