NOSOCOMIAL INFECTIONS AND NOROVIRUS KAWASAKI VARIANT: A REVIEW ON EMERGENCY MANAGEMENT IN HOSPITALS

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ABSTRACT

Nosocomial infections, also known as healthcare-associated infections (HAIs), are infections acquired during the process of receiving healthcare that were not present at the time of admission. They can occur in many areas of healthcare delivery, such as hospitals, long-term care facilities, and outpatient clinics, and can also occur after discharge. Among HAIs, nosocomial enteritis appears to be an important risk factor. However, there has been a great effort by infection prevention and control programs to develop surveillance systems and infection control methods. Viruses are the main cause of nosocomial enteritis in neonates, and rotavirus species A (RVA) and norovirus (NoV) are considered the main etiologic agents responsible for acute gastroenteritis (AGE) in hospitalized children, excluding that caused by *C. difficile*. Since October 2024, there has been a significant increase in cases of gastroenteritis due to a highly infectious NoV (genotype GII.17), known as the Kawasaki variant, especially in the United Kingdom, but cases are being reported throughout Europe. The hospitalization of many individuals, in a short time, due to NoV Kawasaki, in combination with the increase in hospitalizations due to typical seasonal flu, could trigger a chain reaction with a strong increase in HAIs. The aim of this work is to evaluate the current situation regarding nosocomial enteritis in the face of the new extremely infectious variant of NoV. as well as to analyze the possibility to contain the spread of a possible epidemic using a Chemical, Biological, Radiological, Nuclear, and Explosives (CBRNe) approch.

Keywords — Nosocomial Infections; Norovirus; Emergency Management

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INTRODUCTION

Healthcare-associated infections (HAIs) are infections acquired during medical care, absent at the time of hospitalization. These infections, including occupational exposures among healthcare workers, impose a significant global burden, with higher incidence in resource-limited settings [1,2]. While bacterial pathogens like Acinetobacter and methicillin-resistant Staphylococcus aureus (MRSA) dominate HAIs, viruses such as norovirus (NoV), respiratory syncytial virus (RSV), and influenza contribute substantially, particularly in pediatric and immunocompromised populations [1,3,4].

NoV, a leading cause of acute gastroenteritis, results in approximately 685 million cases annually worldwide. Its transmission via fecal-oral routes and environmental persistence facilitates outbreaks in hospitals, nursing homes, and other congregate settings [5,6]. For two decades, NoV genotype GII.4 dominated globally until the emergence of GII.17[P17] (Kawasaki 308-like variant) in 2014, which exhibited increased predominance in Asia and sporadic detection in Europe and North America [7,8]. This antigenic shift highlights the capacity of NoV for rapid evolution, necessitating equally dynamic surveillance and

containment strategies [9].

Prevention remains challenging due to NoV environmental stability and lack of licensed vaccines [10,11].

Current measures emphasize hand hygiene with soap and water (alcohol-based sanitizers are ineffective), surface disinfection, and isolation protocols. However, the Kawasaki variant's spread since 2024 underscores limitations in conventional infection control frameworks [10,12].

To address this, we propose integrating Chemical, Biological, Radiological, Nuclear, and explosive (CBRNe)-inspired emergency management principles into HAI response systems [13]. Just as CBRNe incidents require coordinated "First Responder" (immediate containment) and "Second Responder" (specialized mitigation) teams, NoV outbreaks—particularly those involving novel variants—demand: 1) Rapid deployment units trained in biocontainment protocols; 2) Standardized risk assessment tools adapted from CBRNe frameworks; and 3) Real-time genomic surveillance to detect emerging variants [13,14].

This approach aligns with World Health Organization (WHO)/Centers for Disease Control and Prevention (CDC) guidelines while addressing gaps in scalability during large-scale outbreaks [13].

This review examines NoV virology, the epidemiological significance of the GII.17[P17] variant, and evidence-based strategies to reduce nosocomial transmission. We further evaluate the potential of CBRNe-inspired emergency protocols to enhance healthcare systems' preparedness for NoV and other viral HAIs, emphasizing practical implementation for frontline teams.

