

Epidemiological Report

Epidemiological Investigation of a Norovirus GII.4 Sydney Outbreak in a China Elder Care Facility

Qing-ming Zheng^{†*}, Hua-tang Zeng[†], Chuan-wen Dai, Shun-xiang Zhang, Zhen Zhang, Shu-jiang Mei, Ya-qing He, and Han-wu Ma

Guangming District Center for Disease Control and Prevention, Shenzhen, China

SUMMARY: An outbreak of norovirus GII.4/Sydney_2012 affected a China elder care facility in December 2012. A total of 39 elderly people and staff met the outbreak case definition. The attack rates in the elderly and the staff were 15.9% (31/195) and 23.2% (19/82), respectively, including 13 asymptomatic cases in the staff. The result of gene sequencing revealed that the outbreak was caused by norovirus GII.4 Sydney. The mode of transmission of this outbreak was proven to be person-to-person. The first case (a self-cared elder) was affected outside the elder care facility and was not isolated after returning. Norovirus was transmitted via close contact among the self-cared elderly. Then, through service-related close contact, the attendants promoted the cross-transmission between the self-cared elderly and the nursed elderly. The virus was also spread among the staff via daily contact. In the elder care facility, the asymptomatic cases in the attendants played an important role in the transmission of norovirus, which deserves high attention.

INTRODUCTION

Norovirus causes the majority of nonbacterial gastroenteritis outbreaks worldwide. Five genogroups (GI–GV) and at least 34 genotypes are known, and 3 are pathogenic to humans: GI, GII, and GV (1). In recent years, the GII.4 strain has been identified as being predominant in norovirus outbreaks (2,3). In late 2012, surveillance systems in many countries showed increased levels of norovirus activity compared with the previous season. Data from these countries indicated that this increase was associated with the emergence of a new variant of GII.4 named GII.4 Sydney (4–7). The surveillance data for diarrhea in China have shown that since late 2012, GII.4 Sydney gradually became the predominant strain and induced outbreaks in many provinces (2,8–11). In December 2012, an outbreak induced by GII.4 Sydney occurred in an elder care facility in Shenzhen, which is a city in the south of China. This paper focuses on the transmission process of norovirus during this outbreak and the roles of the attendants in controlling the epidemic situation.

MATERIALS AND METHODS

Case definition: The investigated subjects were the elderly and the staff in this elder care facility. A clinical case was defined as any elderly person or staff in this

elder care facility who had fallen ill with symptoms of vomiting or diarrhea (≥ 3 times/day) since December 12, 2012. A confirmed case was defined as any case whose stool specimen was positive for norovirus. An asymptomatic case was defined as any elderly person or staff who did not exhibit symptoms of vomiting or diarrhea, but whose stool specimen was positive for norovirus.

Epidemiological investigation: Based on medical records and inquiry with a newly designed questionnaire, necessary information was collected for all cases, including the basic characteristics, date of onset, date of recovery, clinical symptoms, and spheres of activity in the previous 3 days before onset. We interviewed the first affected case, the special cases, and some asymptomatic cases and understood their spheres of activity before onset and the people in close contact. From the managers, doctors, nurses, and attendants, we obtained the basic information about this elder care facility, the labor division among the staff, the food supply, and the management of infection. We checked the disinfection facilities and environmental sanitation in the rooms of the elderly, the offices and dormitories of the medical staff, and the public activity areas.

Specimen collection and laboratory tests: In total, 105 stool specimens were collected from the elderly and staff showing symptoms of vomiting and diarrhea as well as from the asymptomatic staff. The nucleic acids of norovirus were measured. Reverse transcription-polymerase chain reaction (RT-PCR) revealed that 39 samples were norovirus-positive. The amplified product of the specific target strip in 10 norovirus-positive specimens was sent to Sangon Biotech Shanghai Co. Ltd. for purification and 2-way sequencing.

