

### **REVIEW ARTICLE**

**OPEN ACCESS** 

# **Emerging Zoonotic Viral Diseases in India: One Health Perspective**

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### Abstract

Emerging zoonotic viral diseases pose significant public health challenges due to their high fatality rates, potential for widespread outbreaks, and profound socioeconomic impact. Human, animal, and environmental health interconnectedness highlights the need for a collaborative One Health (OH) approach to control and prevent these diseases. With its diverse ecosystems and rapid urbanization, India has witnessed several major zoonotic outbreaks over the past two decades, including Nipah virus, Kyasanur Forest Disease (KFD), H1N1 influenza, and the global COVID-19 pandemic. These outbreaks underscore the urgent need for integrated surveillance systems, early detection strategies, and sustainable interventions to mitigate future risks. Contributing factors such as deforestation, climate change, unregulated wildlife trade, and intensive farming practices exacerbate the spread of zoonotic diseases. This manuscript emphasizes the importance of a multidisciplinary OH approach, drawing on evidence-based strategies for disease surveillance, vaccination, vector control, and community engagement. By addressing these challenges through coordinated efforts, India can strengthen its preparedness and response to emerging zoonotic viral diseases while promoting public and ecological health.

Keywords: Zoonotic Diseases, One Health, Nipah Virus, Kyasanur Forest Disease, Surveillance, India, Climate Change

Citation: Mishra VH, Bankar NJ, Tiwari AP, Noman O, Bandre GR. Emerging Zoonotic Viral Diseases in India: One Health Perspective. J Pure Appl Microbiol. 2025;19(1):34-48. doi: 10.22207/JPAM.19.1.40

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### INTRODUCTION

Human activities and stressed ecosystems create opportunities for the emergence and spread of viral diseases. The stress factors such as habitat fragmentation, animal trafficking, agriculture, cattle farming, urbanization, mining industries, climate change, and environmental degradation. <sup>1,2</sup> In recent years, the global community has borne witness to the profound ramifications of emergent viral diseases such as Zika, COVID-19,

and Ebola. These diseases not only engender significant threats to human health but also exert considerable impacts on the environmental and animal well-being.<sup>3</sup> This paradigm embodies a collaborative attempt to acknowledge the intricate interrelations among human, animal, and environmental health domains. Through interdisciplinary cooperation, experts from diverse fields can identify and address the fundamental causes of emergent viral diseases, including factors such as deforestation, climate

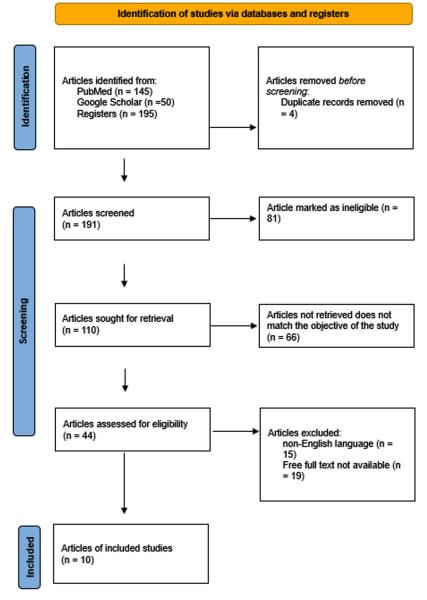


Figure 1. PRISMA9

perturbations, and the proliferation of globalized networks.<sup>4</sup> The efficacy of the OH framework has been substantiated through its successful implementation across numerous nations, bringing advancements in disease surveillance, prophylaxis, and mitigation strategies.<sup>5</sup>

Antimicrobial resistance (AMR) stands out as one of the most significant global health challenges within the OH framework.<sup>6</sup> AMR is linked to all three components due to the excessive use of antimicrobials across diverse sectors, including human medicine, livestock farming, and agriculture. Bacteria acquire resistance genes and mobile genetic elements in response to selection pressure from antimicrobials. These genes can be transferred to other bacteria within the same genus or to new species.7 Due to factors such as mismanagement, lack of infection control, agricultural waste, environmental pollution, and the migration of persons and animals, antimicrobial-resistant bacteria have an increased capability to spread to humans, animals, and the environment.8 This study aims to evaluate the historical and contemporary impact of emerging viral diseases on human and animal populations, considering the potential for zoonotic transmission.