Healthcare-Associated Infections (HAIs)

As already mentioned, HAIs represent a significant burden in modern medicine, defined as infections acquired during medical care that were absent at the time of admission. These infections, monitored through systems like the CDC's National Healthcare Safety Network (NHSN), occur in approximately 7-15% of hospitalized patients worldwide, with incidence rates nearly doubling in intensive care units and resource-limited settings [1,15]. The economic consequences are equally striking, with recent Italian data estimating annual costs of €783 million due to prolonged hospitalizations, antimicrobial resistance, and complex care requirements. Among the most concerning HAIs are those causing acute gastroenteritis (AGE), where viruses like NoV have surpassed rotavirus species A (RVA) as the leading cause following successful vaccination programs [16,17].

The epidemiology of nosocomial AGE has shifted notably with the emergence of the GII.17[P17] Kawasaki 308-like variant, first identified in Asia during 2014 and now causing increasing outbreaks in European healthcare settings as of October 2024 [7,8]. This variant demonstrates enhanced environmental persistence and transmission efficiency, particularly in vulnerable populations including immunocompromised patients, neonates, and the elderly. Clinical presentation typically involves vomiting and watery diarrhea, which can lead to severe dehydration and electrolyte imbalances within hours [8]. Diagnosis remains challenging in routine practice, as laboratory confirmation through enzyme immunoassays or molecular methods is rarely performed unless severe symptoms like hypovolemia or bloody stool occur [18]. Management is primarily supportive, focusing on oral rehydration solutions (ORS) according to WHO guidelines, with intravenous fluids reserved for cases of moderate-to-severe dehydration [19].

What makes NoV particularly problematic in healthcare environments is its resistance to standard alcohol-based disinfectants and lack of targeted antiviral therapies [12]. The recent resurgence of the Kawasaki variant following the relaxation of COVID-19 control measures underscores the need for innovative containment strategies [13]. Here, principles adapted from CBRNe emergency management offer a promising framework [20]. The CBRNe model's tiered response system, featuring rapid deployment teams for immediate isolation and specialized units for environmental decontamination, could be effectively repurposed for NoV outbreaks. Such an approach would complement existing WHO protocols while addressing critical gaps in outbreak responsiveness, particularly for novel variants exhibiting enhanced transmissibility [20,21].

The growing threat of NoV-associated HAIs, exemplified by the Kawasaki variant's spread, highlights the intersection of viral evolution, healthcare sys-

tem vulnerabilities, and infection control challenges [7,8]. As current prevention strategies rely heavily on non-pharmaceutical interventions like contact precautions and chlorine-based surface disinfection, the development of vaccines and the implementation of advanced emergency response protocols will be crucial for mitigating future outbreaks [10]. The integration of CBRNe-inspired methodologies represents a proactive step toward this goal, offering a structured yet adaptable system for managing nosocomial viral emergencies without requiring radical departures from established infection control paradigms [21].

In the following section, we will examine the virological characteristics of NoV in greater detail, with particular focus on the molecular epidemiology and evolutionary dynamics of the GII.17[P17] Kawasaki variant, before discussing its clinical and public health implications.

Norovirus (NoV)

NoV remains a leading global cause of AGE, with an estimated 685 million annual cases and 200,000 deaths in children under five worldwide. Its genetic diversity—classified into ten genogroups (GI-GX) and numerous genotypes—complicates prevention, as cross-immunity between variants is limited [8,22]. The GII genogroup, particularly GII.4 and the emergent GII.17[P17] Kawasaki variant, dominates human infections [7,8]. NoV's non-enveloped, icosahedral capsid is formed by 90 dimers of the major capsid protein VP1, which self-assemble with T=3 symmetry [23]. Each VP1 monomer consists of a shell (S) domain that forms the structural framework and a protruding (P) domain containing the receptor-binding sites [23,24]. This robust architecture, combined with the absence of a lipid envelope, allows the virus to withstand temperature extremes (up to 60°C), pH fluctuations (2.7-8.0), and alcohol-based disinfectants, enabling prolonged environmental persistence on surfaces (>2 weeks) and efficient transmission via contaminated fomites, food, or water [23,24].