Statistical methods: Proportions were compared using the chi-square or Fisher's exact test (when indicated). Incidence clustering analysis was tested by goodness of binomial distribution. The level of statistical significance was established as an alpha error of 0.05. The

Received February 19, 2014. Accepted March 28, 2014.
DOI: 10.7883/yoken.JJID.2014.081

*Corresponding author: Mailing address: Guangming District Center for Disease Control and Prevention, 63 Fengjing Road, Gongming Street Running, Guangming District, Shenzhen, Guangdong, China. Tel: +86 75581733477, Fax: +86 75581733016, E-mail: 281136727@qq.com

[†]These authors contributed equally to this work.

collected data were analyzed using Microsoft Excel. Epi Info and Microsoft Excel were used for statistical analysis.

Ethics statement: According to the Law of the People's Republic of China on the Prevention and Treatment of Infectious Diseases, this investigation was exempted from the ethical committee approval because it was part of the public health interventions to control outbreaks.

RESULTS

The affected elder care facility was a public institution in China, which contains a 7-story building and 152 rooms with independent washrooms. The facility housed 195 elderly whose nursing requirements were classified into self-caring, semi-nursing, full nursing, and special nursing. Eighty-two staff included doctors, nurses, attendants, food handlers, and logistics personnel. Over a period of 15 days, this outbreak involved 11 clinical cases (elderly), 26 confirmed cases (6 staff and 20 elderly), and 13 asymptomatic cases (staff). The total attack rate was 15.9% (31/195) among the elderly and 23.2% (19/82) among the staff.

Clinical symptoms: For the 11 clinical cases and the 26 confirmed cases, the main symptoms were bellyache (86.5%), diarrhea (67.6%), and vomiting (45.9%). Very few cases were accompanied with nausea and fever (Table 1). The disease remitted within 24–72 h. Three elderly cases required hospital admission; however, no deaths occurred.

Description of elderly cases: The elderly cases were aged 69–92 years (median 81), including 11 males and 20 females. The attack rates in males and females were 18.3% and 14.8%, respectively, indicating no differences according to gender ($\chi^2 = 0.38$, $P = 0.53$). The attack rates in the specially-nursed, fully-nursed, semi-nursed, and self-cared elderly were 36.4%, 25.8%, 21.4%, and 11.5%, respectively, indicating a significant difference by chi-square test ($\chi^2 = 7.9$, $P = 0.005$) (Table 2). Based on statistical analysis by floors, the attack rate was the highest on floor 5 (28.1%), floor 3 (24.3%), and floor 2 (21.4%), accounting for 72.9% of

the total elderly cases. Floor 5 was filled with the self-cared elderly, and floor 2 and floor 3 were filled with the specially- and fully-nursed elderly. The specially- and fully-nursed elderly cannot live independently and were taken care of by the attendants; they did not directly contact the elderly on floor 5.

The first case was a 73-year-old self-cared female living in room 501. On December 8 to 14, 2012, she left the elder care facility for a week to visit her daughter, during which they lived in a hotel and ate in restaurants. At 9:00 pm on December 14, she developed diarrhea and bellyache, and by 7:00 am the next day, she had diarrhea 8 times. Her daughter did not have any gastroenteritis symptoms. That night, she returned to the elder care facility and the symptoms disappeared the next day. On December 26, her anal swab detected the presence of norovirus via RT-PCR. During the week from the onset to the disappearance of symptoms, the first case had been visited by 8 self-cared elderly, and 6 of them fell ill in December 17 to 22. After recovery, the first case went to the music room, reading room, and playroom. The second case living in room 521 fell ill on December 17, and the third case living in room 502 fell ill on December 19; both these patients had visited the first case on December 15 and 16.

Description of staff cases: Six confirmed cases and 13 asymptomatic cases were found among the staff. The 8 males and 11 females were aged 39 years on average. They included 8 attendants, 2 nurses, 5 kitchen workers, 1 social worker, and 3 logistics workers. Of them, however, most kitchen workers (4/5) and logistics workers (3/3) never entered the living area of the elderly.

