International Journal of One Health
Available at www.onehealthjournal.org/Vol.9/No.2/16.pdf

REVIEW ARTICLE
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Integration of water, sanitation, and hygiene program with biosecurity: A One Health approach to reduce the prevalence and exposure of antibiotic-resistant bacteria in the livestock community

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Received: 18-08-2023, **Accepted:** 05-12-2023, **Published online:** 28-12-2023

doi: www.doi.org/10.14202/IJOH.2023.181-193 **How to cite this article:** Paramitadevi YV, Priadi CR, Rahmatika I, Rukmana A, and Moersidik SS (2023) Integration of water, sanitation, and hygiene program with biosecurity: A One Health approach to reduce the prevalence and exposure of antibiotic-resistant bacteria in the livestock community, *Int. J. One Health*, 9(2): 181–193.

Abstract

The global spread of antibiotic resistance poses a significant threat to public health and is one of the main causes of this problem. Livestock farming plays a significant role in the horizontal and vertical transmission of treatment-resistant genes and bacteria. These processes involve contact with agricultural products and the environment, raising concerns for public health, and farming communities. The farming community is composed of a staggering 608 million farms worldwide, and their livelihood depends heavily on livestock farming. To address this issue, a multidisciplinary One Health approach focusing on integrated monitoring and intervention for humans, animals, and the environment is essential. Water, sanitation, and hygiene (WaSH) programs have the potential to significantly reduce the risk of exposure to antibiotic-resistant bacteria, particularly extended spectrum beta-lactamase (ESBL) *Escherichia coli*, by obstructing the transmission route between humans and animals. Additional risk reduction measures for ESBL *E. coli* infection in animals include vaccination and biosecurity program implementation. Water, sanitation, and hygiene and biosecurity measures must be combined to maximize the effectiveness of the One Health program. Therefore, this study aimed to describe recent advances in biosecurity and WaSH interventions in the livestock environment, analyze the effects of these interventions on human and animal health, and investigate potential future scenarios within the quantitative microbial risk assessment framework. This study used an integrative literature review through searches of four databases, a review of World Health Organization documents through websites, and an examination of relevant texts from previously obtained reference lists. Although hygiene and sanitation are often combined, there is still a lack of quantitative evaluation of the efficacy of integrating WaSH with biosecurity in livestock. In addition, the integration of the WaSH program with biosecurity has potential as a One Health intervention in the coming years.

Keywords: antibiotic-resistant bacteria, biosecurity, extended-spectrum beta-lactamase *Escherichia coli*, One Health, scenario, water, sanitation, and hygiene.

Introduction

In recent decades, the emergence and spread of antimicrobial resistance (AMR) has become a significant threat to the health of people, animals, plants, and the environment [1]. Antibiotic-resistant bacteria (ARBs) are expected to be responsible for 1.27 million fatalities in 2019 [2], demonstrating the devastating effects of AMR. At present, the transmission of AMR extends beyond clinical and pharmaceutical settings and penetrates the agricultural sector, particularly livestock farming. This sector is of great concern because the horizontal and vertical transmission of ARB and antibiotic resistance genes (ARGs) occurs through contact with agricultural products and the environment [3, 4], leading to various diseases in humans. The main routes of transmission to the human digestive system include oral, skin, and inhalation [5]. The oral route is predominant, usually facilitated by contaminated livestock manure [6] and water polluted with wastewater [7]. As soon as an ARB enters the human body, subsequent colonization and infection can lead to severe disease. Consumption of antibiotics by livestock was positively correlated with the presence of ARB in humans (1.07 [CI 95% = 1.01–1.13], p = 0.020) [8]. Extended Spectrum beta-lactamase (ESBL) *Escherichia coli* is a critically resistant bacterium recommended for in-depth research by the World Health Organization (WHO) [9, 10] due to its ability to cause fatal prolonged diarrhea [11].

The livestock sector accounts for 40% and 20% of developed and developing countries, respectively, with 608 million farms worldwide [12]. Therefore, farmers are highly vulnerable to AMR exposure, which can be influenced by risk factors, such as hazards, transmission routes, and other determinants, often applied in the pathogen mapping process [13]. The most frequent risks include improper use of agents, poor water, sanitation, and hygiene (WaSH) infrastructure, and insufficient measures for infection control and prevention [14]. Pathway factors encompass types of agriculture, environmental routes, and antibiotic consumption [15], whereas indirect factors include urbanicity and multidimensional wealth index [16].

