OPEN ACCESS Advances in Animal and Veterinary Sciences

Research Article

Towards Resilient Shrimp Aquaculture: A Review of Integrative Microbiome, Environment, and Host-Centered Strategies for Sustainable Disease Management

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Abstract | Shrimp aquaculture has become one of the world's most rapidly expanding animal protein sectors and is also a major source of food security, livelihood, and global trade. Nevertheless, infectious diseases caused by viruses, bacteria, fungi, and protozoan parasites are increasingly challenging its sustainability. Disease outbreaks result in significant financial losses and lead to intensive use of antibiotics and chemicals. This review summarizes existing information about key shrimp pathogens, their modes of transmission, and environmental conditions that initiate outbreaks of the disease. This review proposes replacing pathogen eradication with ecosystem resilience as a more sustainable disease management framework. Disease control is examined using three complementary approaches: host-centered, microbiome-centered, and environment-centered. These are immunostimulants, functional feeds, probiotics, biofloc technology, microalgae-based systems, and enhanced management practices in the farms to stabilize microbial communities and enhance innate immune systems. Comparative evidence suggests that while microbiome-centered and environment-centered interventions may offer more consistent long-term disease suppression in controlled settings, their efficacy in field trials is often inconsistent due to varying environmental and ecological conditions. More empirical studies in various real-world systems are needed to determine the condition under which these interventions are always effective. Lastly, the implications on antimicrobial resistance and global shrimp trade are discussed in a One Health framework and critical research gaps include multi-omics validation, long-term pond-scale trials, and regulatory harmonization. These insights together help in the shift to the resilient and antibiotic-reduced shrimp aquaculture systems.

Keywords | Biosecurity, Pathogen, Sustainable, Management, Immunostimulants and resistance

Received | January 31, 2026; **Accepted** | April 27, 2026; **Published** | May 11, 2026
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Citation | Gbaaondo T, Ajiboye KJ, Rahim AIA, Ghazali A, Draman AS, Kasan NA (2026). Towards resilient shrimp aquaculture: a review of integrative microbiome, environment, and host-centered strategies for sustainable disease management Vet. Sci., 14(5):942-960.
DOI | https://dx.doi.org/10.17582/journal.aavs/2026/14.5.942.960
ISSN (Online) | 2307-8316

INTRODUCTION

Shrimp are among the most valuable commodities in the world trade and there has been an unprecedented growth in aquaculture production of shrimp over the past decades. Global shrimp production increased nearly tenfold, from 0.63 million tons in 1980 to 6.0 million tons in 2018. This trend continued into 2022 when the total production of shrimp and lobster amounted to 3.3 million tons (FAO, 2020; FAO, 2024). Shrimp aquaculture is an important element in the process of addressing the increasing nutritional protein needs as one of the fastest-growing industries in the world in aquaculture and international trade (Miao, 2020). In the last forty years, the growth of shrimp farming has played a significant role in meeting the world protein demands. Nonetheless, shrimp production would not be sustainable without the right management practice, especially since disease outbreak regularly happen and cause severe mortalities and financial losses. Consequently, closed cycle rearing techniques have replaced open cycle rearing to focus more on biosecurity and reduce disease transmission (Martínez-Gómez *et al*., 2022). This expansion, however, has been repeatedly challenged by infectious diseases, such as viral infections including white spot syndrome virus (WSSV), bacterial strains, protozoa as well as other devastating pathogens. Research has established that WSSV incurs considerable losses in the world shrimp aquaculture not only by resulting in high mortality and financial losses but also the extensive use of antibiotics and chemical treatment. This, in turn, contributes to environmental pollution and the development of microbial resistance in aquaculture systems (Ji *et al*., 2023). Introducing sustainable pathogen control practices is important not only to mitigate economic losses but also to maintain food safety, environmental health, and long-term industry sustainability. Recent approaches have emphasized biosecurity, pathogen-free stocks, immunostimulants, dietary additives, early detection and surveillance systems, probiotics and manipulating microbial communities. Recent shrimp health management practices are based on multiplex activities and are aimed at the host, the environment, and the pathogen, reducing excessive dependence on the use of chemicals (Haris *et al*., 2024; Kumar *et al*., 2022). More recent approaches involve the design of useful microbiomes that can be used to outcompete pathogens through competitive exclusion, development of immunostimulants and Phyto biotics that can be used to boost innate immune responses, and the use of molecular and surveillance technologies to early pathogen detection. Moreover, the microbial community study can be important in the context of the disease (Rahardjo *et al*., 2023; Negi and Chen, 2025; Khanjani *et al*., 2024). This review goes beyond simply cataloging pathogens or isolated disease control methods. Instead, it offers a unified model that integrates biology, environmental factors and importance of microbiome in management of shrimp disease sustainably It also offers new perspectives on promoting resilience within shrimp aquaculture systems to enable their sustainability in the future by adopting a systems-level perspective.

Pathogens in shrimp aquaculture

The onset of bacterial, viral, fungal, and protozoan diseases in shrimp aquaculture occurs through the interaction between host immune susceptibility, microbiome imbalance, and environmental stressors (Figure 1). Shrimp culture is faced with an extensive repertoire of pathogens that include bacteria, viruses, fungi and protozoan parasites, most of which cause severe disease outbreaks and huge losses in shrimp aquaculture systems, which are facilitated by intensive culture practices, broodstock translocation across the globe and other environmental stressors (Walker and Mohan, 2009).

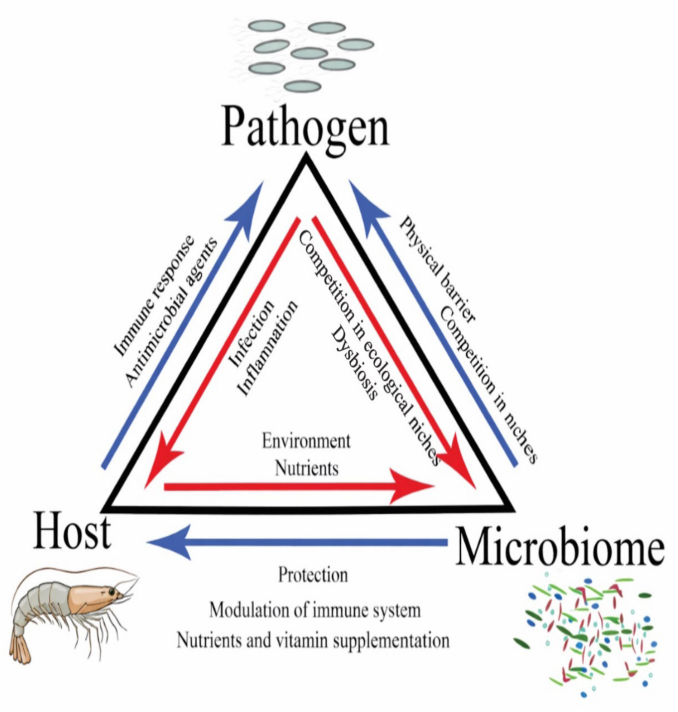

Figure 1: Triangular host–microbiome pathogen interaction framework.

