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Burden of acute gastroenteritis caused by norovirus in China: A systematic review

Hong-Lu Zhou [a,f], Shan-Shan Zhen [a,b,f], Jin-Xia Wang [a,f], Can-Jing Zhang [a,f], Chao Qiu [a], Song-Mei Wang [c], Xi Jiang [d], Xuan-Yi Wang [a,e,*]

[a] *Key Laboratory Medical Molecular Virology, MoE/MoH, and the Institutes of Biomedical Sciences, Shanghai Medical College, Fudan University, Shanghai, 200032, People's Republic of China*
[b] *Shanghai Minhang Center for Diseases Control and Prevention, Shanghai, 201101, People's Republic of China*
[c] *Laboratory of Molecular Biology, Training Center of Medical Experiments, School of Basic Medical Sciences, Fudan University, Shanghai, 200032, People's Republic of China*
[d] *Division of Infectious Diseases, Cincinnati Children's Hospital Medical Center, University of Cincinnati, College of Medicine, Cincinnati, OH, USA*
[e] *Research Center on Aging and Medicine, Fudan University, Shanghai, 200032, People's Republic of China*

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Summary *Background:* To understand the epidemiology and disease burden of norovirus (NoVs) gastroenteritis in China, a systematic review was conducted.
Methods: Studies on acute gastroenteritis (AGE) caused by NoVs from mainland China, published before 2017 were searched. All retrieved articles were screened and reviewed by a standardized algorithm. NoVs detection rates as well as strain variations by ages, seasonal variations and geographic locations were analyzed using random-effects model.
Results: A total of 225 articles were included in the final analysis. Similar detection rates at 21.0% and 19.8% were obtained from the North and the South, respectively. NoVs infection occurred year round, with a peak between October and January in the North and between August and November in the South. High detection rates (~29%) of NoVs were found in adults and the elderly and in children aged 6–35 months (~22%). The predominant strains were GII.4 (70.4%), followed by GII.3 (13.5%).

* Corresponding author. Key Laboratory of Medical Molecular Virology of MoE & MoH, and Institutes of Biomedical Sciences, Shanghai Medical College, Fudan University, 138 Yi Xue Yuan Rd., Shanghai, People's Republic of China.
E-mail address: xywang@shmu.edu.cn (X.-Y. Wang).
[f] Hong-Lu Zhou, Shan-Shan Zhen, Jin-Xia Wang, Can-Jing Zhang contributed equally.

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Conclusion: NoVs cause significant disease burden in China which warrants development of vaccines against NoVs, particularly for children and the elderly who are vulnerable to gastroenteritis diseases. To achieve a broad protection, continual monitoring NoV epidemics and strain variations for selection of proper vaccine strains is critical.

Introduction

Acute gastroenteritis (AGE) is a leading cause of childhood illness in China.[1,2] With the improvement of sanitation and the popularity of safe drinking water, viruses became the major cause of AGE compared with bacteria pathogens. Moreover, it is noteworthy that the rotavirus (RVs) predominance of AGE has been replaced by norovirus (NoVs) with wide implementation of RV vaccination in recent years.[3–5] Though NoVs associated AGE mostly are mild and self-limited, serious cases can lead to death, especially in children under 5 years old (70% occurred in 2 years old), the elderly, and immunocompromised populations. Different from RV infection, in addition to the sporadic year round in the population, NoVs is more frequently associated with outbreak. It was reported that NoVs have triggered at least four pandemics in the past 15-year (1995–1996, 2002–2003, 2004–2005, 2006–2007).[6] Another notable characteristics of NoVs gastroenteritis is that NoVs outbreaks could not be controlled by improvement of sanitation.[7] In the United States, there were 1.9–2.1 million cases of NoV infection reported annually, resulting in 5.6–7.1 million hospitalizations. Of which, most of infection were found in children less than 5 years of age.[8] In Europe, 5.7 million diarrhea episodes caused by NoV infection occurred among children under 5 years of age each year, resulting in more than 50,000 hospitalizations.[9] Studies conducted in Asian and African countries showed that 89% of children acquired at least one episode of NoVs infection in the first two years from birth, and mostly associated with diarrhea (accounted for 22% of all diarrhea).[10] In China, outbreaks of AGE associated with NoVs infection increased continuously since 2006, and raised public health concern.[11] Three VLP-based NoVs vaccine candidates are being developed in China, while the epidemiology data and disease burden, such critical information for vaccine R&D are absent. To this end, we conducted this systematic review.

Methods

Search strategy

Studies on monthly prevalence of acute gastroenteritis, and acute gastroenteritis attributed to NoVs among all ages in mainland china, published before January 1, 2017 were identified using standardized search algorithms for systematic reviews.[12] Scientific articles published in English or Chinese were searched from PubMed (United States), SinoMed (Chinese Bio-Medical Literature Service System, China), and CNKI (National Knowledge Infrastructure, China) databases. Different retrieval formulas were established according to individual retrieval methods of these databases. Standardized medical subject heading (MeSH) term "Norovirus", "Sapovirus", "Caliciviridae", "Gastroenteritis" and free word "Acute", "China" were used for PubMed database; "Norovirus", "Norwalk virus", "Norwalk-like virus", "Sapovirus", "Sapporo-like Virus", "Acute Gastroenteritis" and "Caliciviridae" were set as Subject heading, title and keywords to search CNKI and SinoMed.

Definitions

To facilitate identification of reports, a suspected case of NoVs acute gastroenteritis was defined as a patient was admitted for treatment of acute gastroenteritis to a healthcare facility. A confirmed case of NoVs acute gastroenteritis was defined as a child for whom NoVs infection was proven by means of reverse transcription polymerase chain reaction (RT-PCR) or enzyme immunoassay performed on fecal specimens. The monthly prevalence was defined as the number of cases experienced acute gastroenteritis in the previous 28 days divided by the total number of investigated population. Herein, those multiple episodes were counted as a single episode.

Review strategy

Endnote® (version X7, Thomson Reuters, Inc., Philadelphia, PA) bibliographic software was used to create an electronic library of citations identified in the database searches. PubMed searches were performed using Endnote®, and articles identified through SinoMed and CNKI were imported into Endnote. Duplicate records were deleted. For articles published in Chinese and English, if identical data were presented, the English language article was used. Each study was assigned a unique identification code to enable tracking of reviews and analysis after title/abstract screening. Four reviewers split into two independent groups were trained to perform the title/abstract screening and thereafter full text screening. Disagreements were resolved by consensus between the two groups and the corresponding author. For each article that met the inclusion criteria we used a structured questionnaire to appraise its quality based on study design, sources of specimens, study scope, case definitions, and diagnostic methods. To identify differences in homogeneity among the articles, each question was assigned a score, with zero being the lowest and five being the highest. Mean points per question were calculated for each article. Articles with $\geq 3{\cdot}0$ points/question were considered moderate/high quality. A structured questionnaire was implemented for data extraction,