The WHO, OIE, FAO, and UNEP have established the One Health policy to combat the spread of AMR. This policy aims to achieve holistic health for humans, animals, and surrounding plants [17] through comprehensive transmission analysis, integrated surveillance, interventions, behavioral changes, and economic policies [18]. Biosecurity measures, including restrictions on antibiotic prescriptions and vaccinations, are currently applied in the livestock sector to reduce the risk of AMR transmission. From a medical point of view, biosecurity encompasses cross-sectoral areas such as the prevention of zoonosis, food safety, plant health, animal and plant biosafety, and invasive species control. In the livestock sector, biosecurity programs are the first line of disease control measures and are usually implemented within specific areas of concern [19]. However, there have been limitations, such as inadequate implementation on large farms and lack of stakeholder engagement opportunities [20].

In the field of environmental engineering, WaSH approaches, such as clean water supply, regular water quality checks, periodic cleaning of animal pens, and handwashing practices, are promising for reducing the risk of AMR. This program has been effectively implemented in domestic environments [21, 22], schools [23], and healthcare facilities [24–26]. The World Health Organization and UNICEF launched a monitoring strategy for the 2030 Agenda for Sustainable Development Goal 6, which aims to provide water for all. However, it has not yet been extended to the livestock industry [27]. In view of the urgency of the One Health program to combat AMR, the integration of WaSH and biosecurity programs has significant potential for infection prevention in livestock areas. In view of the close links between people, animals, and the environment in these places, this integration is crucial.

The proposed WaSH program to minimize the spread of AMR in livestock environments [28] remains largely conceptual. On the other hand, the implementation of biosecurity measures to combat AMR remains limited, especially in developed countries [29, 30], due to their complexity. Recently, integrating WaSH with biosecurity has emerged as a means [20, 31] of enhancing control within the One Health program. This review, based on the principles of WaSH and biosecurity, aimed to (1) provide an overview of the global prevalence of ARB, specifically ESBL *E. coli*, (2) describe recent advancements in WaSH and biosecurity interventions in livestock environments within the context of One Health, (3) assess the effects of these interventions on human and animal health, and (4) explore potential future scenarios on quantitative microbial risk assessment (QMRA). Moreover, it emphasizes the examination of sanitation and water elements at points (2) and (3), focusing on environmental engineering aspects of livestock that have not been extensively discussed in the previous research.

Review Method

The literature search was limited to 2007–2022, which encompasses extensive studies conducted on ARBs in livestock over the past decade. The keywords "livestock AND hygiene" and "livestock AND sanitation" were used to search the Scopus, EMBASE, PubMed, and AGRIS. In addition, publications on the WHO website featuring the latest developments in antibiotic resistance was examined. To commence text synthesis, the acquired literature was collated in the Zotero library.

Inclusion criteria, including studies published in English pertaining to animal husbandry and an explanation on hygiene, sanitation, and biosecurity aligned with the objectives of the study, were used to facilitate the text synthesis. This review included 67 studies, including research papers and WHO publications.

Each study was subjected to a rigorous review process and data extraction was performed on elements related to the size of the intervention. Subsequently, the data were grouped and synthesized based on categories such as resistance tendency of *E. coli* to antibiotics, quantitative value of existing interventions, and direction of future interventions.

Worldwide Prevalence of ESBL *E. coli* in Livestock

Extended-spectrum beta-lactamase *E. coli* from livestock and the surrounding environment can be transmitted to humans through both horizontal and vertical mechanisms, with the horizontal mode being more common [32]. Complex horizontal transmission through ARGs occurs mostly in humans, animals, and the environment [33]. In addition, vertical transmission includes the spread of ARB in the same agricultural area or between farms. The transfer process facilitated by ARGs is more common in plasmids, such as transposons, gene cassettes, and integrons than in mobile genetic elements (MGEs) [34].

