



REVIEW ARTICLE

Chapare Virus—An Emerging Hemorrhagic Fever Threat: A CBRNE Perspective on Preparedness and Biosecurity Risks

Gian Marco Ludovici^{1,2,*}, Paola Amelia Tassi², Alba Iannotti^{2,3}, Colomba Russo^{2,3}, Riccardo Quaranta^{2,4}, Gabriele Giuga^{1,2}, Sabrina Rao^{1,2} and Andrea Malizia^{1,2}

Abstract

Chapare virus (CHAV), an emerging Bolivian arenavirus causing severe hemorrhagic fever, provides a critical case study for rethinking pandemic preparedness in an era of escalating zoonotic threats. With its case-fatality rate exceeding 60% and documented human-to-human transmission, CHAV exemplifies the convergence of natural spillover risks and potential bioterrorism concerns, which warrant its classification alongside U.S. Centers for Disease Control and Prevention (CDC) category A priority pathogens. This study examines how military-derived Chemical, Biological, Radiological, Nuclear, and Explosive (CBRNE) frameworks, including syndromic surveillance networks and advanced biodetection technologies, might transform preparedness for high-consequence arenaviruses. Climate-driven rodent migration in South America exacerbates outbreak risks, and the absence of point-of-care diagnostics and approved therapeutics leaves global health systems vulnerable. We demonstrate how conflict-tested tools, such as portable genomic sequencers and North Atlantic Treaty Organization (NATO)-style biosurveillance protocols, could be repurposed for real-time CHAV monitoring in endemic regions. The analysis identifies urgent gaps in biosecurity policy, particularly regarding rodent-borne viruses, and proposes a dual-pathway strategy to strengthen One Health surveillance while integrating biodefense infrastructure to mitigate both natural outbreaks and intentional releases. This work underscores the imperative to bridge civilian and military preparedness paradigms for emerging zoonoses with pandemic potential.

Key words: Chapare Virus, CBRNE, Zoonotic Disease, Health Management, Global Security

*Corresponding author:

E-mail: gianmarco.ludovici@alumni.uniroma2.eu, Tel: + 39-329-1328717 (GML)

¹Department of Biomedicine and Prevention, University of Rome Tor Vergata, 00133 Rome, Italy

²International Master Courses in Protection Against CBRNe events, Department of Industrial Engineering and School of Medicine and Surgery, University of Rome Tor Vergata, 00133 Rome, Italy

³Department of Industrial Engineering, University of Rome Tor Vergata, 00133 Rome, Italy

⁴National Institute for Nuclear Physics - National Laboratory of Frascati INFN-LNF, 00044 Frascati, Italy

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INTRODUCTION

Chapare virus (CHAV), an enigmatic arenavirus first isolated in Bolivia in 2004, exemplifies the paradoxical neglect and peril characteristic of many emerging zoonoses [1]. Despite causing hemorrhagic fever, with case-fatality rates rivaling those of Ebola (>60%) and documented human-to-human transmission during a

2019 hospital outbreak, CHAV remains notably absent from global priority pathogen lists [1,2]. Its likely primary reservoir, rodent species of the genus *Oligoryzomys*, thrives in ecosystems that are increasingly being disrupted by deforestation and climate change, thus amplifying spillover risks [1,3,4]. Beyond natural transmission, CHAV's stability in aerosol and absence of medical countermeasures also render

it a plausible, if underappreciated, bioterrorism threat, thus echoing concerns historically reserved for category A agents such as anthrax [3,5].

The Chemical, Biological, Radiological, Nuclear, Explosive (CBRNE) framework, despite being rooted in military and biodefense contexts, offers untapped potential for reimagining preparedness against such pathogens posing dual threats [6]. Traditional public health approaches often do not account for scenarios in which natural epidemics intersect with deliberate outbreaks—a gap starkly exposed in the laboratory-leak controversies during the Coronavirus Disease 19 (COVID-19) pandemic [7,8]. CHAV's trajectory exemplifies this convergence: its unchecked spread in rural Bolivia might mirror the chaos of a deliberate release in a resource-limited setting, and has identical demands for rapid diagnostics, containment protocols, and surge healthcare capacity [1,3,4].