### Review Search strategy

### Inclusion criteria

Inclusion criteria were (i) studies that focus on zoonosis, emerging viral diseases, and one health approach, (ii) studies published in the past decade, (iii) studies that match the objective of this study, and (iv) studies written in the English language.

### **Exclusion criteria**

Exclusion criteria were (i) Studies written as editorials, book chapters, case series, short communication, or letter to editor; (ii) studies unavailable in full-text; (iii) studies published are not in English language; and (iv) studies whose findings were considered does not match the objective of the study.

### **Data Extraction**

PubMed and Google Scholar search engines were used, Mesh terms were (("zoonoses"[MeSH Terms] OR "zoonoses"[All Fields] OR ("zoonotic"[All Fields] AND "diseases"[All Fields]) OR "zoonotic diseases"[All Fields]) AND ("one health"[MeSH Terms] OR ("one"[All Fields]) AND "health"[All Fields]) OR "one health"[All Fields]) AND ("virus diseases"[MeSH Terms] OR ("virus"[All Fields] AND "diseases"[All Fields]) OR "virus diseases"[All Fields]) AND

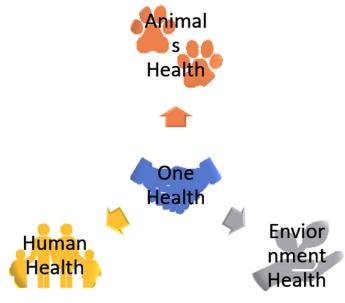


Figure 2. One Health Approach<sup>1,20</sup>

("collaborate"[All Fields] OR "collaborated"[All Fields] OR "collaborates"[All Fields] OR "collaborating"[All Fields] OR "collaboration"[All Fields] OR "collaboratives"[All Fields] OR "collaborative s"[All Fields] OR "collaboratives"[All Fields] OR "collaboratives"[All Fields] OR "collaboratives] OR "collaboratives]

"collaboratives"[All Fields] OR "collaborator"[All Fields] OR "collaborators"[All Fields]) AND ("india"[MeSH Terms] OR "india"[All Fields] OR "indias"[All Fields]))(Figure 1) (Table 1).

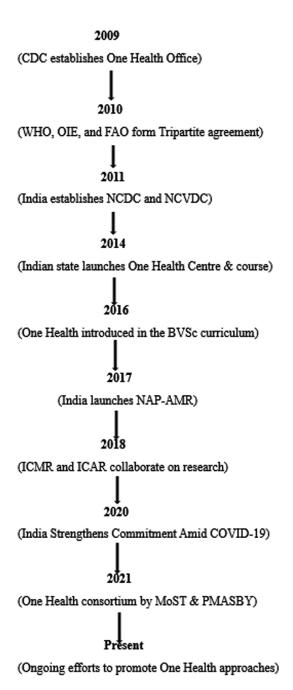


Figure 3. The timeline illustrates the progression of One Health initiatives in India 35,37-40

### Study included

The reviewed studies collectively highlight the significant role of the OH approach in addressing complex health challenges at the human-animal-environment interface. Kumar et al. emphasized the zoological origins of SARS-CoV-2 and stressed the need for a one-health strategy to mitigate future epidemics. 10 Likewise, Filho et al. explain the increasing impact of climate change on the spread of zoonotic diseases and emphasize the need for integrated health interventions. 11 Mourya et al. further demonstrated the effectiveness of one-health interventions. Prejit et al. documented the management and control of successful epidemics of zoonotic diseases in India through cooperation efforts. 12,13 Chatterjee et al. and de la Rocque et al. highlighted the critical gap in policy and the importance of implementing a health plan to improve global health security. 14,15 The detailed study by Tazerji et al. on the transmission of SARS-CoV-2 in animals and Dasgupta et al. on the need for inter-disciplinary cooperation in India, we further highlight the importance of a multidisciplinary approach to the management of zoonotic diseases. 16,17 Finally, Wacharapluesadee et al. long-term surveillance study of Nipah virus in Thailand illustrates the sustained benefits of coordinating.