The labor division for the attendants who nursed the elderly was that the day shift attendants only took care of the semi-, fully-, and specially-nursed elderly residents, while the night shift attendants handled the emergencies of the self-cared elderly on floors 4 to 7. During the outbreak, 6 attendant cases and 2 nurse cases had once handled the excreta and vomitus of the self-cared elderly cases during the night shift. The first affected attendant A was responsible for cleaning the public areas and had fallen ill at 1:00 am on December 24; her anal swab was positive for norovirus detected via RT-PCR. Attendant A once handled the vomitus of a self-cared elder B in the corridor of floor 5 at 11:00 on December 22; the anal swab of elder B was positive for norovirus. On December 19–23, elder C suffered from an acute mental disorder problem; however, because of insufficient attendants, elder C was managed by kitchen worker D and attendant E. The elder C developed diarrhea and vomiting on December 23, and the kitchen worker D developed diarrhea on December 25. The anal swabs of elder C, kitchen worker D, and attendant E were positive for norovirus; however, attendant E was asymptomatic. These findings indicate that norovirus may be cross-transmitted between the elderly and the attendants via the nursing service.

Of the 19 staff cases, 17 cases lived in the dormitory of the elder care facility and 2 cases lived outside. The elder care facility possessed 10 dormitories each with 5–8 beds, and except for security guards and hydropower workers, the nurses, kitchen staff, and attendants lived together. The incidence clustering of dormitories was used for the calculation of the goodness of binomial

Table 1. Clinical symptoms of 37 clinical and confirmed cases

Symptom/sign	No. (%) of cases ($n = 37$)
Bellyache	32 (86.5)
Diarrhea	25 (67.6)
Vomiting	17 (45.9)
Nausea	1 (2.7)
Fever	1 (2.7)

Table 2. Analysis of attack rate in different nursing degree

Nursing degree	No. of people	No. of cases	Attack rate (%)	χ^2	P
Specially-nursed	11	4	36.4	7.9	0.005
Fully-nursed	31	8	25.8		
Semi-nursed	14	3	21.4		
Self-cared	139	16	11.5		
Total	195	31	15.9		

distribution fitting. The results showed that the distribution was gathered in the dormitory (combined $\chi^2 = 9.14$, $df = 1$, $P < 0.005$), indicating that norovirus may be transmitted in the dormitory via close contact.

Epidemic curve: Figure 1 shows that the first case was a self-cared elderly who had fallen ill on December 14, followed by 10 self-cared elderly cases on December 17–22. On day 23, the cases of the nursed elderly (semi-, fully-, and specially-nursed) appeared, and on day 28, the final 2 cases appeared; thus, the outbreak lasted for 15 days. Two peaks of incidence appeared on days 22–23 and days 25–26: the first peak mainly involved the self-cared and non-self-cared elderly, while the second peak involved the non-self-cared elderly and staff. The first affected staff appeared on day 24, and by day 28, 6 staff cases had been affected. On day 23, some attendants were screened to find 2 asymptomatic cases, and on day 25, the stool specimens of all staff were examined to find 11 more asymptomatic cases. On December 22, measures to “restrict the self-cared elderly from going outside the room, send foods to rooms, disinfect external environment, and close public places” were taken, and the number of self-cared cases decreased. On December 25, a measure to “isolate asymptomatic cases” was taken; therefore, this outbreak of norovirus infection ended.

Environment investigation: Each elder room in this elder care facility had a specific mop but not a specific dishcloth. The offices of attendants and the public washrooms had no hand detergent. Except for the cleaning workers, no elderly people or attendants were provided with disinfectants.

The raw materials for all foods were supplied by a food company, and the vegetables and meat were used on that day. We checked the recipes on December 17–30, and the major materials were pork, chicken, beef, and green grocery. Each floor was fitted with a boiled water room, and the attendants sent water bottles to the rooms of the elderly. The affected cases had not consumed unboiled water within the previous week.

Laboratory test results: A total of 105 anal swabs

were collected, and RT-PCR revealed that 39 samples were norovirus-positive, with 13 asymptomatic cases. The nucleic acids for astrovirus, rotavirus, and adenovirus were negative; no routine pathogenic bacteria common in food poisoning (e.g., *Salmonella*, *Shigella*, *Staphylococcus aureus*, *Vibrio parahaemolyticus*, *Bacillus cereus*, *Proteus bacillus vulgaris*, and diarrheagenic *Escherichia coli*) were detected. Three weeks after the end of the outbreak, the anal swabs of 13 asymptomatic cases were collected and were found to be norovirus-negative via RT-PCR.

