



Review

Update on the disease burden and circulating strains of rotavirus in China: A systematic review and meta-analysis



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ABSTRACT

Background: Rotavirus is the most common cause of severe diarrhea in children, and most associated deaths occur in developing countries. Two new internationally licensed vaccines are expected to be launched in the near future in China. We performed a systematic review and meta-analysis of rotavirus studies to update information on the burden of rotavirus disease in China.

Materials and methods: Eligible studies published before 2011 were identified using PubMed/Medline, Embase, Cochrane Library, LILACS, WHOLIS, and two Chinese literature databases, CNKI, and WANFANG. Arc-sine transformations and the DerSimonian–Laird random-effects or fixed-effects models were used for meta-analysis.

Results: A total of 211 studies were included in this review, of which 63 (29.9%) were inpatient studies, 26 (12.3%) were outpatient, 122 (57.8%) were combined. Community subjects were investigated in two combined studies. Rates of gastroenteritis caused by rotavirus in inpatients, outpatients, and community children were 42.6%, 32.5% and 9.3%, respectively. The most common G type was G3 (39.3%), followed by G1 (30.3%), G2 (7.2%), and G9 (3.3%). The most common P types were P[8] (50.2%), P[4] (18.2%), and P[6] (7.2%). The most prevalent G–P combinations were G3P[8] (32.1%), G1P[8] (23.0%), and G2P[4] (7.9%).

Conclusion: Rotavirus is an important cause of both severe and mild diarrheal disease in children <5 years of age in China; G3P[8] is the most prevalent strain. The introduction of an effective rotavirus vaccine to Chinese pediatric immunization programs is necessary.

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1. Background

Rotavirus Group A is the leading cause of severe diarrhea among young children in developed and developing countries. The latest estimate of worldwide deaths due to rotavirus was 453,000 in 2008, with more than half occurring in five Asian and African countries [1]. In addition, 25–50% of all diarrhea hospitalizations in both developed and developing countries and 23 million outpatient visits in young children annually are due to rotavirus diarrhea [2].

Rotavirus vaccines have been developed because of the tremendous disease burden of rotavirus gastroenteritis (RVGE). Two internationally licensed rotavirus vaccines (Rotarix, GlaxoSmithKline Vaccines and RotaTeq, Merck & Co., Inc.) are now available, and have been introduced into both private and public markets

worldwide. The Lanzhou lamb rotavirus vaccine (Lanzhou Institute of Biological Products) for private market is the only one available in China [3]. In 2009, the WHO Strategic Advisory Group of Experts (SAGE) recommended worldwide inclusion of the rotavirus vaccine in national immunization programs, particularly in countries with high diarrhea-related child mortality [4,5]. Rotarix and RotaTeq are expected to be launched in China in the next few years. Precise information on the disease burden of RVGE and the strain distribution are critical for health officials to formulate appropriate policies and recommendations concerning rotavirus vaccination in China.

A recent report estimated that a total of 145,000 deaths per year are caused by rotavirus in Asia, with the majority occurring in Southern and South East Asia [6]. Epidemiological and health economic data relating to rotavirus in China were analyzed in the aforementioned report, but it included articles from only English-language literature databases. We published two review articles on the epidemiology of rotavirus in China with both English and Chinese papers [7]. However, these reviews included papers published before 2005, and a meta-analysis was not performed.

