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Etiology of diarrhea among children under the age five in China: Results from a five-year surveillance

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Summary *Objectives:* Diarrhea is a leading cause of morbidity and mortality for children, although sparse data is available on the etiology of diarrhea in China. This study was conducted to determine main causes that underlie childhood diarrhea and related diseases.
Method: Surveillance data for diarrhea was collected from 213 participating hospitals between 2009 and 2013. These stool specimens, from children aged 0—59 months, were then analyzed for a panel of etiological agents consisting of 5 viruses, 8 bacteria and 3 protozoa. The proportion of children who tested positive for each pathogen was calculated and seasonal patterns for major organisms were determined.
Results: Pathogens were identified in 44.6% of the 32,189 samples from children with diarrhea. The most commonly detected pathogens were *rotavirus* (29.7% of cases), *norovirus* (11.8%), *Diarrheagenic Escherichia coli* (DEC; 5.0%), *adenovirus* (4.8%), non-typhoidal *Salmonella* (NTS; 4.3%), and *Shigella spp.* (3.6%). A strong seasonal pattern was observed for these organisms, including *rotavirus* (winter), *norovirus* (autumn), and DEC, NTS, and *Shigella* (summer).
Conclusion: A wide range of enteropathogens were detected in this five-year surveillance study; *rotavirus* and *norovirus* were most common among children under the age five. These findings should serve as robust evidence for public health entities when planning and developing national intervention programs in China.

Introduction

Diarrhea is one of the leading causes of morbidity and mortality among children aged under 5 and estimated at 1.73 billion episodes and 711,800 deaths each year.[1] China is one of 15 high-incidence countries[1]; an estimated 770 million episodes of diarrhea (0.7 episodes per person year) occur annually, of which 194 million are attributed to children aged <5 years (1.9 episodes per person year).[2] Although infectious diarrheal incidents have been a mandatory notifiable disease/syndrome since 1989,[3] most cases are reported based only on clinical diagnosis. Data regarding trends, etiology and incidence of diarrhea through laboratory-based surveillance study have not been available in China. To address this data gap, a few small scale studies have previously been conducted in China,[4—7] but these have generally focused on a single or limited number of enteropathogens in a hospital or local region, or over a short study period (usually one year); thus these studies did not capture long-term trends or permit robust extrapolation to the entire population of China.

Beginning in 2009, the Chinese Ministry of Science and Technology and Ministry of Health launched a nationwide, multicenter, prospective study: the National Key Science and Technology Project on Infectious Disease Surveillance Technique Platform. This platform was intended to enhance nationwide etiology identification, uncover the major pathogenic agents of epidemic infectious diseases, and inform policy makers on future vaccine and intervention development and enhance recommendations in China. This study presents microbiological results from the first 5 years (2009—2013) of surveillance of diarrheal illness data among children aged <5 years who presented to a hospital outpatient setting in China.

Materials and methods

Case recruitment

From Jan. 1st 2009 to Dec. 31st 2013, ongoing surveillance of diarrhea for all age groups was conducted in 213 participating hospitals ('sentinel' hospitals) throughout the country (Fig. 1). Sentinel hospitals were selected based on their catchment areas, population served, and interest in participating in the study. Three guidelines were adhered to when selecting sentinel hospitals: 1. each of the 31 provinces of mainland China would include a minimum of one hospital; 2. various types of hospitals (e.g., children's, general, urban and rural community health service centers) would be included; and 3. hospitals would have the capability and resources to conduct ongoing surveillance.

Patients visiting outpatient clinics (primarily enteric, pediatric and internal medicine) of sentinel hospitals were registered, and a standard case definition was used to determine eligibility. Diarrhea was defined as ≥3 passages of watery, loose, mucus-, or bloody-stools within a 24-h period. Patients referred from other hospitals or patients not initially diagnosed in sentinel hospitals were excluded from this study. A total sample size of ~10,000 persons per year was selected for the whole country. The total sample size was then allocated and assigned to each sentinel hospital (median = 54 cases/hospital/year), after weighting using the recorded outpatient numbers from the previous year. A convenient sampling method was used in sentinels to recruit that number of participants among eligible cases. To account for seasonal variations of diarrheal illness onset, it was determined that each hospital was to recruit ≥5% of the allocated number on a monthly basis. Information regarding demographics (e.g., sex, date of birth, and address) and clinical characteristics (e.g., signs/symptoms, date of