Bacterial diseases

The main bacterial diseases necrotizing hepatopancreatitis (NHP), acute hepatopancreatic necrosis disease (AHPND), and vibriosis are driven by stress-induced immune suppression and dysbiosis. Hepatobacter penaei, the causative agent of NHP, attacks the hepatopancreas, is exacerbated by high salinity and temperature, thereby inhibiting hemocyte-mediated prophenoloxidase (PPO) immune responses and diminishing immune function metabolic support (Vincent *et al*., 2004). The bacterium Vibrio parahaemolyticus, carrying the pVA1 virulence plasmid, causes AHPND. It kills hepatopancreatic epithelial cells, taking advantage of the shrimp's lack of specific mucosal immunity and cortisol-mediated suppression of hemocytes and PPO activity under the influence of stress (Tran *et al*., 2013; Lee *et al*., 2015; Tang *et al*., 2020). Furthermore, studies reported that Vibriosis is an opportunistic disease caused by Vibrio species, and is a stress-dependent disease where commensal bacteria become pathogenic in the case of impaired immune surveillance due to hypoxia, nutritional deficiencies, or chronic stress

(Ishimaru *et al*., 1995; de Souza Valente and Wan, 2021). In bacterial diseases, dysbiosis of the microbiota through loss of protective Bacillus and lactic acid bacteria (LAB) attenuates immune priming via pathogen-associated molecular pattern (PAMP) signaling and eliminates competitive inhibition of microbes, whereas environmental factors, including organic loading, rising temperatures, and high stocking density, promote pathogen growth (Tang *et al*., 2020; de Souza Valente and Wan, 2021). This indicates that effective control requires combined intervention environmental stabilization, probiotic microbiome restoration, and host immune enhancement rather than any single approach, as individual approaches do not resolve the multi-factorial disease aetiology.

Viral diseases

Viral diseases such as Taura Syndrome Virus (TSV), White Spot Syndrome Virus (WSSV), Infectious Hypodermal and Hematopoietic Necrosis Virus (IHHNV), Infectious Myonecrosis Virus (IMNV), and Yellow Head Virus (YHV) take advantage of the inherent lack of adaptive immunity in shrimp, especially in the absence of adaptive immunity and through the use of hemocyte-mediated pathways (Walker and Mohan, 2009; Lightner, 2011). WSSV is a systemic infection characterised by direct hemocytoplasmic invasion and lethality, as well as encoding proteins that block the Toll/Imd pathways, where environmental stress further reduces immune competence (Millard and Dong, 2022; Hou *et al*., 2020). IHHNV harms hematopoeietic tissues leading to chronic immune deficiency and growth defects, IMNV provokes severe muscle necrosis due to the lack of immunity to the disease, YHV destroys hepatopancreatic and immune tissues with high mortality, and MBV impairs the hepatopancreatic functions in the first stage of development (Dominguez-Mendoza *et al*., 2025; Arunrut *et al*., 2025), Although the microbiota's role in direct antiviral defense is secondary, dysbiosis can still suppress metabolic support and immune priming, impairing antiviral performance through the inhibition of short-chain fatty acid (SCFA) production and immunostimulatory commensals loss (Tang and Lightner, 2005). Viral pathologic outbreaks are generally caused by the spread of water, cannibalism, or vertical transmission of broodstock and enhanced by environmental stressors, including salinity and temperatures, hypoxia, and crowding (Wertheim *et al*., 2009; Srinivasan *et al*., 2026). The appropriate control in this context can only be achieved through a combination of strategies based on biosecurity, selective breeding for genetic resistance, immune and nutritional boost, as well as stabilisation of the environment to avoid stress-related suppression of the immune system.

Fungal diseases

Fungal diseases such as Fusariosis, larval mycosis largely impact the early stages of life or shrimp that has impaired cuticular barriers. Fusariosis caused by the Fusarium species invades due to cuticular damage by either stress or handling, whereas larval mycosis by zoospore-forming fungi (Lagenidium haliphithoros and Sirolpidium) exploits the immature immune system with poorly developed hemocyte and PPO functions, resulting in high larval mortality (Baticados *et al*., 1990). Immature or dysbiotic microbiota fail to provide antimicrobial protection and immune priming, and low standards of water quality in hatcheries, inadequate hygiene, as well as crowding are the key environmental factors that initiate. Management is based on the hygiene control, the optimization of water quality, and the ability to handle it to avoid the compromise of barriers and fungal growth.

Protozoan diseases

Protozoan infections,including gregarine infection and microsporidiosis, primarily exploit the malfunction of the hemocytic immune surveillance system and persistent stress. Gregarines invade the gastrointestinal tract and hepatopancreas, crippling nutrient absorption in the cases of hemocyte-mediated containment failure, particularly in stressed shrimp with diminished immune competence (Baticados *et al*., 1990). Microsporidians are known to cause chronic infection of reproductive tissues, resulting in sterility and opacification of the tissues, usually with a prolonged period of environmental/nutritional stress. Dysbiotic microbiota play a role in eliminating competitive exclusion and decreasing intestinal stability through SCFA. Environmental factors such as crowding, poor sanitation, spawning stress, and nutritional deficiency promote disease transmission and persistence. The focus of integrated control techniques is on the restoration of the microbiome by probiotics, enhanced sanitation and stocking control, biosecurity to protect the broodstock, and nutritional optimization to enhance immune transfer and disease resistance. Table 1 presents an overview of the key pathogens of shrimp aquaculture and the main characteristics of the diseases.

Transmission of diseases and environmental triggers in shrimp aquaculture

The interaction between pathogens, hosts, and the environment (Figure 2) is a dynamic process that leads to the emergence of disease in aquaculture. Environmental conditions such as temperature and humidity define the duration of stay of the pathogen outside the host and influence the multiplication of the vectors that plague the pathogen, which plays a major role in the transmission (Xiao *et al*., 2024). Pathogenicity, which is context-dependent, demonstrates that disease develops by genetic and environmental factors in the hosts (Soni *et al*., 2024). Understanding these interactions is necessary to predict and control the emergence of infectious diseases.

Table 1: Major shrimp pathogens affecting shrimp aquaculture and their core disease characteristics.

Pathogens group	Representative pathogen	Key environmental triggers	Quantitative evidence	References
Virus	White spot syndrome virus (WSSV)	Abrupt changes in temperature and salinity fluctuations, with evidence that low salinity (<10 g L^{-1}) and moulting stress significantly increase risk of WSSV infection, including higher mortality during premoult/ecdysis stages ($P < 0.05$). Fluctuating oxygen levels and ammonia have also been associated with increased disease outbreak risk. Broad environmental stress (storm-related variations) correlates with disease occurrence.	Statistical significance of salinity <10 g/L increasing WSSV infection risk with $p < 0.05$. (Optimal proliferation at ~30 °C and 35‰; reverse at 15 °C)	Van Thuong *et al*., 2016
Virus	Taura syndrome virus (TSV)	Poor water quality and improperly managed environment (including suboptimal water quality parameters such as salinity and temperature) can predispose shrimp to disease episodes. Outbreaks often associated with stressful environmental shifts in pond culture.	Environmental shifts in pond culture linked to TSV outbreaks, though specific p-values and statistical tests are not provided in the cited sources.	Lotz, *et al*., 2005
Bacteria	Vibrio parahaemolyticus (AHPND strain)	Low salinity stress increases susceptibility to V. parahaemolyticus infection, alters gut microbiota, and lowers species richness, promoting pathogen proliferation. Environmental conditions that reduce host immune function (e.g., salinity changes) exacerbate Vibrio infection risk.	$p < 0.05$ for increased Vibrio infection in low salinity conditions. - V. parahaemolyticus thrives in temperatures 5-37°C and salinity 1-3%	Chang *et al*., 2024
Bacteria	Vibrio harveyi complex	Vibrio species activity and pathogenic traits often increase under environmental stress (e.g., temperature changes, poor water quality, salinity fluctuations), which perturb normal microbiota and host defences. Vibrio prevalence in shrimp pond water is linked to environmental factors favourable to bacterial growth.	Specific statistical values are not provided in this review but link environmental stress (e.g., salinity fluctuations) to increased Vibrio prevalence	Valente *et al*., 2020
Protozoa	Gregarines	Poor water quality and chronic stress conditions (suboptimal environmental parameters including low DO and pollution) contribute to increased protozoan infection pressure.	Limited challenge studies for protozoan infections, but general correlations with poor water quality and chronic stress are drawn from disease ecology literature.	Ihwan *et al*., 2022

Overviews the different pathogens that plague the shrimp aquaculture, including the pathogen type, genome type, target tissue, pathogen modes of transmission, important disease consequences, key environmental triggers and the sources of pertinent literature.