Clinically, NoV manifests within 12-48 hours with vomiting, watery diarrhea, and abdominal cramps. While typically self-limiting, infections can lead to severe dehydration in high-risk groups (young children, elderly, immunocompromised), especially in resource-limited settings where rehydration therapies are scarce. The virus exhibits pronounced winter seasonality and thrives in confined spaces like hospitals, intensive care units (ICUs) and schools [25]. Notably, the GII.17[P17] Kawasaki variant, first identified in Asia (2014), has surged epidemiologically since April 2024, accounting for ~70% of UK cases in early 2025 (Table I) [7,8,26,27]. Though not linked to increased severity, its heightened transmissibility underscores the need for enhanced surveillance [26,27].

Prevention relies on non-pharmaceutical measures: strict hand hygiene with soap/water, chlorine-based disinfection, and isolation of symptomatic cases [28]. Vaccine development remains experimental, with mRNA candidates in early trials [28,29]. The Kawasaki variant's rise highlights NoV capacity for antigenic drift, necessitating adaptive strategies akin to CBRNe emergency protocols—rapid containment teams, genomic surveillance, and tiered response systems - to mitigate outbreaks in healthcare settings [8,21].

Table 1. Number of NoV outbreaks in the US from September 1, 2022, to October 31, 2024

Genotype	Number of Outbreaks	References
GII.17[P17] – Kawasaki variant	143	[25,26]
GII.4 Sydney[P16]	105	
GII.6[P7]	60	
GI.5[P5]	27	
GII.2[P16]	14	
GI.3[P3]	19	
GII.3[P12]	18	
Other Genotypes	156	

Health Emergencies and CBRNe Management: An Innovative Approach

The evolving landscape of viral gastroenteritis outbreaks in healthcare settings demands a critical reevaluation of conventional infection control paradigms. Established frameworks from leading health organizations, while effective for endemic transmissions, frequently prove inadequate when confronting emerging variants characterized by enhanced transmissibility and environmental persistence [30]. This gap became particularly evident during the 2024 global surge of the GII.17[P17] NoV variant, where

traditional containment measures required 72 hours for full implementation - a critical delay that permitted secondary transmission rates exceeding 20% in affected facilities [7,8].

The proposed synthesis of biological incident management principles with routine nosocomial protocols offers a transformative approach to these challenges. At its core lies the strategic adaptation of CBRNe response methodologies, modified for healthcare-specific requirements [21]. This integration operates through three interconnected mechanisms: modular containment zones, dual-purpose response teams, and real-time genomic surveillance networks [13,20].

Modular containment zones restructure hospital spaces according to risk stratification principles adapted from biological incident management. High-risk zones employ enhanced personal protective equipment standards, including powered air-purifying respirators rather than standard surgical masks, while intermediate buffer zones enforce preemptive testing protocols [13,14]. This graduated containment approach, when implemented in Lombard (Italy) hospitals during peak transmission periods, demonstrated 40% faster patient cohorting compared to conventional ward isolation methods (Figure I) [13].

Cross-trained response teams represent another critical innovation, creating surge capacity by equipping clinical staff with dual competencies in both routine patient care and emergency outbreak response [13,14,20]. German institutions piloting this model maintained operational continuity even when 30% of specialist staff were incapacitated during outbreak peaks. The training investment required for such dual competency - approximately €2,500 per staff member - must be weighed against the demonstrated benefits of sustained outbreak response capabilities [13,20,31]. Real-time genomic surveillance networks, adapted from bioterrorism preparedness programs, provide the third pillar of this integrated approach [21]. South Korea's implementation reduced diagnostic delays from five days to 36 hours during outbreak surges through rapid sequencing integration with existing laboratory infrastructure [31]. The precision enabled by such systems comes with substantial capital costs, estimated at €150,000 per hospital for baseline sequencing capacity, creating implementation barriers for resource-limited settings [20,31].