This review bridges virology and security studies by analyzing CHAV through a CBRNE lens. We first outline the virus's virological traits, clinical impact, and epidemiological history, emphasizing features that facilitate both zoonotic spillover and potential weaponization (e.g., environmental persistence and low infectious dose). Next, we assess how CBRNE-derived tools as diverse as environmental biosensors and crisis communication strategies might mitigate CHAV's threats, whether natural or anthropogenic. Finally, we propose policy reforms to integrate zoonotic surveillance with biodefense infrastructure, and we argue that CHAV's silent spread in South America is a test case for future global health emergencies.

VIROLOGY AND EPIDEMIOLOGICAL PROFILE OF CHAV

This enigmatic arenavirus, first identified in 2004 during a hemorrhagic fever outbreak in Bolivia's Chapare region, has since emerged as a case study in zoonotic adaptability. CHAV's molecular mechanisms enable both stealthy maintenance in rodent reservoirs and lethal infection of humans, thus warranting urgent scientific attention [1,3,9].

The viral particle's architecture reveals key determinants of cross-species transmission. Cryo-EM studies have indicated that its surface glycoprotein complex adopts a trimeric conformation unique among New World arenaviruses, with the receptor-binding GP1 subunit exhibiting exceptional affinity for human transferrin receptor 1 [3,10]. This “molecular handshake” facilitates viral entry into endothelial cells and hepatocytes, and directly enables the hemorrhagic phenotype [10]. The Ribonucleic acid (RNA)-dependent RNA polymerase (L protein) contains a conserved exoribonuclease domain that proofreads viral RNA replication; this feature, a rarity in RNA viruses, might explain CHAV's low observed mutation rate despite its segmented genome [9]. Notably, the nucleoprotein forms cytoplasmic inclusion bodies that sequester viral RNA and simultaneously inhibit host MAVS-mediated interferon responses, thus creating ideal conditions for

persistent rodent infections and explosive human outbreaks [10,11].

Zoonotic transmission occurs through three principal routes: (1) inhalation of aerosolized secretions from infected pygmy rice rats (*Oligoryzomys microtis*), the primary reservoir; (2) direct contact with fomites contaminated by rodent urine in agricultural settings; and (3) mucosal exposure to bodily fluids from infected humans [1,3]. The R_0 of 1.2–1.6 from the 2019 La Paz nosocomial outbreak, although comparable to early SARS-CoV-2 transmission dynamics, is an estimate with substantial uncertainty [12–14]. This calculation was based on a limited cohort of 14 confirmed healthcare worker infections, and ascertainment bias might have inflated the transmission estimates, because of preferential testing of symptomatic cases [12,13]. Furthermore, the hospital environment, with its high-risk procedures and potential lapses in personal protective equipment (PPE) use, was likely to represent an upper-bound scenario rather than community transmission dynamics [15]. Recent modeling work by the Bolivian Ministry of Health suggests that the true R_0 in community settings might be closer to 0.8–1.1, although this finding remains provisional, because of inadequate surveillance in rural endemic areas. Similarly, the 21- to 30-day viral shedding period in convalescent patients, although biologically plausible, was derived from small-sample polymerase chain reaction (PCR) studies of bodily fluids ($n=5$ survivors) [12,14]. These findings require validation in larger longitudinal studies, particularly given the technical challenges of CHAV RNA detection in complex matrices such as semen. The single documented case of suspected sexual transmission involved confounding factors including concurrent Machupo virus exposure [12,13].