The pathogen-host-environment interaction of shrimp aquaculture is complex and contributes to the spread of diseases. White spot syndrome virus (WSSV), Vibrio species, and acute hepatopancreatic necrosis disease (AHPND) are pathogens that are normally spread horizontally. Transmission occurs through contaminated equipment, waterborne exposure, and infected broodstock. Vertical transmission also occurs especially amongst viral pathogens such as Infectious Hypodermal and hematopoietic necrosis virus (IHHNV) and WSSV, whereby pathogens could be transmitted between infected broodstock to offspring. Several factors that may increase pathogen spread include ineffective biosecurity, poor sanitation, insufficient filtration, and poor farm management practices (Lightner, 2011). Also, high stocking density and a high level of organic matter loading has the potential to stimulate opportunistic bacterial diffusion, elevating the risk of disease outbreaks. Shrimp aquaculture also has disease expression that is highly influenced by the environmental factors that cause outbreaks. Fluctuations in salinity, pH, temperature, and dissolved oxygen can disrupt shrimp immune function, increasing susceptibility to both opportunistic and primary pathogens (Hou *et al*., 2020). Conditions such as high temperatures have been attributed to the virulence of Vibrio parahaemolyticus, the causative agent of AHPND, and fluctuations in salinity with the occurrence of WSSV outbreaks. It has also been revealed that poor water quality, such as a high level of ammonia, nitrite and sediment deposition, may affect hepatopancreatic function and decrease innate immunity in shrimp (Tran *et al*., 2013; Chen *et al*., 2022). Eutrophication and algal

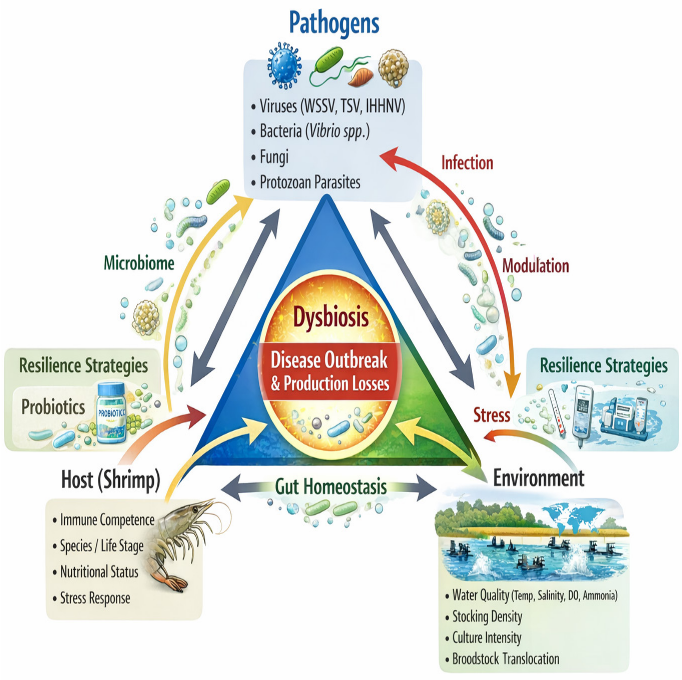

Figure 2: Pathogens, hosts, and the environment interactions.

blooms can cause stress that leads to changes in the bacterial microbiome, which will once again stimulate the growth of pathogen and predispose the disease outbreak. The literature indicates that sustainable disease management requires integrated approaches, including close environmental monitoring, system maintenance, and farming practices that minimize stress and pathogen transmission (Lightner, 2011).Table 2 shows a summary of the key environmental management drivers of disease emergence in shrimp aquaculture.

Sustainable disease management strategies in shrimp aquaculture

Anirudhan *et al.* (2021), state that disease outbreaks are also one of the most chronic problems of global shrimp aquaculture. Although chemical treatments have been extensively employed in managing diseases in intensive shrimp farming systems, there exist long-term implications of these practices, which include environmental pollution, antimicrobial resistance, and food safety. Consequently, interest has increased in strategies of integrated, sustainable disease control that aim at boosting host immunity, manipulating microbial communities, and optimal environmental and farm management practices. These measures are in line with the principles of sustainable aquaculture to minimize the use of chemicals.

Table 2: Effects of environmental stressors on shrimp health and disease associations.

Driver category	Specific stressor	System component affected	Mechanistic effect	Disease association (statistical support)	Quantitative measure/ effect size	Reference
Physical	Temperature fluctuation	Immune homeostasis	Alters viral replication and immune response	WSSV outbreaks correlated with temperature variability; optimal WSSV replication at ~25–28 °C, reduced replication at 15 °C and 35 °C (ANOVA, $P \approx 0.044$)	WSSV copies ~0.626/ng at 15 °C vs 5.94/ng at 35 °C (significant differences, $P < 0.05$)	Gao *et al.*, 2011
Physical	Acute salinity drops	Viral susceptibility	Shrimp are more susceptible to WSSV during low salinity & moulting	Shrimp mortality increased significantly with salinity drops ($P < 0.05$)	Mortality: 6.7% at 10 g/L, 46.7% at 7 g/L, 53.3% at 5 g/L	Van Thuong *et al.*, 2016
Chemical	Elevated ammonia/N	Hepatopancreas, gut microbiota	Tissue damage, microbiota dysbiosis	Hemolymph ammonia-N concentration increased with water ammonia ($P < 0.05$)	Linear regression: hemolymph vs water NH_3-N positive correlation (statistically significant)	Li *et al.*, 2024
Chemical	Ammonia/ nitrite accumulation	Hepatopancreas mortality	Correlated with reduced shrimp survival and tissue damage	Field correlation: ammonia and nitrite positively correlated with EHP prevalence (r = 0.980 & 0.943)	Pearson r ≈ 0.98 (ammonia), 0.943 (nitrite)	Nkuba *et al.*, 2021
Biological	Microbiome dysbiosis (e.g., nitrite)	Gut microbial community	Loss of competitive exclusion; pathogen enrichment	Nitrite exposure associated with significant enrichment of pathogenic bacteria in gut (16S data)	Shift in Photobacterium abundance in diseased vs control groups (statistically distinct clusters)	Wang *et al.*, 2024

Gives a brief report on some of the pathogens that have an impact on shrimp aquaculture. It contains different informations regarding each pathogen such as driver category,specific stressor,component affected,mechanistic effects,didesease association and management implications

Pathogen eradication to ecosystem resilience

The management of diseases in shrimp aquaculture has traditionally been centered on their elimination, and the particular infectious agent has been removed by the use of chemical interventions or exclusion-based biosecurity. However, this approach typically provides only short-term solutions because this approach cannot consider the ecological complexity of aquaculture systems. It may also cause unintentional effects, including antimicrobial resistance, repeated outbreaks of diseases and microbial imbalances (Flegel, 2019). Instead of eliminating pathogens, the new disease management systems targeted at preserving the health of shrimp by stabilizing microbial communities and environmental factors and developing the immunity of the hosts. This paradigm shift is consistent with the ecological concept and has gained more and more interest in recent studies of aquaculture, especially dysbiosis, microbiome structure, and functionalredundancy (De Schryver and Vadstein, 2014).