In 2019, the highest number of projected deaths due to AMR was observed in South Asia, reaching 389,000 cases, with a global disease burden of 619 disability-adjusted life year per 100,000 individuals [2]. These projections were calculated using statistical predictive models based on collected secondary data on sepsis, infection syndromes, case-fatality ratios, pathogen distribution, antibiotic use, resistance prevalence, resistance profiles, relative risk of death, and relative length of hospital stay. Surveillance data are crucial to obtain accurate AMR disease burden values. In livestock environments, AMR surveillance data are primarily obtained through the prevalence of ESBL *E. coli* against one or more antibiotics. Extended Spectrum beta-lactamase *E. coli* testing involves sampling from various sources, including pooled fecal materials, cloacal swabs, feed items, and environmental samples, such as soil, compost products, sewage water, and digester output. Several non-standardized laboratory analysis techniques, such as conventional culture, antibiotic susceptibility testing, microdilution broth, molecular quantitative polymerase chain reaction, whole-genome sequencing techniques, and combinations of conventional and molecular methods, are often employed during the estimation process.

The use of antimicrobials in agricultural activities, such as incorporating antimicrobials into feed, administering antibiotics to animals, and implementing biosecurity measures in the farm area, affects the prevalence of ESBL *E. coli*. As a result, there are differences in the number of ESBL *E. coli* identified on farms between countries [32]. This differs between livestock species, with poultry farms generally having a higher prevalence than ruminants [33].

A comparison of ESBL *E. coli* prevalence between developed and developing countries should be performed with caution. For example, ESBL *E. coli* has been reported at a rate of 39% in Canadian cattle farms [35], whereas pig farms in the United Kingdom reported only 2% [36]. In Italy, the prevalence was 23.3% [37], whereas in France, the prevalence was 5%, and in Japan, it reached 5.2% [38]. In Africa, fecal samples of Ethiopian cattle have a higher prevalence (52%) [39], whereas broiler farms in Zambia have reported lower values [40]. Pig farms in Nigeria recorded 41.2% [41], Cameroon recorded 59.1% [42], and Kenya had the highest value at 81% [43]. In Asia, India reported an occurrence rate of up to 75% [44], whereas Qatar reported 18% [45]. In Indonesia, 35.7% of broiler farms [46] and 52% in Sri Lanka [47] were detected. A study [48] found a greater incidence of ESBL *E. coli* (16.8%) in water samples bathed by buffaloes compared to water used for bathing, washing, and community sanitation.

The prevalence of multidrug-resistant (MDR) *E. coli* has been observed in Asia [49–54], Africa [55–58], and four European countries [59], with varied rates and resistance to more than four types of medicines. Further research is required to understand the transmission mechanism of MDR *E. coli* within agricultural contexts and the risk variables that affect temporal changes.

Water, Sanitation, and Hygiene and Biosecurity Measures in Livestock Environments in the Context of One Health

One Health approach balances human, animal, plant, and ecosystem health. Over the past decade, the implementation of this program has involved cooperation between veterinarians and cross-governmental, multi-sectoral, and environmental experts. In Africa, 21 countries have formed a One Health platform to facilitate resource sharing and evaluate One Health activities [60]. The WHO has developed a Global Action Plan on AMR, which will be implemented in the National Action Plan on AMR by countries worldwide. The effects of NAP on AMR were evaluated every 5 years. For example, Bangladesh NAP study on antimicrobial stewardship (AMS) identified a policy gap in the form of tight operational, monitoring and assessment frameworks, precise funding mechanisms, and guidelines for AMS in the veterinary field [61].

In addition to this collaborative approach, the WHO initiated a surveillance stage to build a database of ARBs in 2015 [62]. Developed countries support developing countries in the implementation of innovative integrated surveillance programs. Cocker *et al*. [63] conducted a longitudinal cohort survey study in rural, peri-urban, and urban areas of Malawi. This study found that the critical risk of ESBL *Enterobacterales* colonization in humans is closely related to environmental sanitation, urbanization, and the rainy season.

Although the prevalence of infections due to exposure to ARBs in livestock and the human environment tends to be lower than that in humans [64], preventive measures to reduce the transmission of bacterial infections in good animal husbandry need to be continuously applied. It is expected that the WaSH program for reducing environmental impacts combined with a biosecurity program to stop the spread of pathogens in the livestock sector will be one of the most effective intervention tools. According to the WHO definition of WaSH, water refers to the provision of safe drinking water, sanitation involves the safe handling of feces, and hygiene focuses on improving basic hygiene practices. The following are the recent developments in WaSH and biosecurity measures to control the spread of pathogens, addressing ESBL *E. coli* and common pathogenic bacteria in livestock.

