

Summary of Doctoral Thesis

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Name: NGUYEN Thanh Gia

Title	RISK ASSESSMENT OF NOROVIRUS INFECTION CONSIDERING INDIRECT IMPACTS OF SEASONAL FLOOD IN SOUTHEAST ASIA
<p>Introduction and objectives (Chapter 1 & 2)</p> <p>Floods are not only the dangerous disaster situation threatening human lives, but they also can pose additional risks for human health. Flood impacts can be divided into direct and indirect impacts. Although floods are likely to indirectly impact on physical health and psychology, these impacts are less paid attention to factors such as foods and water contamination. In terms of physical health impacts, floods are potentially able to cause gastroenteritis diseases outbreaks. While norovirus (NoVs) is well known as a leading causal pathogen for acute gastroenteritis in developed countries, structured data on the prevalence of the disease in developing countries are not available thus far. Due to inadequate access to safe drinking water, poor sanitation and hygiene, I hypothesized that the prevalence of NoVs in case of acute gastroenteritis in developing countries is higher than that in developed countries.</p> <p>Southeast Asia is a region suffered from flood disasters regularly. In most cities in this region, municipal wastewater collection and treatment systems have not been established. Foods cultivated at downstream of these cities are probably contaminated by floods. Risks of gastroenteritis are increased when contaminated foods are consumed.</p> <p>In addition, in terms of psychological impacts, in some areas of developing countries hit by flooding frequently, people seem to adapt their lives to the floodwater so well. People have a high risk of gastroenteritis due to exposure to flood frequently. I hypothesized that facing floods frequently can reduce the</p>	

burden of gastroenteritis by acceptance of this disease. As an indicator of the psychology, people's feeling to diseases is important in the estimation of its burden but it has not been investigated especially for common diseases with a low fatality.

The present study aims (1) to estimate the prevalence of NoVs in cases of acute gastroenteritis in developing countries; (2) to reveal the epidemic of gastroenteritis in a city of a developing country city by monitoring NoV contamination in oysters collected in a downstream lagoon; (3) to assess the risk of NoV infection due to contaminated oyster consumption; (4) to test the hypothesis that facing floods frequently can reduce the burden of gastroenteritis by acceptance of this disease; and (5) to propose a new method to estimate burden of gastroenteritis considering the feeling about the disease.

The prevalence of norovirus in cases of gastroenteritis in developing countries

(Chapter 3)

To estimate the prevalence of NoVs in developing countries, relevant studies were identified by searching PubMed and Web of Science for the period from January 1, 1990 through March 31, 2016. Studies performed in developing countries with a study period of at least 12 months and which provided information on PCR-confirmed NoVs prevalence in patients diagnosed with acute gastroenteritis were included. A meta-analysis was conducted on NoVs prevalence, focusing on viral genogroups GI and GII, in cases of acute gastroenteritis. Using evidence from 178 articles, the estimated NoVs prevalence among 148,867 patients with acute gastroenteritis was 17% (95% CI: 15-18%). The prevalence decreased from 18% (95% CI: 16%-20%) for upper middle-income countries to 15% (13%-18%) and 6% (3%-10%) for lower middle- and low-income countries, respectively. There were no significant differences in NoVs prevalence by age group (under 5 years, 5 years and over, and mixed ages) or severity of symptoms as defined by community, outpatient, or inpatient setting. The pooled prevalence of NoV GII (15%, 95% CI: 13-17%) was significantly higher

than that of NoV GI (1%, 95% CI: 1-1%) in patients with acute gastroenteritis.

Food contamination due to norovirus, urban flood, and health risk (Chapter 4)