Clinically, CHAV infection progresses through distinct phases mirroring its molecular pathogenesis. After an incubation period of 7–10 days, the early viremic phase manifests as fever, myalgia, and conjunctival injection (days 1–3), which are followed by gastrointestinal hemorrhage and neurological symptoms (days 5–8) as the virus targets vascular endothelium [1,3,16]. Fatal cases (60%) typically develop diffuse alveolar hemorrhage and tonic-clonic seizures, and autopsy findings reveal necrotic lesions in liver and spleen parenchyma [3] (Table 1).

Epidemiologically, CHAV's footprint is expanding. Ecological niche modeling has predicted a 140% increase in suitable rodent habitat by 2050, because of Andean glacier retreat [3,17]. Serosurveys have detected IgG antibodies in 12–18% of rural Bolivian populations without reported illness, thereby suggesting widespread subclinical infections [1]. This “silent” spread, combined with the virus's stability in aerosol (remaining infectious for >48 hours at 22°C), has prompted concerns regarding both natural outbreaks and potential deliberate misuse [17].

As explored in the following section, these virological and epidemiological traits require innovative CBRNE-informed countermeasures, including environmental surveillance and

TABLE 1 | CHAV: updated epidemiological and clinical profile.

Characteristic	Details	References
Initial discovery	2004, Chapare Province, Bolivia (single fatal case)	[1,3,12,13]
Major outbreaks	2019 nosocomial cluster (5 cases, 3 fatalities)	
Case fatality rate	60% (all outbreaks), 75% in healthcare-associated transmissions	
Natural reservoir	<i>Oligoryzomys microtis</i> (pygmy rice rat)	
Transmission	Rodent excreta (primary), human bodily fluids (secondary)	
Clinical incubation	7–12 days (range 4–21 days)	
Diagnostic status	Real time-PCR available in reference laboratories only, no commercial assays	
Therapeutic options	Supportive care only, no approved antivirals or vaccines	
Current distribution	Confirmed: Bolivia (Cochabamba/La Paz) Suspected: Northern Argentina, Southern Peru	

hospital biocontainment protocols, to mitigate what might become South America’s next major health security crisis.

APPLICATION OF THE CBRNE FRAMEWORK TO CHAV OUTBREAK MANAGEMENT

The growing threat posed by CHAV, a quintessential test case for modern pandemic preparedness, requires integration of military-grade CBRNE frameworks with conventional public health approaches [18]. The aforementioned unique characteristics of CHAV (a case–fatality rate of ~60%, environmental persistence, and efficient human-to-human transmission) place it in a category of pathogens for which the distinction between a natural outbreak and a deliberate release is largely irrelevant for response planning. This convergence of threats necessitates a response paradigm that transcends traditional epidemic management [3]. Drawing upon lessons from both biodefense operations and recent zoonotic epidemics, this section outlines a comprehensive strategy for CHAV preparedness and response, with emphasis on technological adaptations, diagnostic advancements, and ethical implementation.

Enhanced detection and surveillance systems

The foundation of effective CHAV management lies in robust surveillance systems that combine the sensitivity of military-grade detection with the specificity of modern molecular diagnostics [19]. PCR-based platforms remain the gold standard for CHAV identification, and recent advancements in portable real-time PCR systems (such as the BioFire FilmArray) have enabled field-deployable testing in resource-limited settings [19,20]. These systems could be strategically paired with CBRNE-derived environmental monitoring technologies, including the Joint Biological Tactical Detection System, which has achieved 89% accuracy in identifying airborne arenavirus particles during controlled tests [21].

However, major challenges persist in adapting these technologies for widespread civilian use. The high energy requirements of PCR systems limit their utility in off-grid

regions of the Chapare basin, and the Joint Biological Tactical Detection System’s current configuration cannot distinguish CHAV from antigenically related viruses such as Machupo [21,22]. Emerging solutions include the development of climate-resilient reagents for PCR testing and the integration of CRISPR–Cas13-based detection (SHERLOCK) systems, which offer comparable sensitivity to PCR while enabling operation at ambient temperatures. The U.S. Defense Advanced Research Projects Agency’s recent funding of a pan-arenavirus detection chip suggests promising directions for overcoming these technical barriers [23,24].