Hygiene is often used in large-scale or small-scale intensive and extensive livestock farming worldwide. Hygiene-related efforts include (1) implementing standard procedures [65, 66]; (2) regularly cleaning equipment and maintaining pens [67–74]; (3) using farm clothing and personal protection equipment (PPE) to practice personal hygiene, along with cleaning body parts in contact before and after work [75, 76]; (4) periodically inspecting equipment and PPE [77]; and (5) scheduling the washing of large livestock [78]. Depending on the standard procedures used, various cleaning techniques were applied. These include a combination of washing, rinsing with water, and disinfectant spraying [67, 70, 71, 73], washing with detergent only [69], washing followed by rinsing with an acidic solution [79], and disinfectant spraying only [74].

Recent developments in sanitation include (1) handling livestock feces [80–84] and (2) application of technology to control fecal contamination in the environment [68, 85–87]. Managing livestock feces involves protecting areas by covering storage containers [68]. Other methods include relocating feces during the summer season [80], transferring the collected samples into specific containers or rooms [81], grinding after naturally drying for 100 days [82], and adding straw and sawdust [83, 84]. Fecal contamination can be controlled through anaerobic digestion processes conducted in slurry pits for conversion into biogas and liquid manure [68, 85, 86], composting to obtain solid manure [87], and the conversion of feces into biochar [88].

The processing of feces usually produces agricultural products, biochar, or liquid fertilizers from biodigesters which are directly applied to the soil. Both ARGs and MGEs in fertilizers increased the abundance of native soil ARGs [89]. The soil ARG profile is significantly influenced by the microbial community structure, MGEs, pH, and heavy metals [90]. A setback distance of up to 40 m around the experimental plots with solid manure applied should be installed to prevent runoff from leaching livestock feces into the soil during rainfall [91]. As the distance approached 40 m, the ARGs and MGEs present in the solid manure were carried by runoff water, reducing their impact on the resistome and mobilome in the surrounding area.

Improving the quantity and quality of water is very important for livestock, farmers, and surrounding communities. Water aspects of WaSH include (1) increasing water quantity for domestic purposes [92], (2) ensuring water quality [75, 76, 83, 84, 93, 94], and (3) separating water sources for livestock and human consumption [73]. The approach to water management differs between developed countries and developing countries because clean water in developing countries can originate from various non-piped sources [95]. In addition, rainwater and groundwater are clean sources for livestock farming. Drinking water for workers on large farms is provided in refillable bottles or bottles. Ensuring water quality involves the addition of chlorine [84] and oxygen peroxide [83] to kill pathogens, as well as the application of antibiotics [96] and organic acids [94] in pipeline systems to maintain health or treat poultry diseases. Further, treatments, such as water heating and iron removal systems [97], are employed for non-piped water sources to promote livestock and human health in surrounding areas.

Biosecurity approaches, as described by Constable *et al.* [98], encompass: (1) checking or isolating newly introduced livestock species; (2) controlling visitor contact; (3) managing contact between livestock, pets, and wild animals entering the farm; (4) separating sick livestock; (5) cleaning and disinfection practices; (6) disease monitoring and record-keeping; and (7) conducting communication, training, and employee assessment. According to Pinto Jimenez *et al.* [20], biosecurity programs include bioexclusion, biocontainment, and biomanagement programs. Bioexclusion prevents the emergence of new pathogens, biocontainment restricts their entry, and biomanagement includes the control of existing pathogens in the agricultural environment. The discussion on biocontainment [94] aligned with the overlapping hygiene terminology in the WaSH program.

Farmers can monitor the implementation of biosecurity by means of paper-based or software-based checklists. Biocontainment actions based on the collection of biosecurity checklist examination data and farmer interviews include fencing around farm areas [76, 99–101], venting in livestock barns [101–103], and separation and quarantine measures [66, 68, 76, 80–82, 93, 99, 100, 102]. Other methods include restricting visitors and wild animals from entering the farm area [67, 80, 81, 83, 99, 101–103], limiting the number of livestock herds [103, 104], designing secure livestock housing [79, 81, 83, 105], and properly handling dead livestock [66, 106]. Longitudinal research carried out in Germany focused on the management of pigs suspected to be infected with ESBL *E. coli* through herd eradication followed by health examinations of farmers [106]. Sick farmers were monitored for 3 months and replaced with healthy individuals; they could resume work only if they stopped experiencing diarrhea and showed improvement in the nasal swab. Subsequently, farm owners implemented a shift rotation control. This study demonstrates the importance of eradicating ARB-infected livestock and consistently implementing quarantine measures when introducing new or isolated unhealthy livestock from the herd.