Sequence analysis of 10 positive samples (4 self-cared elderly, 3 nursed elderly, and 3 staff members) amplicons showed 99–100% nucleotide identity, being closest to the variant GII.4 Sydney in GenBank, indicating that the outbreak was caused by a single norovirus strain (Fig. 2).

DISCUSSION

Globally, GII.4 Sydney was first reported in Australia in March 2012; in China, it was first reported in Guangdong province in July 2012 (2) and then spread to many other provinces in China (8–11). Data from August 2012–April 2013 monitored by the U.S. Centers for Disease Control and Prevention indicated that compared with other norovirus strains, GII.4 Sydney outbreaks disproportionately affected older persons, consistent with the observed predilection toward long-term care facilities (12). Patients affected by GII.4 Sydney were more likely to have diarrheal illness and less likely to have vomiting, fever, and abdominal cramps. The surveillance data for diarrhea from October 2012 to March 2013 monitored by Peking University People’s Hospital, a teaching hospital affiliated with Beijing University, showed that GII.4 Sydney caused severe fever, abdominal pain, and a higher frequency of diarrhea clinically compared with other norovirus infections (11). In the Shenzhen outbreak, the attack rates in the elderly and the staff were 15.9% and 23.2%, respectively, and the occurrence rates of bellyache and diarrhea were 86.5% and 67.6%, respectively; however, the occurrence rate of fever was only 2.7%. In several reports, GII.4 Sydney had been transmitted through food and had occurred in schools, restaurants, and mess halls (2,8,13). Therefore, more monitoring data will be required to understand the clinical symptoms and epidemiological features of GII.4 Sydney infection in an elder care facility.

Through epidemiological investigations and laboratory test results, we confirmed that in this outbreak, norovirus was transmitted and diffused among the elderly and staff through the following chains:

1. The cause of this outbreak was that the first case went and ate outside the facility; however, the case was not isolated after returning; thus, norovirus was transmitted in the elder care facility via close contact among the self-cared elderly. It has been reported that within 1–2 weeks after gastrointestinal symptoms disappeared, the virus could still be detected in the feces or stool specimens from norovirus-infected persons and continued to pollute the environment (14,15). On December 22, the elder care facility reported this outbreak to the Shenzhen Center for Disease Control and Prevention

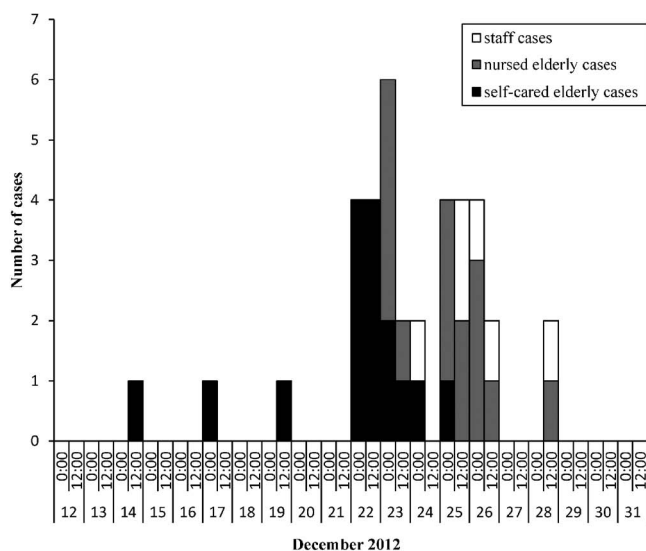


Fig. 1. Distribution of 37 clinical and confirmed cases according to date of onset of symptoms.