### One health approach

One Health approach is a team effort to recognize that the health of animals, humans, and the environment are all connected and that one affects the others. <sup>20</sup> Experts in human health, animal health, environmental science, ecology, and public health work together to find and solve the root causes of new viral diseases, which is why the One Health approach includes specialists from different fields. <sup>21</sup>

The OH approach is not a new concept. It has been recognized since the early 20<sup>th</sup> century, but it gained renewed attention in the 1990s following the outbreak of zoonotic diseases such as SARS and avian influenza. This approach is now widely recognized as an effective way to tackle emerging viral diseases and other health issues that affect multiple species.<sup>22</sup>

This approach has several advantages, including improved disease surveillance, prevention, and control. It also encourages a

more complete and integrated approach to health, acknowledging the connection between the health of people, animals, and the environment<sup>1</sup> (Figure 2).

## The link between emerging viral diseases and the environment

Emerging viral diseases are interconnected with changes in the environment, a relationship grounded in the complex relationship between ecological systems, human activities, and infectious agents.<sup>23</sup> Scientific evidence highlights the pivotal role of environmental alterations, including deforestation and climate change, in driving the emergence and transmission of zoonotic diseases those that originate in animals and spill over into human populations.<sup>24</sup>

Deforestation, often driven by agricultural expansion and urbanization, disrupts natural habitats and ecological balance, bringing humans into closer contact with wildlife species that may harbor novel pathogens.<sup>25</sup> This increased proximity heightens the risk of zoonotic spillover events, wherein pathogens transfer from animals to humans, potentially resulting in outbreaks or pandemics. Similarly, climate change influences the distribution and behavior of vector species, such as mosquitoes and ticks, altering the transmission dynamics of vector-borne diseases and expanding their geographical range.<sup>26</sup>

Globalization and intensified travel patterns have profoundly transformed the landscape of disease transmission, facilitating the rapid spread of infectious agents across borders and continents. The COVID-19 pandemic serves as a poignant illustration of how interconnectedness and international mobility can amplify the dissemination of a novel virus.27 The emerging evidence suggests that the SARS-CoV-2 virus, which is responsible for COVID-19, probably originates from bats and may be transmitted to humans by the intermediate host, possibly pangolin, on a wet market in Wuhan, China.<sup>28</sup> Subsequent international travel facilitated the global spread of the virus, leading to a devastating pandemic.<sup>29</sup>

The approach of one health has become a comprehensive framework for understanding and addressing the complex interdependence between human health, animal health, and environmental

Provides athorough understandingofthe provides a model for future RelevancetoReview of the OH approach effectiveness of the complex impact of climate change on zoonotic diseases. Demonstrates the zoonotic diseases OH approach and ole of animals in **Provides insights** transmission and and the need for into the practice emphasizes the Highlights the OH approach **OH** approach in managing need for an COVID-19 Relies on existing Detailed review Limited to one data; relies on existing cases and outbreak experimental experimental experimental one disease; but no new results may Limitations data; relies district and on existing literature, No new no new studies eports data A comprehensive review of various evaluation of the Detailed review Comprehensive Comprehensive animal studies on SARS-CoV-2 of data using experimental OH approach analysis, and bibliometric visualization Network for out no new data; relies VOSviewer on existing Strengths cases and using the outbreak reports Canada, Australia, Italy, pathogens and vectors, most active in research Climate change alters a significant reduction The review highlights and Germany are the viruses; the USA, UK, preventive measures. West Nile and Usutu eading to increased coordination among crucial in managing scores in a systemic the zoonotic origin, early detection and controlling the KFD spread of zoonotic stakeholders were Collaboration and the conditions for in impact through The OH approach and the need for diseases such as its transmission, a OH approach. outbreaks and; Main Findings Degree of OH-ness, and transmission among animals Disease spread, infection rates literature and effectiveness SARS-CoV-2 bibliometric and control Analysis of Measures response, measures outbreak Outcome outbreak trends control Table 1. Summary of research on one health strategies and their impact implementation Forest Disease investigations OH approach (KFD) control for Kyasanur Intervention SARS-CoV-2 /Exposure change on Impact of Outbreak approach Infection zoonotic diseases and OH climate with Not specific populations population of Wayana, Population Population Various Various in India species to any Kerala animal 2022 2021 2022 2022 /ear Mourya et al. 12 Kumar et al.<sup>10</sup> Prejit et al. 13 Filho et al. 11 No. Author(s) 7 m 4