Host-centered strategies

Host-centered disease management (Figure 2) involves boosting the inherent immune system of the shrimp to increase their resistance to disease. The main strategies involved are bioactive compounds, immunostimulants, immunization and functional feeds. Even though shrimp do not have the adaptive immune response, there is potential in using vaccines, such as subunit vaccines, toxoids, live attenuated vaccines, and bacterins, which induce innate immune response (Anirudhan *et al*., 2021). Heat shock proteins (HSPs) serve as both stress biomarkers and immune enhancers, and especially Hsp70 and its bacterial counterpart Dna K. The proteins are involved in pathogen recognition, immune activation and antigen presentation in the crustaceans. Research has indicated that dietary supplementation with HSPs has the potential of enhancing cellular immunity, e.g. phagocytosis and hemocyte activity, which has protective effects against Vibrio infections in shrimp. Also, the short-chain fatty acids (propionate, acetate and butyrate) dietary supplement has been reported to enhance the growth performance, immune gene expression, feed efficiency and resistance to diseases in penaeid shrimp (Robert, 2003; Defoirdt *et al*., 2009). Short chain fatty acid supplementation has increased gene expression, like those of prophenoloxidase, lysozyme, crustins, and penaeidins, and has boosted resistance to Vibrio alginolyticus. These results emphasize the need to use a combination of various methods of disease management, even though the improvement of the immune system does not necessarily result in direct antimicrobial action (Defoirdt *et al*., 2009; Defoirdt *et al*., 2011). Plant-based immunostimulants represent another important host-directed approach. The use of extracts of such seaweeds as Gracilaria tenuistipitata, Sargassum duplicatum, Gelidium amansii, and Sargassum fusiforme has been reported to enhance hemocyte counts, respiratory burst activity and resistance of vibriosis in penaeid shrimp. These natural compounds offer safer, low-cost alternatives to chemical therapies (Hodt and Kraan, 2011; Mulyad. *et al*., 2019).

Microbiome-centered strategies

Probiotics typically Bacillus species and lactic acid bacteria are among the most widely studied disease management tools in shrimp aquaculture, which is usually a collection of Bacillus species and lactic acid bacteria. Probiotics are found to enhance growth performance, minimize the cases of vibriosis and other positive benefits such as augmented feed utilization, immune stimulation, pathogenic bacteria suppression, and increased survival rates. Probiotics have provided a more predictable and viable disease control practice than antibiotics by altering the microbiome of the shrimp instead of its direct attack (Liu *et al*., 2018). Another essential microbiome-focused approach is microalgae-based biocontrol, which is also referred to as green water technology. The microalgae secrete bioactive metabolites which restrict the pathogenic Vibrio species and improve immune-enhancing factors like erythrocyte and leucocyte populations. Besides suppressing diseases, microalgae are also known to give nutritional support as well as improve water quality. Nevertheless, additional screening and optimization is necessary because microalgae-based biocontrol is pathogen-specific in its effectiveness (Anirudhan *et al*., 2021). Biofloc technology is a technology that combines nutritional and environmental advantages with microbiome manipulation. Biofloc technology enhances the water quality, in-situ microbial protein generation and shrimp immune competence by stimulating growth of heterotrophic bacteria by balancing carbon and nitrogen, thereby improving water quality. The microbes that are attached to biofloc have antagonistic properties against bacterial and viral pathogens resulting in nonspecific immune responses. Studies have indicated that shrimp reared in bioflocs grow with high survival rates, immunogenic gene expression, and antioxidant responses to pathogenic conditions (Emerenciano *et al*., 2013).

Environment-centered strategies

This is the practice of environmental management and farm management to ensure that shrimp remains healthy (Figure 2), it is necessary to maintain the best environmental conditions in the form of temperature, salinity, dissolved oxygen, pH, and water quality. The management of water quality minimizes physiological stress and improves innate immune functions and finally, minimizes the risk of disease epidemics. To minimize organic matter and decrease the frequency of pathogenic microbial blooms, it is beneficial to have ideal water conditions and use biofiltration systems, which include seaweed or shellfish (Flegel, 2019). The proper stocking densities, proper pond preparation, and periodic monitoring of the ponds, are important elements of reducing disease outbreak due to good farm management. Dense stocking densities are also likely to result in stress and augmentation of disease outbreaks whereas normal stocking densities maintain resilience and steadiness in shrimp production. Ecological buffering of different ecological conditions could be achieved by having several species in the polyculture systems that may aid in enhancing the biodiversity, stabilizing the environmental conditions, and decreasing the spread of pathogens. Such systems stimulate the proliferation of desirable microorganisms, which outcompete pathogenic species of Vibrio microorganisms (Tendencia *et al*., 2011; De Schryver and Vadstein, 2014).

Synthesis and comparative perspective

Investigations always indicate that microbiome and environment-based approaches especially probiotics and biofloc systems provide the most environmentally friendly options in terms of disease suppression. Host-based approaches, including short chain fatty acids (SCFAs), immunostimulants, and plant extracts give specific immune boosting and greater protection but their efficacy is greatest in combination with microbial and environmental management strategies. All these combined measures decrease the use of chemical treatments and minimize the risks of antimicrobial resistance, which promotes sustainable aquaculture systems and ecosystem management (FAO, 2020; Defoirdt, 2011). Table 3 compares the sustainable disease control strategies in shrimp aquaculture.

Table 3: Comparison of sustainable disease control strategies in shrimp aquaculture.

Intervention category	Consistency across contexts	Primary mechanism	Management skill required	Effect size / quantitative evidence	Confidence / statistical indication	Reference
Host-Centered	Low context dependent	Immunostimulants activate innate host defenses	Low–Moderate	Qualitative evidence of immune activation and improved disease resistance in shrimp (e.g., increased immune markers)	No pooled effect size reported in reviews; benefits noted qualitatively	Ramena and Sharma, 2025
Microbiome-Centered (Probiotics)	Moderate influenced by strain, dose & context	Competitive exclusion, immune modulation, pathogen inhibition	Moderate–High	Meta-analysis of ~100 studies reported up to ~95% survival increase in probiotics vs controls	Positive impact across multiple parameters (survival, immunity); statistical measures vary by study	Amiin *et al*., 2023
Microbiome-Centered (Biofloc)	Moderate High benefits seen across systems	Nutrient recycling + microbial protein + immune stimulation	High	Quantitatively higher survival & immune parameters in biofloc vs control, e.g., immune markers elevated (total hemocyte count, phagocytic activity) and phenoloxidase activity higher ($p < 0.05$)	Multiple challenge trials show improved disease resistance (statistically significant differences)	Gustilatov *et al*., 2022
Environment-Centered	High generally applicable across systems	Stress prevention + water quality stability	Moderate	Biofloc and polyculture reviewed as broadly beneficial with improved water quality and reduced pathogen prevalence though numerical effect sizes vary by system	Generally, consistently positive across farm contexts, but metrics differ by system	Nazarudin *et al*., 2025
Integrated / Combined	Highest robust across diverse conditions	Synergistic host + microbiome + environment resilience	High	Evidence indicates integrated strategies reduce disease risk and improve outcomes across multiple parameters; quantitative effect sizes vary by study	Integrated approaches recommended widely but rarely reported as single effect size	Patanasatienkul *et al*., 2023

Gives a brief history of some pathogens that are related to the culture of shrimp. It contains relevant information concerning each pathogens including their strategy,intervention,mode of action,target level,strength ,limitations and approximate Cost/Complexity (Low/Med/High).

Comparative quantitative analysis of existing studies has shown that there are different efficacy patterns between categories of interventions. The efficacy of intervention procedures in shrimp disease management, shown in Table 4, is highly differentiated. Host-centered (immunostimulants, HSP70) interventions are highly context-dependent (Anirudhan *et al*., 2021; Defoirdt *et al*., 2009; Defoirdt *et al*., 2011), whereas the microbiome-centered (probiotics) interventions are moderately constant (Calcagnile *et al*., 2024). Most interventions involving the environment such as water quality management and temperature have proven to be diversely applicable across systems (Hou *et al*., 2020; De Schryver and Vadstein, 2014). Nevertheless, their efficacy may differ according to species, climatic regions, and agricultural activities, therefore, additional field research should be conducted to define in which conditions these interventions may work most efficiently and consistently in various settings.

Specific immune boosting and greater protection but their efficacy is greatest in combination with microbial and environmental management strategies. All these combined measures decrease the use of chemical treatments and minimize the risks of antimicrobial resistance, which promotes sustainable aquaculture systems and ecosystem management (FAO, 2020; Defoirdt *et al*., 2011). **Table 3** compares the sustainable disease control strategies in shrimp aquaculture.

Standards and harmonization of regulations.