One Health research mainly focused on surveillance [107] to understand the transmission process. However, studies on interventions are limited [31]. The WaSH biosecurity program can be integrated into a series of intervention steps to address this gap. As outlined by O'Cathain *et al.* [108], these steps include problem identification, literature review, preparation, feasibility testing through pilot tests, optimization, evaluation, and long-term implementation. In addition, One Health-based WaSH biosecurity intervention program can take the form of managerial, structural, educational/behavioral, biological/chemical, and physical/infrastructural approaches [31].

As a first step in the intervention research offered by the WaSH biosecurity program, integrative WaSH biosecurity scenarios must be tested on an integrated farm. In the course of the test, the risk recipient targets must include humans, animals, and the environment.

One health issue should be considered by optimizing (1) WaSH with human and environmental health targets and (2) biosecurity through livestock health targets.

The Effects of Existing WaSH and Biosecurity Strategies

The odds ratio (OR) of ESBL *E. coli* and common pathogen bacteria in the literature was used to review the function of WaSH and biosecurity applications, representing a comparison between farmers who implemented the interventions and their counterparts (Table-1) [72, 76, 80, 84, 92, 99]. The ORs were derived entirely from interviews with the farmer population who indicated the magnitude of the impact of the implementation of both programs. The higher values suggest a greater expected impact, thereby reducing the risk of ARB infection in farmers and livestock.

An adequate supply of clean water significantly contributes to the operational aspects of livestock farming, with an OR of 1.89 ([CI 95% = 1.1–2.78], p = 0.05) [92]. Disinfection efforts for drinking purposes had an OR of 1.96 ([CI 95% = 0.52–7.39], p = 0.32) [76]. The OR for hygiene, which includes cleaning followed by disinfection, was 3 ([CI 95% = 1.2–7.5], p = 0.05) [72]. Similarly, the use of PPE had an OR of 3 ([CI 95% = 0.6–15.9], p = 0.2) [80]. Sanitation interventions were assessed based on the log removal value (LRV), which indicates the level of ARB reduction in logarithmic units after completion of the sanitation process. Composting, ordinary biodigestion, and biodigestion with a bioslurry pit can achieve bacterial LRVs of 1–2 [87], 1–2 [86], and 6.11, respectively, for ESBL *E. coli* [85]. Another aspect of sanitation, such as the addition of straw to litter [84], has an OR of 0.87 ([CI 95% = 0.57–1.33], p = 0.53).

According to Mridha *et al.* [76], the overall implementation of biosecurity has an OR of 3.37 ([CI 95% = 0.71–16.06], p = 0.12), whereas another investigation [99] reported a lower OR of 1 ([CI 95% = 0.16–0.94], p = 0.035]. Moreover, recent biosecurity interventions on poultry farms and slaughterhouses in the Netherlands to address *Campylobacter* spp. (a pathogenic bacterium) have focused on disease occurrence that affects the health of broiler chickens for human consumption [109]. The combined effectiveness of insect control efforts, barn cleanliness, and visitor control resulted in a minimum reduction of 5%–10%.

In Burkina Faso, studies on small-scale chicken farms have used a different approach to disrupt

Table-1: WaSH and biosecurity intervention based on the OR of previous studies.