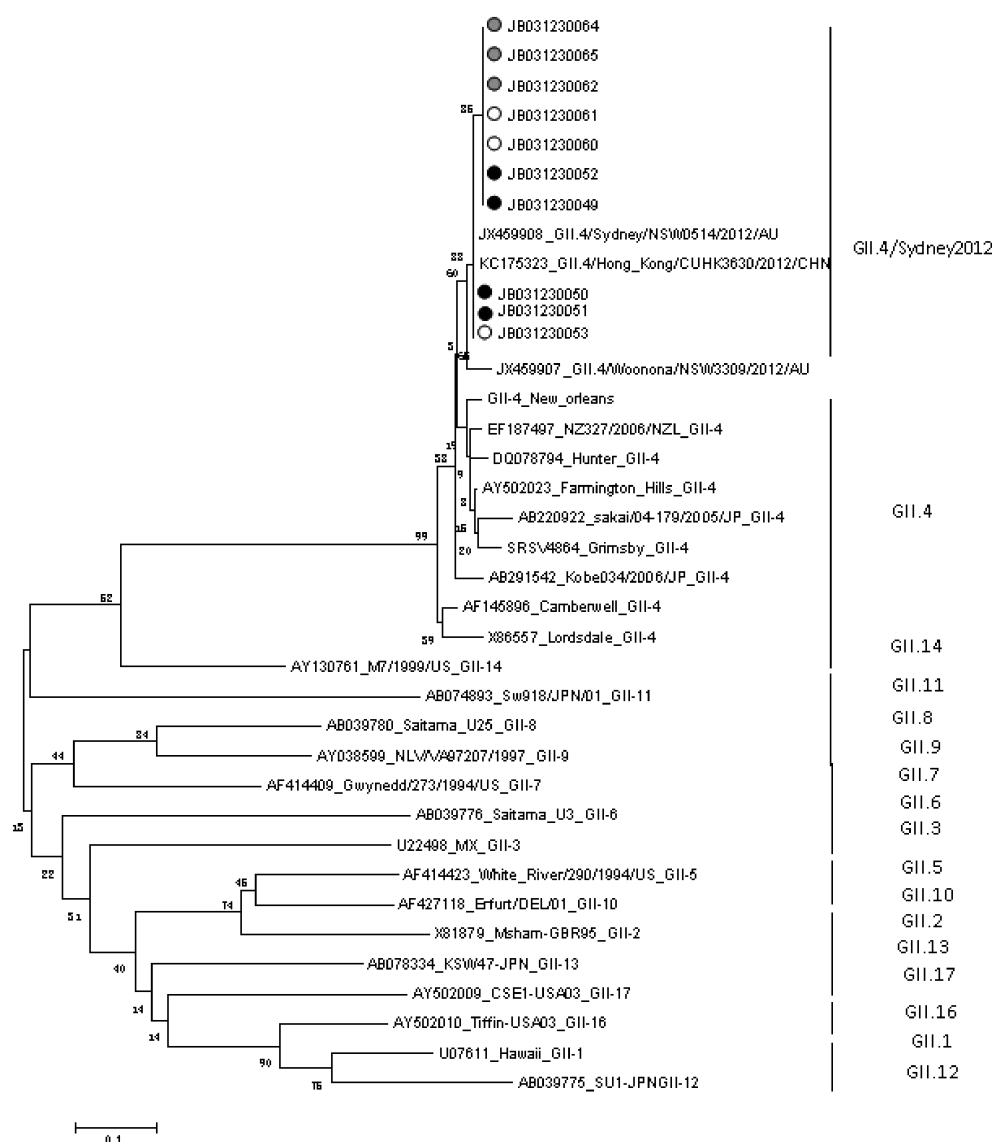


Fig. 2. Phylogenetic analysis of the partial capsid sequence of the norovirus strains in 10 cases. ●, samples of self-cared elderly; ○, samples of nursed elderly; ●, samples of workers.

(CDC). Three cases before December 22 were not isolated from the other elderly and staff; the stool specimens of 2 cases were still norovirus-positive after the gastrointestinal symptoms disappeared, indicating that the infection source inducing virus transmission continued to exist.