| implementation<br>in similar contexts  | Provides a policy perspective on the importance and integration in national health strategies.   | Provides a framework for improving OH implementation and enhancing global health security   | Provides insights into the transmissiondynamics of SARS-CoV-2 between humans and animals, highlighting the need for a OH approach  |
|--|--|---|--|
| generalizable  | Focuses on<br>policy analysis,<br>lacks<br>empirical data  | Limited to<br>analysis, lacks<br>implementation<br>data   | Relies on existing reports and studies, no new experimental data   |
| Evaluation of<br>One Health<br>(NEOH)<br>framework                                   | Critical analysis<br>of policy<br>framework,<br>highlighting<br>gaps and<br>missed<br>opportunities  | Comprehensive<br>analysis of IHR<br>capacities and<br>OH implementation   | Detailed genomic<br>and phylogenetic<br>analysis of<br>SARS-CoV-2<br>isolates from<br>animals  |
| organization and OH thinking; and identified areas for improvement in OH sharing and | The paper discusses the missed opportunities in integrating One Health approaches in India's national health policies, emphasizing the need for intersectoral coordination to address emerging | The study highlights The importance of operationalizing OH roadmaps to improve IHR capacities and health security, identifying gaps and recommending improvements for better coordination at the human- animal-environment interface. | The study reviews reported cases of SARS-CoV-2 transmission to animals, emphasizing the need for further research to understand the dynamics of the disease in humans and animals. |
|  | Policy gaps<br>and<br>recommendations  | Evaluation of<br>IHR capacities<br>and health<br>security   | SARS-CoV-2 infection rates among animals, genomic and phylogenetic analyses  |
|  | Policy<br>analysis<br>and review   | One Health<br>roadmap<br>implementation   | Transmission of SARS-CoV-2 from humans to animals  |
|  | Various<br>stakeholders<br>in India  | Various   | Various<br>animal<br>species   |
|  | 2016   | \$ 2021   | 2020   |
|  | Chatterjee et al. <sup>14</sup>  | de la Rocque et al. <sup>15</sup> 2021  | Tazerji et al. <sup>16</sup>   |
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| The importance of a coordinated OH approach in addressing zoonotic diseases and other public health challenges in India   | Demonstrates the effectiveness of long-term OH surveillance in managing zoonotic disease outbreaks  | Provides insights into the current landscape of OH activities at the local level in India, emphasizing the need for formalized and sustained intersectoral coordination  |
|---|---|--|
| Focuses on<br>policy analysis,<br>lacks empirical data  | Limited to surveillance data, no new experimental data  | Limited to published literature and personal experiences, potential bias   |
| Comprehensive policy recommendations, practical framework for implementation  | Long-term<br>surveillance<br>data,<br>comprehensive<br>analysis of<br>Nipah<br>virus trends   | Comprehensive landscape assessment, highlighting real-world examples of intersectoral coordination   |
| The study emphasizes the need for intersectoral collaboration and the establishment of OH Committees at state and district levels to address public health challenges effertively | The study reviews two decades of OH surveillance of Nipah virus in Thailand, highlighting the effectiveness of a coordinated surveillance approach in detecting and managing outbreaks. | The review identifies key themes and examples of local OH activities, demonstrating that intersectoral collaboration primarily occurs through specific research activities, during outbreaks, and community outreach efforts. Limited formal coordination among veterinary, medical, and environmental professionals at the district/sub-district levels is noted. |
| Policy<br>recommendations,<br>framework for<br>OH Committees  | Nipah virus<br>infection rates,<br>surveillance<br>effectiveness  | Local intersectoral activities and collaboration examples  |
| OH policy<br>implementation   | Surveillance<br>ssof Nipah<br>virus   | Intersectoral<br>coordination<br>and<br>collaboration  |
| Various<br>populations<br>in India  | Various Surveilla<br>animal speciesof Nipah<br>in Thailand virus  | Various<br>populations<br>in India   |
| 2021  | 2018  | 2023   |
| Dasgupta et al. <sup>17</sup>   | Wacharapluesadee<br>et al. <sup>18</sup>  | 10 Taaffe et al. <sup>19</sup>   |
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health. The goal of a health approach is to identify and mitigate the root causes of emerging viral diseases by promoting cooperation between experts from a variety of fields, such as medicine, veterinary sciences, ecology, and public health. This collaborative effort involves proactive surveillance, early detection, and preventive interventions aimed at mitigating the risks posed by environmental factors, thereby reducing the likelihood of future outbreaks and pandemics.