Reference	Type of intervention	OR
Dohmen *et al*. [80]	Hygiene intervention:	
	Using gloves when treating piglets	3 (CI 95% = 0.6–15.9), p = 0.2
Caudell *et al*. [92]	Water intervention:	
	Increased water supply for domestic purpose (non-livestock)	1.89 (CI 95% = 1.1–2.78), p = 0.05
Mridha *et al*. [76]	Water intervention:	
	Maintain water quality	1.96 (0.52–7.39 CI 95%; p = 0.32)
	Hygiene intervention:	
	Attendants' hand rinse water	0.41 (0.12–1.34 CI 95%; p = 0.14)
	Biosecurity intervention:	
	Overall biosecurity on farm application (provision of perimeter fencing, netting of the farm, footwear clean entry in the farm, all-in all-out practice)	3.37 (0.71–16.06 CI 95%; p = 0.12)
Adebowale *et al*. [99]	Biosecurity intervention:	
	Presence of isolation bay for sick animals, Quarantining of new animals on arrivals, Restriction visit to other farms, Access to farms by farm buyers, Access to farms by feed transport vehicles, Ownership of farm equipment, Use of farm equipment from other farms.	1 (0.16–0.94 CI 95%)
Coffman *et al*. [72]	Hygiene intervention:	
	Conducted any pesticide application or cleaning activity	3 (1.2–7.5 CI 95%)
	Used any PPE	0.3 (0.1–1.5 CI 95%)
	Washed hands at least 8 times per shift	0.3 (0.1–0.8 CI 95%)
Sanni *et al*. [84]	Water intervention:	
	Dug-up well using chlorination	0.42 (0.3–0.58 CI 95%, p < 0.001)
	Sanitation intervention:	
	Litter materials for litter management	0.87 (0.57–1.33 CI 95%, p = 0.53)

PPE=Personal protection equipment, WaSH=Water, sanitation, and hygiene, OR=Odds ratio the transmission of pathogens. The experts concerned [110, 111] focused on the children of farmers and provided supervision for hand hygiene, feeding practices, and biocontainment of animal feces. To reduce inadvertent soil and fecal ingestion in children, participatory behavioral change sanitation programs combined with biocontainment were implemented through two-way communication. Similar participatory behavior-based sanitation programs have been practiced in pastoralist communities in Ethiopia [112], raising awareness of the importance of maintaining clean water and sanitation infrastructure. Strengthening WaSH and biosecurity measures in livestock farming disrupts the chain of disease transmission between animals and reduces the risk of exposure in animals and humans. These strategies can reduce the incidence of disease in livestock, leading to a reduction in antimicrobial use, in particular antibiotics, thereby suppressing the possible emergence of ARB.

Research on the combined implementation of WaSH and biosecurity programs over the last 5 years has highlighted the impact of these programs. While there is a significant amount of literature on WaSH or biosecurity, the impact of these interventions has not been analyzed using OR, which is a limitation of this review. Literature on other pathogenic bacteria has also been included due to a lack of literature on ESBL-specific *E. coli*.

Quantitative Microbial Risk Assessment Framework in the Livestock Environment for Farmers

Antibiotic-resistant bacteria in farm areas can originate from feed, antimicrobial use, and medications for sick livestock. Antimicrobials, antibiotics, and feed consumed by livestock are processed in the gut and excreted in the feces. Animal feces are considered hotspots due to the presence of pathogens, both in their original state and in processed forms, such as manure and slurry [113].

Manure or slurry tends to bind to pathogens, antibiotic residues, and chemical stressors compared with raw animal waste. These materials are referred to as hotspots for ARGs and MGEs even though their concentration depends on processing method and storage conditions. Moreover, gene transfer can occur immediately after the application of manure or slurry to the soil, even under unfavorable conditions [114]. feedwater, soil, and feed are potential exchange points for ARGs and ARBs between humans and animals. The resistant pattern of *E. coli* has been found in soils with direct or processed contact with animal feces. In Thailand, Tanzania, Peru, and Bangladesh, they are also observed in humans, cattle, and soil [33]. The risk of exposure to resistant *E. coli* is higher in individuals who maintain animals near their homes than those who separate livestock areas from their living spaces [115].

The risk of human exposure to microorganisms has been evaluated using deterministic or stochastic QMRA method [116]. This model involves hazard identification, exposure estimation, dose-response calculation, and risk characterization through ARB transmission across the oral route. According to QMRA research, individuals can be directly or indirectly exposed to animal feces through airborne, oral, or fomite transmission routes [11]. Inhalation exposure by farmers in direct contact with raw and processed manure and slurry differed from the exposure of workers to the digestive system. Research conducted in Beijing, China, revealed that inhalation exposure due to manure being a hotspot is less than that from drinking water or ingesting waste and soil while working [117]. There are limited specific investigations of AMR indicating which exposure pathway is associated with a higher risk.