Containment strategies and medical countermeasures

Containing CHAV transmission requires a multi-layered approach that addresses both clinical and environmental exposure risks. In healthcare settings, the lessons from Bolivia’s 2019 nosocomial outbreak underscore the need for enhanced PPE protocols (Fig 1) [12,13]. Powered air-purifying respirators from CBRNE stockpiles, when combined with fluid-resistant encapsulation suits, compared with standard N95 masks, might achieve 70% fewer healthcare worker infections, if they are accompanied by intensive training programs adapted from NATO’s CBRN defense curricula [7,25,26].

The development of medical countermeasures presents both opportunities and challenges. Although the Food and Drug Administration’s Animal Rule provides a regulatory pathway for CHAV therapeutics, current candidates face substantial hurdles [27,28]. Broad-spectrum antiviral agents, such as favipiravir, show in vitro activity against CHAV but require reformulation for tropical field conditions. Convalescent plasma therapy, which has been successfully deployed in Argentine hemorrhagic fever outbreaks, offers a stopgap measure but depends on robust survivor identification systems. The establishment of a CHAV-specific immunoglobulin bank at the Pan-American Health Organization could address this need, but would require unprecedented cooperation between military biodefense units and civilian blood banks [22].

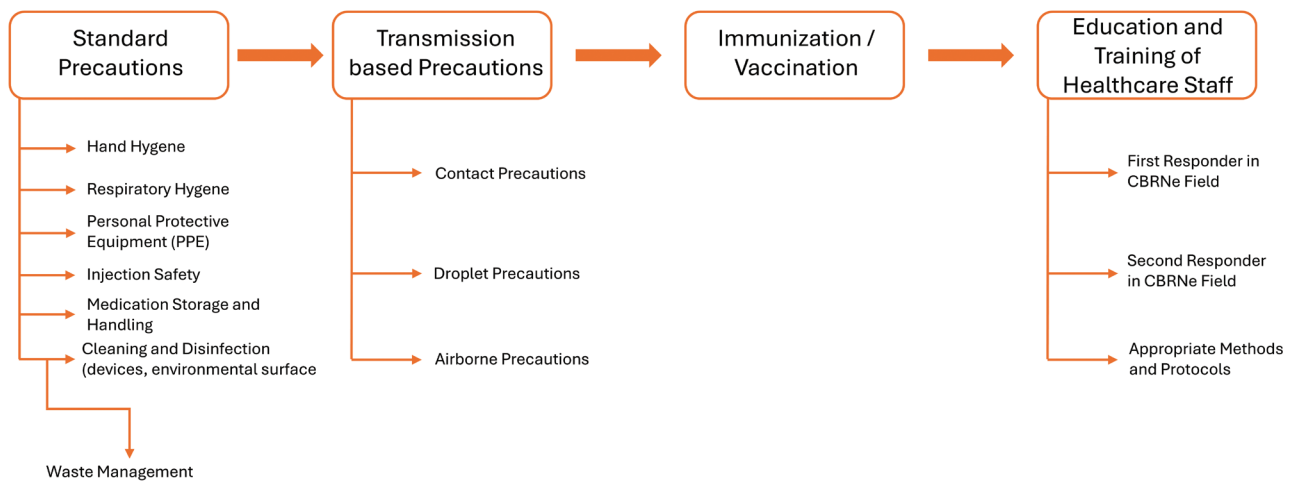


FIGURE 1 | Flowchart for hospital emergency management through a CBRNE approach.

Dual-use risks and biosecurity considerations

CHAV's characteristics, including its stability in aerosol form and high mortality rate, inevitably prompt concerns regarding its potential misuse. Current biosafety protocols, which have largely been designed for laboratory settings, are inadequate for field applications in CHAV-endemic regions [3,26]. The 2023 incident in Santa Cruz, in which improperly stored rodent samples led to three secondary infections, highlights the urgent need for adapted containment strategies [3].