In short, the bridge between emerging viral diseases and the environment highlights the urgent need for interdisciplinary cooperation, evidence-based interventions, and sustainable practices to safeguard human health and ecological integrity.<sup>30</sup> By adopting a comprehensive and integrated approach, informed by scientific and ethical studies, we can address the complex challenges associated with new infectious diseases and promote the resilience of the global health system to environmental changes.<sup>31</sup>

### **Indian Government**

The Government of India plays an important role in the implementation of a one health approach that addresses the interdependence of human, animal, and environmental health and mitigates the risks of emerging infectious diseases. As a diverse and populous nation facing numerous health and environmental challenges, the Indian government's actions and policies have significant implications for public health and ecological integrity.<sup>32</sup>

In terms of public health, the Indian government is tasked with enhancing disease surveillance, early detection, and response capabilities to combat infectious pathogens. This involves strengthening laboratory infrastructure, expanding diagnostic capacity, and developing robust public health systems capable of rapidly detecting and containing outbreaks. Additionally, promoting research and innovation in fields such as epidemiology and virology is essential for understanding the dynamics of disease emergence and transmission.<sup>33</sup>

Furthermore, the Indian government plays an important role in environmental governance and biodiversity conservation, addressing factors such as habitat destruction and deforestation that contribute to the emergence of zoonotic

diseases. Policies aimed at conserving ecosystems, preserving wildlife habitats, and promoting sustainable land-use practices are integral to a OH approach. Initiatives to regulate the wildlife trade, promote responsible agriculture, and mitigate climate change impacts are also essential for minimizing ecological drivers of disease emergence.<sup>34</sup>

In terms of international collaboration, the Indian government engages with global health organizations and regional alliances to exchange knowledge and resources related to OH initiatives. Participation in forums such as the World Health Assembly and the Convention on Biological Diversity allows India to contribute to collective efforts to address emerging health and environmental challenges.<sup>35</sup>

However, challenges such as resource constraints, infrastructure gaps, and socioeconomic disparities pose obstacles to effective OH implementation in India. To tackle these challenges, strong political support is needed, along with investment in building skills and community involvement. This will help ensure fair access to healthcare services and environmental resources for everyone.<sup>36</sup>

The Indian government's role in implementing a OH approach is multifaceted, encompassing public health, environmental management, and international collaboration. By prioritizing interdisciplinary cooperation, evidence-based policymaking, and community participation, the Indian government can help in the prevention, detection, and control of emerging viral diseases while promoting the health and resilience of ecosystems and communities across the country (Figure 3).<sup>35</sup>

### History of Viral diseases outbreak reported in India

Zoonotic viral diseases have a long history of impacting humans and animals, with notable outbreaks occurring throughout the ages. Rabies, a disease that dates back to ancient times, affects dogs, bats, and wild carnivores and is primarily transmitted by saliva. In the 1950s, Japanese Encephalitis emerged, affecting birds and pigs, transmitted by Culex mosquitoes. Kyasanur Forest Disease, discovered in 1957, primarily affects monkeys and is transmitted by ticks.