The regulatory systems governing the utilization of antimicrobial and microbial supplements, as well as environmental release, differ greatly in various countries that produce shrimps. Such disparities may negatively affect international commerce and the introduction of the new disease control measures. There is an urgent necessity of harmonization of regulatory standards in the safe use of microbial products, ecosystem health indicators monitoring, and antimicrobial resistance (AMR) surveillance. The regulatory harmonization will also enable the producers to satisfy the export requirements, besides promoting responsible innovation in the aquaculture industry (Desbois *et al*., 2025). It is noteworthy that the three largest markets of shrimp imports (United States, the European Union, and Japan) do not as yet enforce resistance gene surveillance as a prerequisite to market entry of shrimps, but each is moving towards this direction, making such a requirement conceivable in the medium term. Regulatory harmonisation, in this regard, can be seen as the practise that must take place simultaneously on at least three (3) levels: firstly, creating internationally validated standard operating procedures to detect resistance genes in aquaculture matrices; secondly establishing scientifically based thresholds which could be integrated into Codex risk assessment models; and lastly capacity-building programmes in the producing countries to enable the required laboratory infrastructure to be established progressively with international technical and financial help. In the absence of this sequenced methodology, the imposition of resistance gene monitoring as a regulatory measure would be a burden that most countries involved in production are not able to meet.

Table 4: Comparative analysis of intervention efficacy patterns in shrimp aquaculture: mechanisms, effect sizes, and management requirements.

Intervention category	Consistency across contexts	Primary mechanism	Management skill required	Effect size	References
Host-Centered	Low: highly context-dependent	Rapid immune response through stress adaptation	Low - Moderate	Cohen's d = 0.3	Nolasco-Alzaga *et al*., 2025
Microbiome-Centered (Probiotics)	Moderate: requires management quality	Competitive exclusion + PAMP-mediated immune priming	Moderate - High	Cohen's d = 0.5	Khanjani *et al*., 2024
Microbiome-Centered (Biofloc)	Moderate–High: system-wide approach	Nutrient cycling + microbial protein + continuous immune stimulation	High	Cohen's d = 0.7	Nisar *et al*., 2022
Environment-Centered	Highest: universally applicable	Stress prevention + immune homeostasis	Moderate - basic husbandry	Cohen's d = 0.6	Doan *et al*., 2025
Integrated/Combined	Highest: robust across diverse conditions	Synergistic: rapid support + system-wide resilience + stress prevention	High	Cohen's d = 0.8	Tong *et al*.,2025

shows a comparative quantitative analysis of existing studies which shows that there is dissimilarity in efficacy patterns between categories of interventions. The efficacy of intervention procedures in shrimp disease management.

Microbiome dysbiosis as a unifying mechanism of shrimp disease

Microbiome dysbiosis is increasingly recognized as a key factor in shrimp disease pathogenesis. It can act as a primary factor predisposing the host to pathogen development, a consequence of infection, or part of a two-way feedback loop that promotes disease progression (Xiong *et al*., 2017; Negi and Chen, 2026; Yu *et al*., 2018). Environmental stresses selectively deplete native microbiota like high organic loading, variations in temperatures, and salinity differences, causing pathogenic colonisation to occur. The outbreaks of AHPND have shown that high temperatures (> 28 °C) cause the population of obligate anaerobes, such as Bacillus and lactic acid bacteria, to decrease, whereas the populations of thermally tolerant and fast-growing Vibrio species increase (Tran *et al*., 2013; Tang *et al*., 2020). It has been demonstrated in several studies of aquatic animals and in other marine systems that the major changes in microbial community structure sometimes referred to as dysbiosis can precede the onset of apparent disease or even prior to the recognition of clinical pathogens and as such, a dysbiosis state may be an indication of early predisposition to disease or even a precursor to disease. Indicatively, cases of dysbiosis have been seen to precede death in stressed shrimp, in which cases, the occurrence of sudden changes in the microbial community were apparent before disease outbreak, suggesting that microbial instability is a predictable early biomarker of incumbent disease outbreak in controlled shrimp systems. In isolation, the studies in larger systems of marine hosts like sea stars demonstrate that observed changes in microbial diversity and composition precede the appearance of wasting disease, as expected in the case of early ecological dysbiosis. These results are consistent with the new knowledge that microbiome alterations are linked with disease progression, but much of the evidence is observational, but not mechanistic, in most aquaculture host-pathogen systems. Notably, how early dysbiosis is causally related to establishment of pathogens has not yet been established. The majority of available studies do not include the adequate densities in time sampling or controlled trial studies, which are required to prove that dysbiosis is infections and not a manifestation of initial, low level pathogen replication or host stress responses in other words, it is not always clear that dysbiosis is a cause or a predictor of disease risk in a broader context review on microbial causality. Framing should remain cautious until a study that directly measures whether restoring a pre dysbiotic microbiome prevents disease in the presence of pathogens, is conducted. Thus, although dysbiosis is becoming a widely accepted early sign of microbial imbalance, which is associated with disease susceptibility, longitudinal and interventional studies with regular sampling and experimental control of the microbiome are required to reveal the temporality of dysbiosis, exclude replication of undetected pathogens, and support any causal argument of the connection between dysbiosis and disease emergence (Thompson *et al*., 2024; Holt *et al*., 2021; Egan and Gardiner, 2016;).

On the contrary, some of these agents, like WSSV, TSV, and Vibrio toxins, causing AHPND directly cause damage to the intestinal epithelia, decreasing the complexity of the microbial habitats and altering oxygen gradients needed by microbiota diversity. The simplified and nutrient-enriched environment produced by the epithelial necrosis and loss of mucus typical of AHPND result in dominance by pathogenic Vibrio and inhibition of slower-growing protective anaerobes, dysbiosis may also result directly from pathogen-mediated tissue damage (Tran *et al*., 2013). Dysbiosis reduces microbial functional redundancy, collapsing diverse communities of 20-40 protective taxa to 5-10 dominant organisms, which exposes microorganisms to ecological instability and pathogen survival (De Schryver and Vadstein, 2014). Concomitantly, microbiota diversity loss diminishes the generation of a wide range of protective metabolites (i.e., short-chain fatty acids, bacteriocins, quorum-sensing inhibitors, immune-modulating products), which lessens the ability of the microbiota to suppress pathogens despite the elimination of environmental stressors (Li *et al*., 2018). Also, the competitive exclusion processes do not work since pathogenic Vibrio can be 30-50% of the microbial population, creating the stable dysbiotic state that cannot be reversed (De Schryver and Vadstein, 2014). Dysbiotic Vibrio communities also maintain the domination by antibiotic cross-feeding in which extracellular proteases and lipases hydrolyze the antimicrobial peptides released by the beneficial bacteria and release nutrient substrates that promote the survival of pathogens under antibiotic conditions (Xiong *et al*., 2017). Lastly, a decrease in the production of metabolites, including butyrate and propionate, undermines intestinal epithelial tight junctions to permeabilize to bacterial antigens and lipopolysaccharides, which sparks chronic inflammation and further destabilizes microbiota recovery (Li *et al*., 2018).

Studies have demonstrated that diseased shrimp forfeit microbial diversity in the gut and change functional profiles, such as lost antimicrobial property of commensal bacteria (De Schryver and Vadstein, 2014). Alterations in salinity, temperature, pH and dissolved oxygen are also environmental stressors that directly influence the dynamics of microbial growth and immune competence of the host. The immunosuppression caused by stress undermines the capability of the shrimp to maintain control of microbial populations and this provides an opportunity to the opportunistic bacterial growth. The nutrient and high loads of organic matter favor the growth of fast-growing

R-type, such as Vibrio species, which further disrupts the microbial network. The effect of these can be reduced by probiotic and biofloc based systems to enhance the microbial population, optimize functional redundancy, and enhance the resilience of systems. This is because one of the primary causes of chronic microbiome disruption is due to the extensive and regular prophylactic applications of antibiotics in shrimp aquaculture. Antibiotics put relevant pressure on microbial communities, eliminating the helpful bacteria and result in proliferation of pathogenic antibiotic-resistant microorganisms. This does not only worsen antimicrobial resistance but it also compromises natural microbial barriers that protect shrimp against disease. Literature has also demonstrated that antibiotic-treated systems have a longer period of dysbiosis, a larger number of Vibrio, and are prone to recurring disease events (Flegel, 2019; De Schryver and Vadstein, 2014). Table 5 shows the operational microbial signatures defining healthy versus dysbiotic states in shrimp aquaculture for a guided management decision.