Once hazard identification was conducted, the next step in QMRA was to calculate the exposure through hand-to-mouth contact while handling animal feces, which was estimated by multiplying the ARB concentration by the manure ingestion rate. Exposure through soil ingestion when feces were applied to agricultural land was estimated by multiplying the concentration of ARB by the soil ingestion rate. We performed a Monte Carlo simulation to calculate the uncertainty of the parameters and conducted a statistical sensitivity analysis. Ingestion rates in occupational farming are currently limited, and empirical data are mostly based on ingestion rates in the general adult population. Behavioral factors such as hierarchical health and safety interventions (e.g., engineering and administrative controls, PPE use) that can reduce intake or exposure time during hotspot handling are currently unavailable in developing countries [118]. Limited research has been carried out on exposure to ESBL *E. coli* and dose-response assessments for farmers, partly because most studies have focused on non-ARB microorganisms [119, 120], and relevant data on antimicrobial exposure remains lacking. Antimicrobial exposure includes vulnerability, resistance, tolerance, and persistence [121]. Therefore, ingestion rate and dose-response assessments of ESBL *E. coli* in farmers are potential opportunities for future research.

Potential Scenarios for Future WaSH and Biosecurity Interventions within the QMRA Framework

The incorporation of WaSH biosecurity into the QMRA framework can reduce the risk of exposure of farmers to ESBL *E. coli* and reduce the incidence of inadvertent soil and livestock feces ingestion. It is possible to reduce the frequency and duration of farmers' daily interactions with soil and animal waste to reduce the rate of accidental ingestion. Reducing ESBL *E. coli* concentration should consider the WaSH principles outlined in the F-diagram [122], whereas biosecurity principles can be derived from

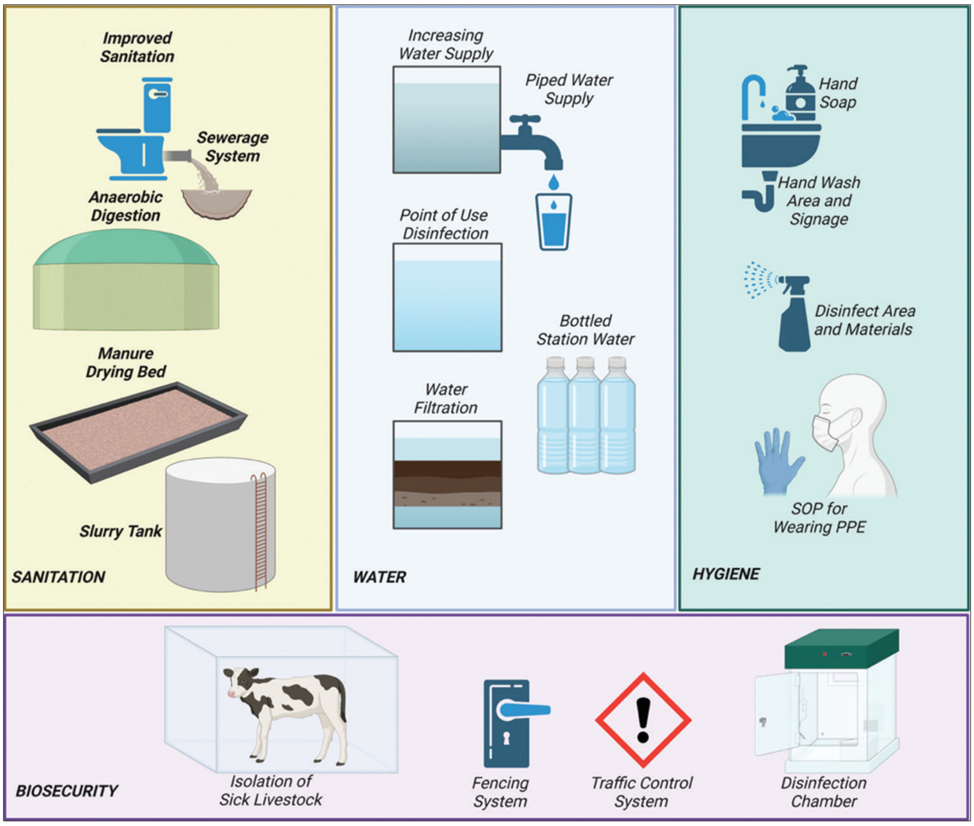

Figure-1: Water, sanitation, and hygiene–biosecurity program framework as an option to reduce extended spectrum beta-lactamase concentrations of *Escherichia coli* in livestock [Source: Prepared by Yudith Vega Paramitadevi using BioRender.com].

biocontainment and biomanagement. Implementing the WaSH biosecurity program involves biocontainment and biomanagement, with water and sanitation components emphasizing fecal management, enhancing drinking water quality, and increasing farmers' cleanliness [31]. Figure-1 alternatives for incorporating WaSH biosecurity to lower the concentration of *E. coli* ESBL.

