REVIEW 10.1111/j.1469-0691.2009.02846.x

Norovirus seasonality and the potential impact of climate change

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Abstract

Seasonal variation in norovirus infection is a recognized but poorly understood phenomenon. It is likely to be based on biological, environmental and behavioural factors that regulate transmission, virulence and persistence of the virions in host populations. Understanding the seasonal dependency of norovirus infection is an important step towards understanding its epidemiology, with subsequent implementation of efficient measures of surveillance and control. Whether or not climate change could influence the seasonal patterns of norovirus infection, by impacting on its transmission, geographic distribution and prevalence, has not yet been considered. This review addresses the question.

Keywords: Climate change, norovirus, persistence in populations, seasonality, transmission

Clin Microbiol Infect 2009; **15:** 524–527

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Introduction

Noroviruses are non-enveloped with a single-stranded RNA genome. They are classified in the family Caliciviridae, and are considered to be one of the most important aetiological agents of food-borne gastroenteritis worldwide. Noroviruses display a broad genomic diversity, with approximately 40 genotypes clustering in five genogroups; GI, GII and GIII infect humans, whereas GIV and GV exclusively infect other animals. To date, no noroviruses have been recognized as zoonotic agents.

They are highly infectious viruses, largely as a result of their resistance to physicochemical environmental factors and the low infectious dose required to cause disease. A recent report in which volunteers were challenged with the Norwalk virus showed that less than ten genome equivalents were sufficient to induce the disease [1]. When considered in the context of human population density, the expression of this high infectivity is the dramatic increase in number of outbreaks observed over the past decade. This increase stimulates questions concerning norovirus transmission, pathogenicity, evolution, tropism and its association with environmental factors that may play a role in their modulation, such as climate change or genetic variability.

Climate change relates to local, regional or global changes in rainfall patterns, surface and air temperature, winds and ocean currents [2]. It is predicted to affect viral infections at three levels: change in transmission patterns, change in the ecology of the host and socio-economical changes affecting host populations [2]. Climate change may modulate epidemiological outcome, as well as morbidity and mortality of viral infectious diseases. Therefore, if the occurrence of norovirus outbreaks is attributable to weather fluctuations, climate change may influence the incidence and the spread of the infection.

The aim of this review is to investigate the possible influence of climate change on norovirus infection, by asking the following questions. What are the determinants of seasonality in norovirus infection? Do norovirus infections display a preferential geographic distribution and climatic pattern? Is there any evidence of an association between climate change and the incidence of norovirus infection?

Norovirus Seasonality

Seasonality of pathogens can be defined as the appearance of recurrent epidemics at defined periods of the year [3]. Norovirus epidemic characteristics, and timing, are remarkably consistent from year to year, with a peak incidence during the wintertime (from October to April) and specific peaks in February and March [4]. However, outbreaks of norovirus do occur during the summertime, typified by

the persistence of norovirus gastroenteritis in the so-called off-season (May to September), although at a reduced rate and with an absence of epidemic spread to geographically remote areas. These observations cause us to ask why do norovirus infections peak in wintertime and display a reduced incidence in summertime, without disappearing altogether? According to Dowell *et al.* [3], the seasonality of pathogens is associated with (i) their appearance and disappearance, (ii) the environmental changes and (iii) host-behavioural changes.

Norovirus appearance and disappearance

One possible explanation for the sporadic norovirus outbreaks in the summertime may lie in the limited circulation of virus during this time of the year, showing long-term survival in the host population and spasmodic seasonal reactivation. There are some arguments in favour of this possibility: (i) noroviruses cause self-limiting disease, lasting from 24–48 h in otherwise healthy patients, but shedding of noroviruses occurs for up to 4 weeks after infection; (ii) viral shedding occurs at very high loads; and (iii) the occurrence of asymptomatic shedding with time, and at high loads, enables noroviruses to be transmitted efficiently and silently from asymptomatic to non-infected individuals, with subsequent chain-to-chain transmission.