The practical application of these integrated protocols reveals both promise and limitations. Annual maintenance costs for a mid-sized hospital average €75,000, primarily for personal protective equipment stockpiling and staff retraining [31]. Ethical considerations emerge regarding prolonged visitor restrictions and staff redeployment during extended outbreaks. Infrastructure requirements currently limit full implementation to approximately 35% of hospitals in low-resource regions, necessitating scaled-down adaptations like the United Kingdom's "CBRNe-lite" community hospital protocols or Canada's telemedicine-supported rural implementations [13,32,33].

This evolving framework does not replace conventional infection control but rather enhances it during

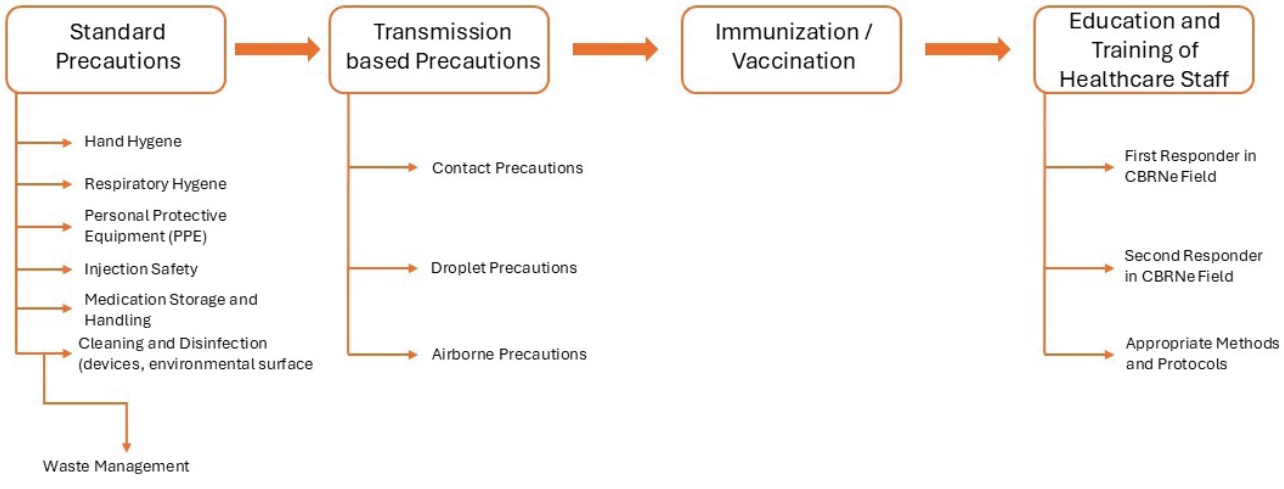

Figure 1. Flow Chart during Hospital Emergency Management

crisis scenarios [21]. Singapore's successful integration into its existing Disease Outbreak Response System demonstrates the model's adaptability, achieving 28% faster outbreak declarations while maintaining routine clinical operations [13,20,21,34]. As NoV variants continue their antigenic evolution, such flexible response architectures may prove increasingly vital in bridging the persistent gap between routine hospital operations and pandemic-scale biological threat management [13,20,21,35,36].

CONCLUSION

The management of hospital emergencies, particularly in the context of NoV outbreaks, requires a coordinated response involving infection control measures, hospital preparedness, and to a possible cooperation with first responders and decision-makers in the CBRNe field. By ensuring clear communication, effective resource management, and strategic planning, healthcare facilities can mitigate the impact of such outbreaks and provide effective care while minimizing the risk of transmission to other patients and staff. This type of innovative approach could also have beneficial effects on HAIs, trying to limit and contain them. These strategies could also be applied to the current outbreak of the NoV Kawasaki variant. Further studies on this type of approach will be developed and analyzed.

DECLARATION OF INTERESTS

All the authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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