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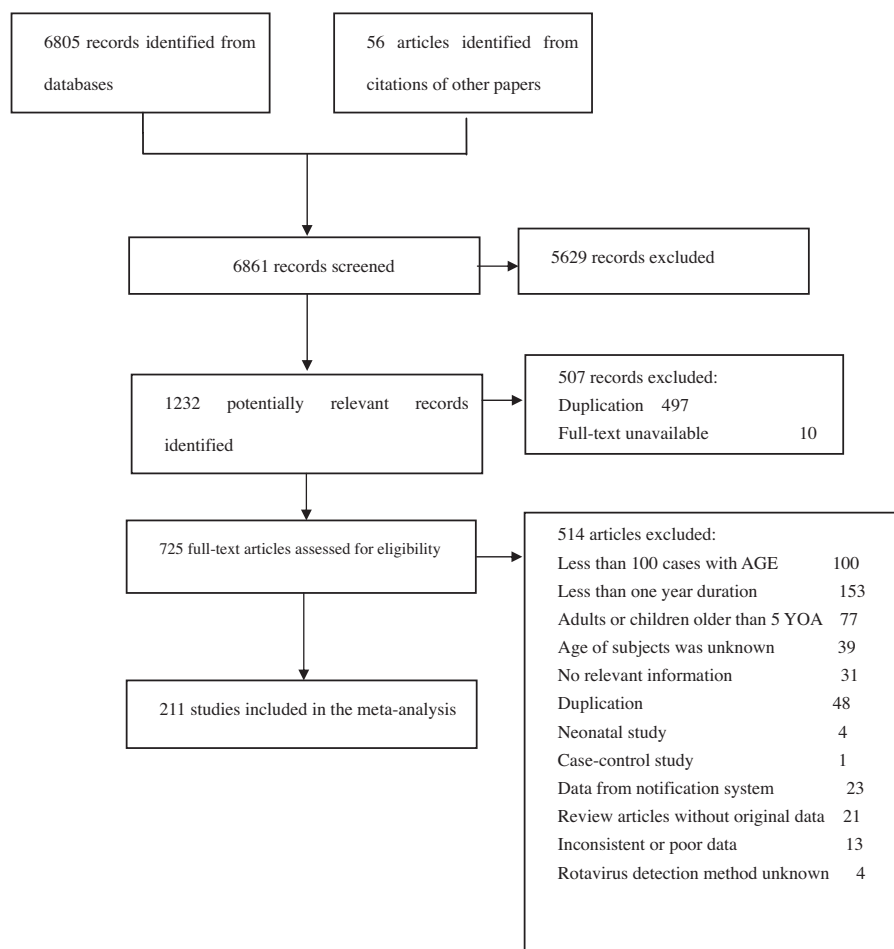


Fig. 1. Flow of information through the phases of the systematic review.

This study updates epidemiological data regarding rotavirus in China, and precisely estimates the distribution of rotavirus-related diarrhea among Chinese children less than 5 years of age (YOA). Also, the circulating rotavirus strains are evaluated.

2. Materials and methods

2.1. Search strategy and selection criteria

We systematically searched for English papers published before 2011 using PubMed/Medline, Embase, Cochrane Library, LILACS, and WHOLIS. CNKI and WANFANG were used for Chinese papers. “Rotavirus AND China” were the search terms in English databases, and “Rotavirus” was used for Chinese databases. The selected publications were narrowed to studies relevant to disease burden and serotype distribution. Target studies report either the proportion of rotavirus disease among children with gastroenteritis or the prevalence of rotavirus genotypes, G, P or both. Studies were required to include at least 100 acute gastroenteritis cases and be of at least 1-year duration. Studies included the following methods for detecting rotavirus in fresh samples: enzyme immune-assay (EIA), polyacrylamide gel electrophoresis (PAGE), reverse-transcription polymerase chain reaction (RT-PCR), viral isolation, latex agglutination (LA), electronic microscopy (EM), indirect immunofluorescence, and immuno-chromatography (IC) or gold immuno-assay (GA). Studies based only on asymptomatic infections, health carriers, neonates, outbreaks, hospital-acquired infections, adults, or children older than 5 years were excluded.

Articles without original data, duplicate studies, case-control studies, case analysis studies, and methodological studies were also excluded. Studies using notification systems were excluded since hospitals reported data passively, and so the results are not representative of the true rotavirus incidence. Citations from the two previous review articles published in China were also considered for inclusion.

2.2. Screening and data extraction

Papers were screened based on titles and abstracts by one researcher. Full-text versions were obtained for potentially eligible studies. Two independent researchers assessed the full text to confirm whether they met the inclusion criteria. Data were extracted by the researchers who assessed the full texts using a predefined Microsoft Office Excel database.

2.3. Assessment of risk of bias

The risk of bias for the reports was assessed by two independent researchers using the tool developed by Linhares et al. (web appendix 1) [8]. The tool was based on a checklist of essential items stated in STROBE [9], and two methodological studies [10,11]. Disagreements were resolved by discussion with a third reviewer.

2.4. Statistical analyses

A proportion meta-analysis was conducted to analyze the extracted data. An arc-sine transformation was used to

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