The prevalence of NoVs in cases of gastroenteritis in developing countries was lower than my expectation. This prevalence was comparable to that in developed countries. However, poor surveillance about NoVs and the tendency of people in developing countries not to use medical services for mild diseases such as gastroenteritis caused by NoVs could cause the underestimation of the prevalence in developing countries. To overcome these limitations, a field survey was conducted in a city of a developing country. Some previous studies indicated that NoV contamination in oysters was reported to be well correlated to the number of gastroenteritis cases in some developed countries. Monitoring the level of NoV contamination in oysters harvested at a lagoon in Hue City, Vietnam for 17 months (August 2015 to December 2016), was applied to reveal the epidemic of gastroenteritis in the city. Hue City is known as a flood city. About two-thirds of the city's residents are likely exposed to flooding when a heavy rainy occurs. Since the city has no wastewater treatment plant, domestic wastewater is discharged directly into drainage channels, although a part of wastewater passes through septic tanks. The channels flow directly into the Perfume River. Oysters cultivated in the downstream of the river are probably affected by contaminants from the city where urban flooding occurs regularly. This area has potential to show indirect impacts of flood as above described and so it was selected for the field of this study. A total of 34 oyster samples were collected at two sampling sites in the lagoon. NoV GI was more frequently detected than GII (positive rate 79% vs. 41%). Maximum concentrations of GI and GII were 2.4×10^5 and 2.3×10^4 copies/g, respectively. Co-contamination with GI and GII was observed in 35% of samples. NoV GII concentration was higher at station A in the flood season than in the dry season ($P= 0.04$, Wilcoxon signed-rank test). Six genotypes (GI.2, GI.3, GI.5, GII.2, GII.3, and GII.4) were identified in both wastewater and oyster samples, and genetically similar or identical sequences were obtained from the two types of samples. These observations suggest that urban drainage and seasonal flooding contribute to NoVs contamination of oysters in the

downstream. On the other hand, due to this impact of flood, monitoring of NoVs concentration in oysters seemed ineffective to reveal the epidemic of gastroenteritis in the city. Estimated risk of NoV infection due to consuming oysters harvested in the lagoon was quite high (36.3 to 72.2%).

Psychological impacts caused by floods (Chapter 5)

As another indirect impact of flood, its impact on psychology was investigated by a cross-sectional study involving 293 people living in flooding areas and 365 people in non-flooding areas in T. T. Hue province, Vietnam, and three provinces in Cambodia. A questionnaire was developed for this investigation. As the result, the participants felt that diarrhea, severe diarrhea, cough, fever, skin problems, and eye problems happened more frequently during/after flooding. The feeling about all those diseases of the people living in the flooding areas, except eye problems, was significantly different from that of the people living in non-flooding areas in Cambodia ($P < 0.05$). The same results were observed in Vietnam for diarrhea and cough. In Vietnam, factors associated with the feeling about diseases that happened more frequently during and after flood, were age and education. According to this finding, a new method was proposed to incorporate psychological impact of floods into health burden of gastroenteritis, which was estimated by Disability Adjusted Life Years (DALYs), by modifying the disability weight.

Conclusions and recommendations (Chapter 6)

Overall, the findings from the study demonstrated that seasonal floods were able to cause indirect impacts on not only physical human health but also psychological one. The estimated prevalence of NoVs in cases of acute gastroenteritis in developing countries was lower than in developed countries, rejecting my hypothesis. This may be due to the poor surveillance system and the tendency of people in developing countries not to use medical services for mild diseases such as gastroenteritis caused by NoVs. For revealing the real situation of gastroenteritis in developing countries, a field study was conducted in Hue city, Vietnam to monitor NoVs in oysters. The monitoring was ineffective to reveal the epidemic of gastroenteritis in the city. This

may be due to virus transportation enhanced by flood. However, urban drainage surely contributed to the oyster contamination with NoVs in the study area. A risk of NoV infection due to consuming oysters was noticeable. People facing floods frequently could not reduce the burden of gastroenteritis by acceptance of this disease. A new method was proposed to incorporate the psychological impact of floods into the burden of the gastroenteritis, which was estimated by DALYs. The disease burden was lower than that calculated using the original disability weight. This is not due to the impact of flood, but possibly to less impact of people living in developing countries as a result of more frequent occurrence of gastroenteritis than in developed countries. Therefore, strengthening communication and knowledge regarding of food safety especially during the seasonal flooding may help prevent future NoVs-associated infection outbreaks. More supports to those who are frequently affected by floods with considering of psychology could contribute to reduction of adverse impacts of floods. Further studies are needed to clarify the relationship between the epidemic of NoVs in cases of gastroenteritis and NoV concentration in oysters in the study site, considering some potential factors such as water temperature, salinity, flow direction, etc. Further studies should be conducted to understand more deeply the feeling of people living in flood-affected areas about infectious diseases by application of cohort study. Moreover, modification of disability weight for common diseases that happen more frequently in flooding areas should be continued.