2. Some nurses and attendants were infected by norovirus after contacting the feces and vomitus of the self-cared cases; then, they transmitted the virus to the specially- and fully-nursed elderly via daily services such as bathing, feeding, and helping with bowel relief. Therefore, the asymptomatic cases of attendants played an important role in the transmission and spread of norovirus. During the case investigation into the attendants, we found that most attendants did not know that norovirus could be transmitted via daily contact, or that close contact to vomitus or diarrhea was risky. The epidemiological investigations into norovirus infection outbreaks in other elder care facilities and hospitals also showed that the asymptomatic staff can cause the transmission of norovirus (1,16–18).

3. Many norovirus outbreaks occurring in elder care facilities, summer camps, and hospitals were due to the food handler who were infected with the virus (13,18–21). In the Shenzhen elder care facility, the nurses, kitchen workers, and attendants cross-lived in the dormitory, and norovirus spread among the staff via daily contact in the dormitory; this affected the kitchen workers who had no direct contact with the elderly and induced foodborne transmission risks.

Norovirus is characterized by a low infection dose, prolonged virus shedding time, strong survival ability, and high variability, which make its transmission quick; the infection can be transmitted via person-to-person or by water, food, environment, or air (2). The outbreaks of norovirus illness in healthcare settings may be disruptive and costly and can cause significant complications, including chronic illness and deaths; therefore, controlling the outbreak of norovirus infection can be very challenging (22). During the Shenzhen outbreak of norovirus infection, Shenzhen CDC stayed at the elder care facility every day to conduct an epidemiological

investigation and improved the control measures according to the Trend of Epidemic. First, the CDC took measures to “restrict the self-cared elderly from going outside the room, send foods to rooms, disinfect the external environment, and close public places,” thereby blocking the close contact among the self-cared elderly so that the number of cases in this group would be reduced. After one specially-nursed elder was affected, the CDC immediately evaluated the stool specimens of the entire staff, isolated the asymptomatic case, and promptly blocked the cross-transmission between the attendants and the elderly and between attendants and other types of workers. According to the results of the epidemiological investigation, we suggested that the elder care facility in Shenzhen establish a gastroenteritis case isolation system; all acute gastroenteritis cases, particularly those that developed after eating outside, should be isolated until the symptoms have disappeared for 2–3 days. The facility should also reasonably arrange the labor division for the attendants and appoint the attendants to fixed floors and fixed rooms to reduce the pathogen cross-transmission risks. To control an outbreak of norovirus infection, it is necessary to analyze the stool samples from all staff (symptomatic and asymptomatic) and to pay attention to staff education on hand washing and disinfecting feces and vomitus appropriately.

In this investigation, an “asymptomatic case” was defined as “any elderly person or staff who did not exhibit symptoms of vomiting or diarrhea, but whose stool specimen was positive for norovirus.” However, we found that some asymptomatic cases did not present with vomiting or diarrhea but had nonspecific symptoms, including nausea and anorexia. We failed to record the detailed dates of occurrence for these symptoms. It has been reported that norovirus could be commonly excreted in formed stools, and there was no significant difference in the norovirus-positive rate of formed stools with norovirus compared with loose and liquid stools with norovirus (14). The appearance of stools is not a reliable indicator of the presence or absence of norovirus in an outbreak setting. Therefore, we suggest that for controlling norovirus outbreaks in elder care facilities, the definition of cases can be loosened, and attention should be paid to the identification of cases with nonspecific symptoms.

Acknowledgments This work was supported by grants from the Shenzhen Field Epidemiology Training Program.

Conflict of interest None to declare.