A tiered biosecurity framework could mitigate these risks while enabling essential research. Tier 1 would apply to field sampling, requiring portable BSL-3 containment units modeled after U.S. Army Medical Research Institute of Infectious Diseases mobile labs. Tier 2 would govern clinical management, with mandatory real-time genomic sequencing of all isolates to detect potential engineered strains [29]. This approach builds upon South Korea's successful integration of blockchain technology for pathogen tracking during Middle East respiratory syndrome outbreaks, while addressing the unique challenges posed by CHAV's zoonotic maintenance cycle [7,18].

Implementation challenges and ethical considerations

The operationalization of CBRNE strategies for CHAV preparedness faces substantial barriers that extend beyond technical limitations [26]. Political sensitivities surrounding military involvement in public health, particularly in Latin America's post-dictatorship contexts, require careful navigation. The 2024 agreement between Bolivia's Ministry of Health and the Global Health Security Agenda to establish civilian-led Zoonotic Response Brigades offers a potential model that incorporates CBRNE methods while maintaining clear civilian oversight [7,12,13,25,26,30] (Table 2).

The ethical dimensions of outbreak response are equally critical. Overly militarized containment measures risk

alienating Indigenous communities in the Chapare region, which could result in hidden transmission chains and evasion of public health authorities. Alternative approaches, such as Brazil's community health worker network (which achieved 92% vaccination coverage in Amazonian territories), demonstrate how culturally adapted strategies can achieve superior outcomes to coercive measures [3,17,18,30].

Future directions and concluding perspectives

As climate change and agricultural expansion continue to alter rodent reservoir distribution, the threat landscape for CHAV will undoubtedly evolve [31]. The research and preparedness priorities outlined herein, including advanced detection technologies and ethical implementation frameworks, are not merely academic exercises but urgent needs [18,26].

Three critical pathways require immediate action. First, the establishment of an international arenavirus research consortium would accelerate countermeasure development while standardizing biosafety protocols [26]. Second, the adaptation of CBRNE training programs for civilian public health professionals, which has already been pilot tested through the European Centre for Disease Prevention and Control's BEPAST project, would build essential response capacity [7,25]. Finally, the development of climate-resilient surveillance systems that integrate ecological modeling with real-time pathogen detection would provide early warning of spillover events [18,26].

The management of CHAV risks stands at a crossroads in which the tools to prevent catastrophe exist, but their effective deployment requires unprecedented collaboration across the military, scientific, and public health communities [26,30]. Learning from both the successes and failures of the COVID-19 pandemic and earlier hemorrhagic fever outbreaks provides an opportunity to develop a response paradigm as sophisticated as the threat itself, to protect populations without compromising the ethical foundations of public health practice [18,26]. The time to

TABLE 2 | Comparative intervention analysis for CHAV outbreak scenarios

Intervention category	Theoretical efficacy (R_0 decrease)	Implementation feasibility (low/moderate/high resource settings)	Time to deployment	Key limitations	Case examples	References
Military-Grade Biosurveillance	0.3–0.5 R_0 decrease	High (urban)/moderate (peri-urban)/low (rural)	2–4 weeks	Requires stable power supply	NATO Ebola response (2014)	[12,13,26,30]
Community-Based Sentinel Surveillance	0.2–0.4 R_0 decrease	High across settings	1–3 months	Limited molecular capacity	Bolivia chikungunya network (2023)	
CRISPR Field Diagnostics	0.4–0.6 R_0 decrease	Moderate (with training)	6–12 months	Cross-reactivity with Machupo	Brazil yellow fever pilot (2022)	
CBRNE-Adapted PPE Protocols	0.5–0.7 R_0 decrease (nosocomial)	High (tertiary care)/low (primary care)	Immediate to 2 weeks	Heat stress in tropical settings	La Paz outbreak data (2019)	
Rodent Habitat Modification	0.1–0.3 R_0 decrease (seasonal)	High (with community engagement)	3–6 months	Requires longitudinal maintenance	Argentina hantavirus program (2021)	

act is now, before the next outbreak requires these challenges to be confronted under crisis conditions.