Trade-off and limitations of natural disease control methods

The effectiveness of the microbiome-based interventions and probiotics in the controlled environments has demonstrated promise, however, their performance in the field (especially open shrimp farming system) can be affected by multiple factors. Probiotics are biologically diverse and cannot be considered as one type of intervention. The various strains have different means of action and the environmental conditions such as competition with other microorganisms and changes in conditions can restrict their steadiness and endurance. This leads to temporary colonization and short run gains, requiring constant reapplication that would raise the costs of operation and management issues. The problems such as probiotic death in the feed pellets and the possibility of probiotics to be in the viable but non-culturable (VBNC) conditions also make them even more problematic, though they are not frequently addressed in the literature. The future studies should be aimed at strain-specific intervention, given the parameters of probiotic survival, colonization of the gut, and inter-microorganism competition to enhance the efficacy of probiotics. It is important to learn the behaviour of probiotics in various environmental factors and delivery systems (e.g. water based vs. feed) in order to create more stable and efficient products. The study of VBNC states and die-off and the gut colonization mechanism may provide useful information about the failure of some probiotics and contribute to better suitability of successful interventions in aquaculture, which will reduce the number of regular applications and enhance the survival of probiotics (Thakur *et al*., 2025; Elsegeny *et al*., 2025; Pazos-Rojas *et al*., 2023 microbial diversity and functional redundancy. The effect of probiotics is to inhibit Vibrio species of well managed systems but provide little protection of poorly managed systems, in which opportunistic pathogens may have a competitive advantage. Likewise, biofloc systems enhance microbial stability and disease resistance, yet they are not as easy to manage as traditional systems because of the strict control over aeration and carbon-nitrogen ratios (De Schryver and Vadstein, 2014; Verschuere *et al*., 2000).

System-level combination

Individual disease control measures are usually limited, but when combined to form a system, it offers a more sound and valid method of controlling the health of the shrimp. The failure of systems commonly causes disease outbreaks in aquaculture due to environmental stress, pressure of the pathogens, host nutritional condition, and poor management of the farm (Flegel, 2019). Biosecurity has formed a part of preventing diseases, especially to exclude foreign pathogens such as Vibrio parahaemolyticus, which causes AHPND. Nonetheless, techniques of modern biosecurity must no longer be based on only disinfection, but should be expanded into the category of supposed ecological biosecurity, in which the defensive layers themselves, rather than their composition, are constituted by the microbial community (De Schryver and Vadstein, 2014). Low water exchange, the growth of intake water by microbes, and non-selective sterilization practices are among the practices that preserve useful microbial groups that have the natural ability to control populations of pathogens. However, over-disinfection has the unintended effect of exacerbating disease as well as eliminating competitive biota and leaving vacant ecological niches that are soon occupied by opportunistic pathogens (Verschuere *et al*., 2000). Nutrition is one more important but frequently neglected determinant of microbiome stability and immunity of shrimp. Shrimp diets are known to influence the structure of the gut microbes, host immunity and metabolite generation that consequently affects disease susceptibility. Prebiotic combinations with optimized protein feeds have the potential to increase the numbers of diverse microbes and indicator of enhanced gut immune system functionality improving the pathogen-rich environments indirectly. Studies have demonstrated that such dietary interventions can balance the gut microbiota and improve resistance to Vibrio pathogens and that such measures are more effective when used in conjunction with probiotic supplementation (Ringø *et al*., 2016; Li *et al*., 2018). Microbiome management combined with biosecurity and nutrition provides a more holistic and constant approach to the control of the disease. Instead of temporally repressing pathogens, this system level integration enhances resilience of shrimp populations in the long run. Although this integrated approach requires substantial technical coordination; the necessity of regular checks of water quality, the maintenance of high reliability of sourcing and cold-chain management of probiotic products, accuracy in feed dosage and timing, and the possibility to amend the management practises according to the perceived conditions in the pond. This provides a more viable and efficient mechanism of disease control as compared to the use of one single intervention. Such a strategy also changes the traditional model of disease management based on the usage of chemicals into the model where resilience is the primary goal of contemporary shrimp aquaculture (Tayyab *et al*., 2025).

Table 5: Operational microbial signatures defining healthy versus dysbiotic states in shrimp aquacult.

Signature class (mechanistic rationale)	Specific, measurable microbial features	Healthy state (operational pattern)	Dysbiotic state (operational pattern)	Practical assay / readout	Effect size / variability	References
Alpha Diversity & Evenness (Ecological Buffering Capacity)	Shannon, Simpson, Pielou's Evenness; Observed ASVs/ OTUs; Faith's PD	Stable diversity and evenness within cohort and life stage	Reduced evenness and/or abrupt diversity collapse with dominance by few taxa	16S rRNA amplicon; Shotgun Metagenomics	Moderate	Rungrassamee *et al*., 2014
Beta Diversity Displacement & Dispersion (Anna Karenina Principle)	Bray-Curtis / UniFrac distance to healthy centroid; β-dispersion	Tight clustering around baseline centroid; low dispersion	Large centroid displacement and increased dispersion under stress/ disease	16S/Shotgun + Ordination	Moderate to large	Zaneveld *et al*., 2017
Temporal Stability & Resilience (Cause vs Consequence Inference)	Turnover rate; Variance and autocorrelation; Recovery time after perturbation	Rapid recovery and return to baseline after disturbance	Delayed or incomplete recovery; rising variance preceding disease	Longitudinal 16S/Shotgun	Moderate	Xiong *et al*., 2017
Absolute Opportunist/ Pathobiont Load (True Overgrowth vs Compositional Shift)	Absolute Vibrio spp. load (qPCR/ddPCR); Total bacterial load	Low–moderate Vibrio load without persistent blooms	Sharp increase in absolute Vibrio abundance preceding or accompanying disease	qPCR/ddPCR; Culture Counts	Large	Han *et al*., 2015
Taxonomic Dominance / Opportunist Blooms (Bloom Ecology)	Relative dominance of Vibrionaceae, Photobacterium, Alteromonadaceae	No persistent dominance by opportunistic taxa	Opportunist families dominate community structure	16S/Shotgun (relative) + Absolute Load Confirmation	Moderate	Gao *et al*., 2023
Virulence Determinant Burden (AHPND Specificity)	pirA/pirB (PirABvp) toxin genes; secretion systems; plasmid markers	Virulence genes absent or at baseline	Enrichment of pirA/pirB and associated virulence functions	Targeted qPCR; Shotgun Metagenomics	Moderate to large	Lee *et al*., 2015
Quorum Sensing & Biofilm Potential (Self-Reinforcing Dysbiosis Loops)	QS Regulators, AHL/ AI-2 pathways; EPS/ Biofilm genes	No enrichment beyond baseline	Upregulated QS/ biofilm potential supporting persistence	Shotgun Metagenomics; qPCR	Small to moderate	Defoirdt, 2018
Resistome & Mobilome Expansion (Selection-Stabilized Dysbiosis)	ARGs (tet, sul, qnr, bla); Integrons; MGEs	Low ARG background consistent with inputs	Expanded ARG/ MGE burden following antimicrobial pressure.	Shotgun Metagenomics; ARG Arrays	Moderate	Fhang *et al*., 2021
Pond–Host Microbiome Coupling (Environmental Forcing)	Source tracking from water/biofloc/sediment to gut	Gut microbiome distinct from pond water	Strong coupling: Gut shifts mirror pond blooms	16S/Shotgun + Source Tracking	Moderate	Md Zoqratt *et al*., 2018
Composite Dysbiosis Index (Diagnostic Operationalization)	Weighted score: centroid distance, dominance, Vibrio load, virulence genes	Low, stable score	Elevated and rising score preceding disease	Multivariate Statistical Model	Large	Xiong *et al*., 2017

Synthesizes ecological, taxonomic, and functional microbial signatures that operationally distinguish healthy from dysbiotic states in shrimp aquaculture, connecting measurable microbiome features to mechanical interpretation and practical diagnostic assays.