REFERENCES

- Lai CC, Wang YH, Wu CY, et al. A norovirus outbreak in a nursing home: norovirus shedding time associated with age. *J Clin Virol.* 2013;56:96-101.
- Zhong XS, Huang Q, Li H. Progress research on epidemic situation of the norovirus genotype II.4 variants. *Chin J Epidemiol.* 2013;34:849-51. Chinese with English summary.
- Bull RA, Eden JS, Rawlinson WD, et al. Rapid evolution of pandemic noroviruses of the GII.4 lineage. *PLoS Pathog.* 2013;6:e1000831.
- Fonager J, Hindbak LS, Fischer TK. Rapid emergence and antigenic diversification of the norovirus 2012 Sydney variant in Denmark, October to December, 2012. *Euro Surveill.* 2013;18:pii=20413.
- van Beek J, Ambert-Balay K, Botteldoorn N, et al. Indications for worldwide increased norovirus activity associated with emergence of a new variant of genotype II.4, late 2012. *Euro Surveill.* 2013;18:pii=20345.
- Bennett S, MacLean A, Miller RS, et al. Increased norovirus activity in Scotland in 2012 is associated with the emergence of a new norovirus GII.4 variant. *Euro Surveill.* 2013;18:pii=20349.
- Fu JG, Ai J, Qi X, et al. Emergence of two novel norovirus genotype II.4 variants associated with viral gastroenteritis in China. *J Med Virol.* 2014;86:1226-34. Epub October 17, 2013.
- Cai WF, Xie HP, Liu YF, et al. An epidemiological investigation on a food-born outbreak of norovirus caused by Sydney 2012 GII.4 strain. *Chin J Epidemiol.* 2013;34:804-7. Chinese with English summary.
- Fu JG, Ai J, Jin S, et al. Molecular characteristics of acute gastroenteritis outbreaks caused by norovirus, in Jiangsu province. *Chin J Epidemiol.* 2013;34:808-11. Chinese with English summary.
- Sun LM, Li H, Tan XH, et al. Epidemiology and etiological characteristics of diarrheal disease among children under 5 year of age in Guangdong province, in 2012. *Chin J Epidemiol.* 2013;34:989-92. Chinese with English summary.
- Mai H, Jin M, Guo X, et al. Clinical and epidemiologic characteristics of norovirus GII.4 Sydney during winter 2012–13 in Beijing, China following its global emergence. *PLoS One.* 2013;8:e71483.
- Leshem E, Wikswo M, Barclay L, et al. Effects and clinical significance of GII.4 Sydney norovirus, United States, 2012–2013. *Emerg Infect Dis.* 2013;19:1231-8.
- Maritschnik S, Kanitz EE, Simons E, et al. A food handler-associated, foodborne norovirus GII.4 Sydney 2012-outbreak following a wedding dinner, Austria, October 2012. *Food Environ Virol.* 2013;5:220-5.
- Goller JL, Dimitriadis A, Tan A, et al. Long-term features of norovirus gastroenteritis in the elderly. *J Hosp Infect.* 2004;58:286-91.
- Rockx B, de Wit M, Vennema H, et al. Natural history of human *Calicivirus* infection: a prospective cohort study. *Clin Infect Dis.* 2002;35:246-53.
- Qian ZY, Zhang YW, Zhou Q, et al. An outbreak of nosocomial norovirus gastroenteritis. *Chin J Nosocomiol.* 2012;22:2573-5. Chinese with English summary.
- Gallimore CI, Cubitt D, du Plessis N, et al. Asymptomatic and symptomatic excretion of noroviruses during a hospital outbreak of gastroenteritis. *J Clin Microbiol.* 2004;42:2271-4.
- Medici MC, Morelli A, Arcangeletti MC, et al. An outbreak of norovirus infection in an Italian residential-care facility for the elderly. *Clin Microbiol Infect.* 2009;15:97-100.
- Barrabeig I, Rovira A, Buesa J, et al. Foodborne norovirus outbreak: the role of an asymptomatic food handler. *BMC Infect Dis.* 2010;10:269.
- Schmid D, Kuo HW, Hell M, et al. Foodborne gastroenteritis outbreak in an Austrian healthcare facility caused by asymptomatic, norovirus-excreting kitchen staff. *J Hosp Infect.* 2011;77:237-41.
- Ozawa K, Oka T, Takeda N, et al. Norovirus infections in symptomatic and asymptomatic food handlers in Japan. *J Clin Microbiol.* 2007;45:3996-4005.
- Koopmans M. Noroviruses in healthcare settings: a challenging problem. *J Hosp Infect.* 2009;73:331-7.