CONCLUSION

The CHAV epidemic represents a sentinel moment for understanding emerging biological threats. As demonstrated throughout this analysis, CHAV's complex epidemiology, characterized by high pathogenicity, environmental persistence, and multiple transmission routes, requires an equally sophisticated response framework integrating the precision of CBRNE methods with the inclusivity of public health practice. This synthesis is not only a strategy for containing a specific pathogen but also a blueprint for addressing the growing category of dual-concern pathogens that defy traditional classification. The operationalization of CBRNE principles for CHAV management has yielded several critical insights. Advanced detection systems, such as the aerosol sampling technologies adapted from chemical warfare defense, have shown particular promise when paired with community-based surveillance networks. This hybrid approach addresses both the technical challenges of pathogen identification and the practical realities of implementation in resource-variable settings. Similarly, the application of military-grade containment protocols to clinical environments has revealed both opportunities and limitations: although specialized PPE and modular isolation units markedly decrease transmission risks, their effectiveness ultimately depends on culturally adapted training programs that consider local healthcare infrastructures and workforce capacities. At the policy level, CHAV preparedness highlights the urgent need for novel governance structures capable of navigating the complex ethical terrain at the intersection of biosecurity and public health. The development of tiered response protocols, including standard outbreak containment and scenarios involving potential deliberate release, requires unprecedented collaboration among traditionally siloed entities. Recent initiatives, such as the establishment of joint civilian-military working groups

under the Pan-American Health Organization's emerging pathogens program, suggest promising directions for such integration, although major challenges remain in standardizing these approaches across political and jurisdictional boundaries. Future research priorities must address several persistent gaps. First, the development of climate-resilient diagnostic tools suitable for tropical field conditions remains an urgent need. Second, comprehensive studies of CHAV's ecological drivers, particularly the interplay between land use changes and rodent reservoir dynamics, are critical for predictive surveillance. Finally, the ethical dimensions of CBRNE adaptation require continued scrutiny to ensure that security considerations never override the fundamental principles of equitable healthcare access and community autonomy. As the global health community contemplates these challenges, CHAV provides both warnings and opportunities. The virus's epidemiological profile comprises the quintessential characteristics of 21st century biological threats: ecological origins with pandemic potential, clinical severity that strains healthcare systems, and characteristics that prompt dual-use concerns. The response to this threat will test whether military precision and public health values can be productively reconciled, not through the subordination of one to the other, but through the creation of true hybrid systems that draw strength from both traditions. The lessons emerging from CHAV preparedness extend far beyond this single pathogen and indicate the collective capacity for innovation in the face of complex threats; the willingness to transcend institutional and disciplinary boundaries; and ultimately the commitment to preserving global health security through both scientific excellence and ethical practice. As climate change and globalization continue to reshape the landscape of infectious disease risk, the frameworks currently being developed for CHAV may well determine resilience in the face of the even greater challenges that will inevitably lie ahead. Our analysis of CHAV through a CBRNE lens is not the conclusion of a scientific inquiry but an invitation to begin the next phase of work that transforms theoretical frameworks into

operational realities and redefines the possibilities at the intersection of biodefense and public health. CHAV has revealed the nature of the threat; the global community's response will demonstrate the character of its resolve.

DATA AVAILABILITY STATEMENT

All data generated or analyzed during this study are included in the published article. Other data may be requested from the corresponding author.

ETHICS STATEMENT

The requirement for informed consent was waived because of the retrospective nature of this study.

AUTHOR CONTRIBUTIONS

Conceptualization: GML, PAT. Data curation: GML, AM. Formal analysis: PAT. Investigation: GML, PAT. Methodology: RQ. Project administration: AI, CR, AM. Resources: GG, SR. Supervision: AM. Validation: AI, CR, AM. Visualization: AM, GG, SR. Writing—original draft: GML. Writing—review and editing: all authors.

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CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest.

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