This form of silent transmission is similar to the transmission of influenza virus between humans. Indeed, noroviruses display patterns of evolution similar to influenza (i.e. antigenic drift punctuated by antigenic shift every 2–3 years) [5]. This pattern of evolution enables noroviruses to persist in human populations, escaping host immune pressure through antigenic drift and/or penetrating naïve populations [6].

Changes in the natural environment

Changes in the environmental conditions, such as humidity [7–9], temperature cycles [10,11], rain patterns and winds, are associated with seasonality of infectious diseases. For gastrointestinal infectious agents such as rotaviruses, changes in humidity have been reported to facilitate viral persistence, increasing the risk of transmission through contaminated surfaces. Similar observations were made for influenza viruses [3,12,13]. In poliovirus, a positive association between disease prevalence and air humidity has been reported [9]. In the case of noroviruses that are transmitted not only through the faecal–oral route, but also through aerosols (vomitus), increased humidity may potentially facilitate an increased transmission efficiency of the virions. It is tempting to postulate that changes in humidity and temperature may influence norovirus resistance, transmission and/or virulence. We have previously reported on the prevalence of noroviruses in sewage water during the floods generated by the river Elbe overflowing its banks [14]. According to our observations, low water temperatures were associated with an increase in norovirus prevalence, indicating a possibly favourable physical environment for the virions. However, further studies are required to investigate the possible influence of temperature and humidity on norovirus incidence and seasonality.

Changes in the behaviour of the host

Crowding of populations is frequently cited to explain increased transmission and the subsequent incidence of infectious diseases [3]. Models of transmission of infectious diseases in children show that transmission patterns depend on contact rates, with infection cases increasing during school terms and decreasing during vacations, underlying the role of host behaviour in disease transmission [15,16]. Similarly, crowding of individuals in hospital wards or cruise ships may partly explain the occurrence of norovirus outbreaks independently of the season. This is in line with a recent study on norovirus outbreaks where the risk of transmission of norovirus on cruise ships was positively correlated with host behaviour [17]. Thus, human behaviour may be invoked as one of the facilitators of norovirus transmission during wintertime. Although being intuitively attractive, this hypothesis lacks empirical data enabling the quantitative association of the risk of transmission of noroviruses with change in human behavioural patterns as a consequence of seasonal variation.

A further aspect relates to the seasonal susceptibility of humans to norovirus infection. Seasonal fluctuations modulate host cellular and humoral immune function, potentially increasing the susceptibility of mammals to infection [18]. Vitamin D is an important regulator of phagocyte function and is associated with the antiviral response to influenza virus infection by immune cells. During wintertime, diminished UV-radiation reduces vitamin D synthesis, with subsequent impairment of the immune response [18], and possible higher susceptibility to infections. Whether or not this applies to norovirus infection remains speculative, but may prove to be an interesting direction towards understanding norovirus seasonality. This is discussed in more detail below.

Geographic Distribution of Noroviruses

If seasonal variations in temperature, sunlight and humidity do influence norovirus incidence, then, on average, one could expect an incidence variation over a 6-month period, particularly between the northern and southern hemisphere, with a subsequent low incidence in equatorial areas, as observed for

other viral disease patterns, such as that of influenza virus [19,20]. Similar observations have been reported for enteroviruses, which do exhibit a summertime preference. They display a decrease of virus activity in equatorial regions [3]. This loss of seasonality of viral infections with increasing proximity to the equator suggests that environmental factors may also play a role in the genesis of the seasonal periodicity.

Norovirus infections have been reported in various countries in both the northern and southern hemisphere, as well as in the equatorial regions [21]. However, it remains unknown whether seasonality inversion exists for noroviruses (i.e. leading to their migration from the northern to the southern hemispheres, depending on the season). In the case of other viral gastroenteritis pathogens, such as rotaviruses, there is no evidence of migration of these pathogens from one hemisphere to the other, although seasonal recurrence is observed [22,23]. Therefore, because noroviruses and rotaviruses display similar patterns of transmission (i.e. faecal–oral route) and tropism (i.e. the enteric cells), one can reasonably presume that noroviruses behave similarly to rotaviruses in terms of seasonality.