Mosquito (Aedes aegypti, Aedes albopictus) 50 Mosquito (aedes albopictus, aedes aegypti)<sup>45</sup> Mosquito (aedes albopictus, aedes aegypti)<sup>44</sup> Direct transmission (Respiratory droplets)<sup>48</sup> Direct transmission (Respiratory droplets)<sup>51</sup> Direct transmission (Bird secretions)46 Direct transmission (bat secretions)<sup>54</sup> Sandflies (Phlebotomus species)<sup>53</sup> Direct transmission (saliva/bite)<sup>41</sup> Ficks (Haemaphysalis spinner)<sup>43</sup> Ticks (Hyalomma species)49 Mosquito (culex species)<sup>42</sup> Livestock (cattle, sheep, goats) Bats, Pangolins (Suspected) Dogs, bats, wild carnivores Non-human Primates Non-human primates Non-human primates Poultry, wild birds **Affected Animals** Bats (fruit bats) Not specific Pigs, birds Monkeys 2006 (major outbreak) 2001 (West Bengal), **Historical** (ancient) Year of Detection/ Table 2. Emerging, remerging zoonotic viral diseases in India 2018 (Kerala) Outbreak 1960s 1950s 1957 1965 2006 2009 2011 2017 Crimean-Congo Hemorrhagic Fever (CCHF) (yasanur Forest Disease (KFD) H1N1 Influenza (Swine Flu) lapanese Encephalitis (JE) Avian Influenza (Bird Flu) SARS-CoV-2 (COVID-19) Zoonotic Viral Disease Chandipura Virus **Dengue Fever** Chikungunya Nipah Virus Zika Virus Rabies

The 1960s saw the emergence of Dengue Fever, transmitted by Aedes mosquitoes and affecting non-human primates.44 Chikungunya, another mosquito-borne disease, caused a major outbreak in 2006, primarily affecting non-human primates.45 Avian Influenza, or Bird Flu, emerged in 2006, impacting poultry and wild birds through direct transmission.46 The Nipah Virus, identified in 2001 and 2018, is associated with fruit bats and direct contact with bat secretions.47

In 2009, the H1N1 Influenza, or Swine Flu, emerged, primarily affecting mainly pigs and spreading through respiratory droplets. 48 Crimean-Congo Hemorrhagic Fever, identified in 2011, affects livestock and is transmitted by ticks. 49 Zika Virus gained prominence in 2017, transmitted by Aedes mosquitoes and impacting non-human primates.<sup>50</sup> Recently in 2020, SARS-CoV-2, which causes COVID-19, emerged, possibly from bats and pangolins, spreading through respiratory droplets in humans.51 These diseases underscore the ongoing challenge of zoonotic infections and the importance of understanding their dynamics for effective prevention and control measures (Table 2).

Collaboration between veterinary, environmental, and public health sectors to monitor bat populations, educate communities, and implement surveillance and control measures to prevent future outbreaks come under a OH approach.52

### Emerging, remerging zoonotic viral diseases in India

### Implications for future

The imperative for active disease management necessitates a collaborative approach to surveillance, vaccination, vector control, wildlife management, environmental stewardship, community engagement, and policy formulation, all supported by research and capacity-building initiatives.55 Integrated monitoring systems are necessary for human, animal, and vector surveillance to detect disease emergence easily. Simplified by enhanced data sharing among health, veterinary, and environmental agencies, timely dissemination of information is essential for effective response.56

Vaccination campaigns targeting both animals and high-risk human associates joined