The WaSH principles in the F-diagram, in sequential order, include: (1) animal and human fecal sanitation, (2) water quality improvement, and (3) personal hygiene, equipment, and food. The measures referred to in points (2) and (3) may be implemented together with biocontainment. Therefore, the combinations to reduce ESBL *E. coli* exposure following environmental engineering disciplines include (a) sanitation-biocontainment, (b) sanitation-water-biocontainment, (c) sanitation-hygiene-biocontainment, (d) sanitation-water-hygiene-biocontainment, and (e) addition of biomanagement to options (a) to (c). Decision analysis can be facilitated by various multicriteria decision-making tools commonly used in conjunction with QMRA using a participatory group discussion approach involving the community or stakeholders.

All available options must be analyzed according to the needs of farmers, farming types, other risk factors such as vaccination programs for livestock, policies restricting the use of antibiotics exclusively for sick animals, and farmers' understanding of antibiotic use. In addition, indirect factors, such as location and multidimensional wealth index, must be taken into account, especially in the case of farms located in developed or developing countries. The implementation of comprehensive biosecurity measures may be difficult in developing countries where small-scale farms are predominant. Therefore, optimizing the integration of the WaSH program with biocontainment has been proposed as the best practice for reducing the prevalence of ESBL *E. coli.* In developed countries, additional risk factors, such as pathway factors, should be included in the implementation of WaSH biosecurity programs. The adoption of a single health approach through the consistent implementation of WaSH biosecurity activities involving stakeholders will reduce the exposure of ARBs to the farm environment.

Conclusion

The prevalence of critically resistant bacteria such as ESBL *E. coli* varies due to the use of antibiotics in livestock farming. As a result, there are difficulties in comparing developed and developing countries. In the livestock sector, it is essential to maintain high levels of hygiene to ensure the well-being of animals and prevent the spread of diseases. As part of the WaSH program, regular cleaning of equipment and barns is emphasized to maintain optimal hygiene standards. Sanitation involves processing animal feces into manure, biogas, liquid fertilizer, and biochar to control pollution. The quality of water was ensured by adding chlorine, organic substances, and advanced treatment methods. In addition, biosecurity programs focus on biocontaining or limiting the entry of pathogens into agricultural areas. In this study, we assessed the roles of WaSH and biosecurity based on the intervention effects obtained from interviews with farmers. Technological aspects of sanitation were evaluated using LRV. Water, sanitation, and hygiene and biosecurity programs are often carried out separately; however, both reduce the risk of disease transmission from humans and animals to humans. Several combined WaSH and biosecurity programs exist, but their intervention effects are typically described qualitatively. The development of WaSH biosecurity scenarios within the QMRA framework involved the identification of hazards and estimation of ESBL *E. coli* exposure with a view to reducing its prevalence and minimizing inadvertent soil and fecal ingestion rates. Scenarios should be considered on the basis of associated risk factors.

Authors' Contributions

YVP: Conceptualized the review and drafted the manuscript accordingly. CRP and IR: Edited and revised the manuscript. AR and SSM: Literature search and commented on it. All authors have read, reviewed, and approved the final manuscript.

Acknowledgments

The study was funded by the Ministry of Education and Culture of Indonesia (Grant Number: 125/E5/PG.02.00/PT.2023). The authors are grateful to Yuni Resti from the Universität für Bodenkultur Wien, Vienna, for reviewing the quality of the literature in the field of livestock, and Henny Endah Anggraeni from IPB University, Bogor, for reviewing the literature quality in the field of veterinary science. Furthermore, the authors thank Editage (www.editage.com) for editing English language.

Competing Interests

The authors declare that they have no competing interests.

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