Climate Change and its Possible Impact on Norovirus Infection

During the coming decades, climate change is predicted to directly influence, temperature, precipitation, seasonal length and intensity of episodes, and atmospheric CO_2 concentrations [24]. Winter temperatures are predicted to increase, although summer temperatures are expected to remain relatively unchanged. Climate warming will change rainfall patterns, with increased humidity and risks of floods [25,26]. Warming will affect continental regions and the northern hemisphere more than equatorial regions.

Extreme weather variations, such as cold winters, heat waves, floods and temperature changes, are important modulators of the transmission of infectious agents and their survival in natural environments. Extreme temperature changes may impact natural phenomena, such as the El Nino Southern Oscillation (ENSO) [26]. ENSO is a periodic change in the thermal gradients in the Pacific Ocean and the intensity of the east-to-west trade winds [27]. ENSO influences rainfall patterns in countries of the southern hemisphere, subsequently affecting the incidence of waterborne infectious diseases. ENSO events have been identified as an important risk factor for influenza [20], arboviral infections [28] and viral gastroenteritis [11]. For example, an increase in the cases of infectious gastroenteritis to more than 200% was reported in Lima, Peru as a result of the ENSO, when the ambient temperature increased to >5°C above the expected values for the winter season [11].

Climate change may therefore affect norovirus seasonality with subsequent impact on (i) norovirus transmission, (ii) host susceptibility to norovirus infection and (iii) resistance of norovirus to environmental conditions. Furthermore, climate change may influence the interaction of noroviruses with their host. Indeed, human migration may become significantly altered as the result of climate change. As a consequence of floods or droughts, massive displacement of populations and crowding in refugee camps may facilitate the introduction of noroviruses into immunologically naïve populations, resulting in epidemics and the emergence of new norovirus strains. In this context, climate change may modulate norovirus evolution by favouring periods of elevated transmission or facilitating transmission and evolutionary bottlenecks through rapid mutation or recombination events. This may in turn cause larger oscillations in the prevalence of the disease than are currently observed.

Challenges and Future Prospects

The prospect that climate change may influence the current seasonality patterns of noroviruses is challenging. However, to understand completely the likely impact of climate change on norovirus epidemiology, we need to understand all of the factors that determine seasonality (i.e. host behaviour and susceptibility, virus transmission and virus fitness in its natural environment). Therefore, epidemiological surveillance of norovirus outbreaks should be tightly linked to climate monitoring. This will require multidisciplinary approaches involving virologists, climatologists, ecologists and epidemiologists. Additional research methods need to be created and implemented, aiming to assess the significance of the ecological context in the epidemiology of noroviruses, as well as addressing the public health challenge in the long term. Such approaches should include (i) a geographically focused analysis of norovirus incidence in association (or not) with abrupt climate changes caused, for example, by tornadoes, hurricanes or floods, in developed and industrialized countries; (ii) an assessment of transmission risk in the context of demographic, economic and social characteristics; and (iii) an analysis of historical data where climate variability was extreme, as well as its association with infection rates.

It would also be of interest to investigate in depth the seasonality of noroviruses by (i) generating knowledge on host and pathogen biology and ecology, (ii) increasing the accuracy of surveillance systems aiming at generating epidemiological data, and (iii) improving the precision and accuracy

of the methods for predicting epidemics, or even pandemics. Clearly, a greater understanding of the long-term influence of climate change on norovirus epidemiology should facilitate an improvement in disease control and therefore reduce human suffering as well as the associated costs to the public health services.

Transparency Declaration

The author is funded by the European Consortium "Vizier" (www.vizier-europe.org). He has no conflicts of interest.

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