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| Area                                       | Strategies  |
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| Surveillance and Early<br>Detection        | <ul> <li>Integrated monitoring means creating systems to keep track of diseases in people, animals, and insects that spread diseases.</li> <li>Data sharing means improving teamwork between agencies that focus on human health, animal health, and the environment so they can quickly share important information.<sup>62</sup></li> </ul> |
| Vaccination and<br>Treatment               | <ul> <li>Vaccination Campaigns can conduct vaccination programs in animals (e.g., rabies, avian influenza)</li> <li>and at-risk human populations.</li> <li>Access to antiviral drugs can improve healthcare through early treatment.<sup>63</sup></li> </ul>   |
| Wildlife and Livestock<br>Management       | • Zoning and biosecurity can be implemented in livestock biosecurity measures and wildlife management strategies.<br>• Educate communities on the safe handling of domestic and wild animals.   |
| Vector Control and<br>Management           | <ul> <li>Source reduction of breeding sites for vectors such as mosquitoes or ticks.</li> <li>Biological control by using biological agents or natural predators to reduce vector populations.<sup>55</sup></li> </ul>  |
| Community Engagement<br>and Education      | <ul> <li>Public Awareness to educate communities on preventive practices, safe animal handling, and recognizing disease symptoms.</li> <li>Cultural Adaptation to give messages and strategies to local cultural practices for better adoption.</li> </ul>  |
| Environmental and<br>Ecological Management | <ul> <li>Deforestation control can limit habitat disruption and manage land use changes to minimize wildlife-human contact.</li> <li>Water management to reduce contamination and ensure proper waste disposal.<sup>26</sup></li> </ul>   |
| Policy and Legislation                     | <ul> <li>Establish strong legal regulatory frameworks for disease control, wildlife trade, and livestock management.</li> <li>Cross-sector cooperation to promote multi-disciplinary coordination between health, agriculture, and environmental sectors.</li> </ul>  |
| Research and Capacity<br>Building          | <ul> <li>Research on disease ecology helps us understand how diseases spread between different species.</li> <li>Training programs to build capacity in epidemiology, veterinary science, and environmental health for sustained expertise.66</li> </ul>  |

with improved access to antiviral therapeutics, establishment is an essential component of disease management strategies. Together, vector control measures, including source reduction and biological agents, aim to restrain vector-borne disease transmission.<sup>57</sup> Implementation of zoning protocols and biosecurity measures in livestock and wildlife management, alongside community education on safe animal handling, foster disease containment.<sup>58</sup>

Environmental management interferences, such as deforestation control and water sanitation measures, moderate habitat disruption and minimize pathogen spillover. Community engagement initiatives, emphasizing preventive practices and culturally adapted messaging, increase public awareness and adopt behavioural change. Policy frameworks, surrounding disease control, wildlife trade, and interdisciplinary cooperation, provide the regulatory support necessary for effective implementation. 60

The research aims to explain disease ecology dynamics across species and capacity-building initiatives in epidemiology, veterinary science, and environmental health to support institutional resilience against emergent threats. This collaborative approach, supported by scientific accuracy and interdisciplinary collaboration, embodies a positive attitude toward the protection of public health and ecological integrity in the evolving infectious disease challenges (Table 3).<sup>61</sup>

### CONCLUSION

The one health approach connects the health of people, animals, and the environment, making it essential for managing new diseases that can spread from animals to humans in India. Success requires teamwork across various fields, effective monitoring, vaccination efforts, controlling disease-carrying insects, managing wildlife, and engaging communities. The Indian government plays a crucial role by creating policies, collaborating with other countries, and building the necessary skills to address these health issues. Tackling challenges like antibiotic resistance and environmental damage through sustainable practices can help prevent future

outbreaks of zoonotic diseases. By adopting a comprehensive and evidence-based strategy, India can enhance public health and foster a healthier balance between people and nature.

### **ACKNOWLEDGEMENTS**

None.

### **CONFLICT OF INTEREST**

The authors declare that there is no conflict of interest.

### **AUTHORS' CONTRIBUTION**

All authors listed have made a substantial, direct and intellectual contribution to the work, and approved it for publication.

#### **FUNDING**

None.

### **DATA AVAILABILITY**

All datasets generated or analyzed during this study are included in the manuscript.

### **ETHICS STATEMENT**

Not applicable.

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