Implications for antibacterial resistance and global shrimp trade

The shrimp farming methods have been highly intensive and have extensively depended on chemicals, especially antibiotics, to manage disease outbreak. Although these measures provide short-term advantages in terms of disease management, the long-term effects of such measures are dangerous, especially when it comes to the development and spread of antimicrobial resistance (AMR). This is a great concern for aquaculture as well as human health. Farming of shrimps with antibiotics is directly associated with the emergence of resistant bacterial species and transfer of resistance genes in pond systems (Okeke *et al*., 2022). In particular, aquaculture ponds provide favorable conditions in which resistance genes can be transferred horizontally. Selective pressure in these systems is caused by antibiotic residues, which in turn enables different resistance characteristics to be transferred to the microbial communities. These genes may be transmitted through mobile genetic elements, e.g., plasmids and integrons and may be transferred between bacterial species, including human pathogenic bacteria (Preena *et al*., 2020; Mourao *et al*., 2025). The international trade has far reached consequences regarding the spread of AMR bacteria in shrimp farming. Shrimp is a highly traded marine food product, and the international market has strict standards concerning microbiological and residue requirement in an effort to ascertain the safety of imported products. Detection of AMR bacteria in the shrimp shipments can lead to trade bans and recall of products as well as negative publicity to the exporting countries. Thus, although residue-based testing is a routine in food safety assurance, it cannot alone raise the issue of the wider societal health concerns that AMR presents in aquaculture. In addition to needing overarching supervision, the ingestion of infected shrimp or other goods, and the likelihood of the AMR bacteria spreading in the food chain, adds further importance to the necessity (Thornsba *et al*., 2021). The regulatory organizations like the Codex Alimentarius and the World Organization of Animal Health (WOAH) have put rules that seek to control the use of antimicrobials in aquaculture. Nevertheless, the regulations are not easily implemented, particularly in the large shrimp-producing nations (FAO, 2018). The identified obstacles to implementation are several interrelated types. To begin with, laboratory limitations in key producing countries imply that basic testing of the residue is not consistently conducted on farms, and the transition to molecular detection of resistance genes, involving PCR facilities, trained experts, and certified guidelines, is a massive technical challenge (Tran *et al*., 2021; Allegra *et al*., 2024).

Secondly, the unit pricing of metagenomic or qPCR-based surveillance of resistance genes is significantly greater than traditional residue immunoassays, which present cost barriers that are prohibitive to national food safety agencies within the financial limits (Shay *et al*., 2023; Davis *et al*., 2025). Thirdly, the internationally agreed technical standards of what resistance genes ought to be monitored, what detection limits, what sample matrices, and what frequency are lacking, i.e., even well-endowed countries have no standard to follow (Zhao *et al*., 2026). Fourth, in most producing countries, AMR surveillance in aquaculture is in direct competition with more immediate national health needs, thereby limiting political will to invest in proactive environmental monitoring (Alwisi *et al*., 2025). It is crucial to diagnose these challenges before the prescription of reforms; it is not mere regulation challenges, but the lack of the technical, financial, and institutional infrastructure to make more advanced surveillance functional. Regardless of these frameworks, little has been accomplished as far as curbing the occurrence of AMR in aquaculture environments is concerned and especially in settings where use of antibiotics is at very high levels. The question then comes in, do food safety standards, based on residues, alone have the capacity to reduce the potential human health risk of AMR caused by aquaculture? Considering the accumulating evidence of mobile genetic element transfer in pond systems, it becomes more apparent that the trade regulations will need to change. Instead of using residue testing as a sole method in final product testing, direct detection of resistance genes in aquaculture setting such as pond water, pond sediment, and shrimp microbiomes may be required. This would give a broader picture of the AMR dynamics in the whole aquaculture ecosystem and would enable more specific interventions. For example, tracking the microbiomes of shrimp and the pond environment around it would aid in detecting AMR hotspots and prevent the transmission of resistance before even reaches the international markets. Although the current regulatory frameworks, such as Codex and WOAH guidelines, have helped in controlling the AMR risks in aquaculture, the frameworks should be extended to include more proactive monitoring of the resistance genes in the aquaculture environment itself. Such practice would fit trade laws with the changing characteristics of AMR transmission, which would contribute to the improved protection of the health of the population and international commerce (Costa Ortega *et al*., 2026; Fang *et al*., 2021). It is worth noting that this suggested change of residue-based monitoring to resistance gene-based monitoring is yet to be manifested in the import certification mechanisms of key shrimp markets. The United States (through FDA), the European Union (through Regulation EC 470/2009 and its implementing measures) and Japan (through the Food Sanitation Act) are already using maximum residue limits (MRLs) of approved antimicrobials as the basis of shrimp import controls, and neither of the jurisdictions has yet taken the step of mandatory environmental AMR surveillance as a market entry requirement (Karunasagar, 2025), although the Farm to Fork Strategy and the WHO Global Action Plan on AMR allude to a directional shift to broader One Health-suited food safety standards (Narciso and Fonte, 2021). The review thus defines the resistance gene monitoring as a scientifically necessary future; instead of a currently enforceable standard, and concurs specifically that its establishment as a trade certification means would need prior accord of reference methods, threshold values, and legal interpretation of non-conformity with WTO provisions Sanitary and Phytosanitary (SPS), as of non-conformity. The critical practical question, which has to be answered in this situation, is what should an importing country do when a shrimp consignment is proven to be positive in the environment of the aquaculture, but is proven to have no traceable antibiotic residues in the end product. According to the existing trade legislation, there is no legal ground to deny such a shipment, as SPS-compatible restrictions to import must be based on a scientific risk assessment associated with a quantifiable risk to the commodity itself.

Future work and research gaps multi-omics requirement

Multi-omics method validation is vital for defining the specificity and sensitivity of microbial communities in various populations and in varying environmental conditions. In shrimp, microbial communities, environmental and host genomes interact to make the process of understanding health and diseases more difficult. Although 16S rRNA gene surveys have been found to be helpful in the characterization of microbial community organization, they cannot reveal information on the functional dynamics of disease resistance and microbiome dysbiosis. To overcome this weakness, it is important to combine multi-omics methods, such as metagenomics, meta proteomics, meta transcriptomics, and metabolomics, with 16S rRNA gene sequencing. This integration would provide deeper insight into the microbiome's role in the health of shrimps to identify the microbial pathways that underpin resilience or increase susceptibility to disease. These multi-omics systems will enable the identification of health biomarkers in various aquaculture systems, which will eventually lead to creation of more specific and efficient probiotics (Xiong *et al*., 2017). Integrating metagenomics and meta transcriptomics could move the field from correlation to causation by addressing a fundamental question like: How do individual microbial taxa and their expressed metabolic functions influence the immune response of the host and result in disease resistance in shrimp? Metagenomics gives a detailed perspective of the genetic potential of microbial communities whereas meta transcriptomics reflects real time functional activity by profiling gene expression which provides dynamic information on the interaction between microbes and their host environment. With their combination, we will be able to determine which microbes are functionally active in healthy conditions versus pathological, and this will further our capacity to attach microbial activity to host immunological response as opposed to taxonomic presence. Considering this causal relationship between the activity of the microbes and the host immunity, the research-based community can advance beyond observational relationships to implement direct cause effect relationships, and eventually, generate mechanistic information on which a given intervention can be applied in the aquaculture system. Moreover, these integrative multi-omics systems are now also being identified as critical to understanding microbiome interactions and their impact on host physiology in complex ecosystems (Aguiar Pulido *et al*., 2016; Tayyab *et al*., 2025).

Long-term pond-scale trials

Numerous experiments related to the control of natural diseases and microbiome focused approaches are held in a controlled laboratory environment. Nevertheless, the environment of aquaculture is extremely dynamic and elastic to unstable elements including the stocking density, water quality, feed programs, and seasonal stressors. Extensive and prolonged experiments are required to determine the cost efficiency, uniformity, and environmental effects of such measures as probiotic regimes, biofloc systems, and functional feeds under the conditions of commercial reality. These trials would distinguish short-term suppression from durable disease control (Calcagnile *et al*., 2024).

Environmental interaction

The host pathogen interactions do not only dictate disease breakdowns in shrimp aquaculture but also other environmental factors such as changes in temperature, salinity, organic load, and eutrophication. Predictive models that would relate these environmental factors to disease outbreaks and microbiome instability are in great need. These models would inform adaptive management approaches based on the particulars of a specific area and thus prevent instead of responding to disease outbreaks (Murugan *et al*., 2024).

Socioeconomic research

Future research needs to deal with socioeconomic improbabilities of adopting sustainable disease control mechanisms. The lack of knowledge among farmers, financial issues, and inaccessibility to quality inputs are some of the factors that are critical in deciding whether science innovations are applied in practice or not. To address these problems, social sciences should be integrated with aquaculture systems biology so as to develop strategies that are efficient and also accessible to the farmers. This cross-functional strategy will assist in the effective disease containment methods to be widely adopted in the shrimp aquaculture sector (De Schryver and Vadstein, 2014). However, it is important to note that most of the studies used in this study are of the shrimp-producing nations in Asia, which is more a result of the biases towards geographic coverage of published aquaculture studies and areas of intense shrimp production than a deliberate omission of others. Although the biological concepts of microbiome stability, host immunology, and pathogen interactions are probably generalizable to any production setting, the intervention thresholds, environmental variables, and management guidelines identified in the reviewed studies might not be directly applicable to any other production environment (biological infrastructure, water quality patterns, climate, regulations, and climate and value chain organization vary significantly). The main implication that this review has for producers who do not belong to the Asian research setting is the ecological and systems-level framework that it offers, which shifts disease management from the principles of pathogen eradication to the principles of resilience-building. This model of conceptualism is not geography-dependent, although local validation of particular reviewed inputs may still be lacking. Validation research in underrepresented producing countries on a region-specific basis is thus deemed highly desirable as a research priority in the future.

The socio economic, institutional, and environmental aspects play a significant role in promoting sustainable aquaculture practices such as climate smart and integrated farming methods among small holder farmers with barriers to the uptake of innovations as a result of low education level, financial accessibility and extension services, as well as household characteristics of small holders. The socioeconomic studies have not received much emphasis in learning the barriers to adoption (e.g., cost, knowledge gaps, and risk aversion) but these are some of the greatest barriers to effective integrated approaches in aquaculture. The most important question to small scale farmers in developing nations with complex biosecurity, nutrition and microbiome management in place is how they can determine which entry point into the resilience paradigm is the most impactful and the least expensive.

Research should focus on ensuring that implementation undertakings are planned to be scaled and implemented in phases so that farmers can implement the practices step by step without straining their already scarce resources. Participatory strategy with steps can enable farmers to start with the small, manageable interventions, which are sustainable in the long run and wider adoption (Mdoe *et al*., 2025; N'Souvi *et al*, 2025). To make this practical, in a small-scale ponds farming, with no regular extension assistance, commercial probiotic supplementation added to the feed is advised because it is operationally simple, only in that it requires correct dosing at the time of feeding, it also directly act on the microbiome stability and Vibrio suppression pathways that have been most consistently demonstrated as disease-initiating conditions in shrimps, lastly its activity is not contingent on pond or culture conditions. This approach not only gives priority to interventions based on their availability, but also on their lack of technical support.

In addition to education and financial access, it is also important to note that there are multi-dimensional interlocking barriers to adoption in shrimp aquaculture. The unreliability of supply chains of probiotics and other biological inputs, the failure to provide consistent quality of products, and the lack of long-term after-sales technical services are equally reported limitations that can sabotage adoption even in cases where there is awareness among farmers and early interest. The next round of studies should focus on the main factor of adoption failure instead of focusing on the knowledge gap or capital constraints. The most important thing is that the available literature has given little consideration to situations where farmers who had initially embraced probiotic-based or integrated disease management systems later deserted them. It is necessary to know the circumstances under which adoption is reversed, be it that it is in the long-run cost of inputs, inconsistency of observed effects, withdrawal of technical support, or market-level volatility, so that interventions can be designed that are durable in practise, rather than being merely effective under controlled or ideal conditions. The systematic study of such adoption cases that have failed or been discontinued is a critical gap in the current literature that future socioeconomic research must first identify so that the proposed interventions are not merely scientifically valid but also remain practically viable in the context of various production settings.

CONCLUSION

The use of pathogen-centered interventions is not enough in the treatment of diseases in shrimp aquaculture. As evidenced in this review, disease outbreaks are consequences of host immunity-pathogen interactions as well as interactions among host immunity, microbiome stability, and environmental stressors. The discovery of microbiome dysbiosis as a primary pathogenesis in significant shrimp disease is redefining the concept of disease control by then turning the emphasis from eliminating pathogens to proactive resilience enhancement. The future direction in sustaining shrimp production and minimizing the use of antibiotics and the possibility of antibiotic resistance should be centered on the interpretation of ecological and multiomics data into real-world solutions that will meet regulatory requirements. These integrated methods will be primarily dependent on long-term field validation to achieve success. Finally, these methods assist in ecosystem resilience and not pathogen eradication, which represents a fundamental shift in current shrimp health management practices in aquaculture to become more sustainable. The evidence base of this review is geographically focused in Asia, and transferability of the particular findings to other major producing regions like Sub-Saharan Africa and Latin America would still be determined in the future through region-specific field validation. In addition, the examination of failed instances or adoption challenges, (i.e. those in which farmers that previously considered the integrated approach to disease management later dumped it), is also a significant gap in the existing literature that the socioeconomic research in the future must focus on in an effort to make sure that the proposed interventions are not merely scientifically valid, but they are also practical in various production settings.

ACKNOWLEDGEMENT

This work was funded by the Universiti Malaysia Terengganu (UMT) through the Strategic Research Grant-IPhD (SRG-IPhD) [Vot No. 55612]. All authors would like to express special gratitude to the Higher Institution Centre of Excellence (HICoE), Institute of Tropical Aquaculture and Fisheries (AKUATROP), Universiti Malaysia Terengganu, Malaysia, for providing facilities for this research.

NOVELTY STSTMENT

This review presents a new systems-based approach to sustainable shrimp disease management that focuses on ecosystem resilience and moves away from the eradication of pathogens. Rather than treating pathogens and control measures as discrete entities, it integrates host immunity, microbiome stability, and the environment into an all-encompassing approach to disease prevention. Analyses of immunostimulants, functional feeds, probiotics, biofloc technology, and microalgae-based systems, as well as best management practices, underscore the potential of coordinated, ecology-based approaches for implementing antibiotic-free shrimp aquaculture. It also pinpoints the main gaps, such as multi-omics validation, long-term tests under field conditions in ponds, and harmonisation of regulatory aspects in a One Health context.i

AUTHOR'S CONTRIBUTION

Gbaaondo Terzungwe wrote the first draft of the manuscript. Kayode Joseph Ajiboye wrote the second draft; Ahmad Ideris Abdul Rahim visualized the manuscript. Azmie Ghazali,
Ahmad Shuhaimi Draman revised the manuscript, and Nor Azman Kasan conceptualized and supervised the writing process. All authors critically revised the manuscript and approved the final version.

Generative AI and AI assisted technology statement

The authors declare that no generative AI and AI assisted technology was used in the creation of this manuscript.

Conflict of interest

The authors have declared no conflict of interest.

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