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Estimating rotavirus gastroenteritis hospitalisations by using hospital episode statistics before and after the introduction of rotavirus vaccine in Australia

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ABSTRACT

Introduction: Hospital discharge records and laboratory data have shown a substantial early impact from the rotavirus vaccination program that commenced in 2007 in Australia. However, these assessments are affected by the validity and reliability of hospital discharge coding and stool testing to measure the true incidence of hospitalised disease. The aim of this study was to assess the validity of these data sources for disease estimation, both before and after, vaccine introduction.

Methods: All hospitalisations at a major paediatric centre in children aged <5 years from 2000 to 2009 containing acute gastroenteritis (AGE) ICD 10 AM diagnosis codes were linked to hospital laboratory stool testing data. The validity of the rotavirus-specific diagnosis code (A08.0) and the incidence of hospitalisations attributable to rotavirus by both direct estimation and with adjustments for non-testing and miscoding were calculated for pre- and post-vaccination periods.

Results: A laboratory record of stool testing was available for 36% of all AGE hospitalisations ($n = 4948$) the rotavirus code had high specificity (98.4%; 95% CI, 97.5–99.1%) and positive predictive value (96.8%; 94.8–98.3%), and modest sensitivity (61.6%; 58–65.1%). Of all rotavirus test positive hospitalisations only a third had a rotavirus code. The estimated annual average number of rotavirus hospitalisations, following adjustment for non-testing and miscoding was 5- and 6-fold higher than identified, respectively, from testing and coding alone. Direct and adjusted estimates yielded similar percentage reductions in annual average rotavirus hospitalisations of over 65%.

Conclusion: Due to the limited use of stool testing and poor sensitivity of the rotavirus-specific diagnosis code routine hospital discharge and laboratory data substantially underestimate the true incidence of rotavirus hospitalisations and absolute vaccine impact. However, this data can still be used to monitor vaccine impact as the effects of miscoding and under-testing appear to be comparable between pre and post vaccination periods.

1. Introduction

Rotavirus is the leading cause of severe acute gastroenteritis (AGE) in early childhood globally [1]. In Australia before vaccine introduction, rotavirus gastroenteritis caused approximately 10,000 hospitalisations, 22,000 emergency department and 115,000 general practitioners visits in children under 5 years of age, with one rotavirus-related death each year [2]. Two live attenuated oral rotavirus vaccines, RotaTeq (pentavalent rotavirus vaccine [CSL/Merck]) and Rotarix (monovalent rotavirus vaccine [GlaxoSmithKline Biologicals]) were funded under the Australian National Immunisation Program from 1st July 2007. By end of 2009 national coverage for a full rotavirus vaccine course by 12 months of age was 84% and in New South Wales (NSW), which uses Rotarix in a two dose course, was 86.5% [3].

In developed world settings like Australia, the major population benefit expected from rotavirus vaccination is a decrease in hospital admissions [4,5]. In pre-licensure clinical trials both rotavirus vaccines significantly reduced rotavirus gastroenteritis (85–96%) as well as all-cause gastroenteritis (42–59%) hospitalisations in young infants [6–8]. Similarly, high effectiveness of RotaTeq against hospitalisations assigned the rotavirus specific diagnosis code and all AGE diagnosis codes has been reported from early assessment of vaccination programs in USA and Australia [9–11]. Vaccine

Abbreviations: AGE, acute gastroenteritis; NIP, National Immunisation Program; NSW, New South Wales; ICD-10 AM, International Classification of Diseases 10th edition Australian Modification; CHW, Children's Hospital at Westmead; PPV, positive predictive value.

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Table 1
ICD 10 codes/categories and rotavirus test status in hospitalisations with primary diagnosis of AGE in children <5 years of age, 2000–2009.

AGE code category		ICD 10 code	Number (%)	Number tested for Rotavirus (%)
Diarrhoea of determined aetiology	Bacterial	A01–A07 (excluding A02.2, A06.4, A06.5, A06.6, A06.7)	155 (3.1)	103 (66.5)
	Parasitic	A06–A07	22 (0.4)	13 (59.1)
	Rotavirus	A08.0	534 (10.8)	477 (89.3)
	Other viral	A08.1–A08.4	2241 (45.3)	591 (26.4)
Diarrhoea of undetermined aetiology	Presumed infectious	A09	1907 (38.5)	556 (29.2)
	Presumed non-infectious	K52, R198	89 (1.8)	34 (38.2)
Total			4948 (100)	1774 (35.9)

effectiveness estimates for Rotarix in USA are not yet available [12]. Estimates of Rotarix vaccine effectiveness in Indigenous Australian children in rotavirus outbreaks have varied widely [13,14].

Validated and reliable methods to estimate hospitalisations associated with rotavirus diarrhoea are essential to accurately monitor the impact of rotavirus vaccination on the gastroenteritis disease burden [15]. Active surveillance with laboratory confirmation is the ideal method to measure disease but requires substantial resources [15,16]. Previous studies in Australia have used either routinely collected hospital discharge code data, laboratory testing results or both, reported separately, to estimate vaccine impact [2,17–19]. A specific diagnosis code for rotavirus enteritis was introduced in the International Classification of Diseases (ICD) in 1993 (ICD-9, 008.61) and was revised in 1999 in the ICD-10 to the current code (A08.0) [20], which is also in the Australian modification, ICD-10 AM.

Hospital discharge coding practices, utilisation and performance of laboratory testing and management practices all potentially affect the accuracy of disease incidence estimates from routine hospitalisation data. The sensitivity of the rotavirus specific diagnosis code to capture hospitalisations due to rotavirus disease, assessed in the USA, was low. [11,21]. However, when adjusted for under testing, rotavirus hospitalisation estimates from diagnosis codes were shown to be consistent with active surveillance data [16,21].

The estimated declines in hospitalisations coded as rotavirus gastroenteritis since vaccine introduction are dependent on the comparability of hospital discharge coding practices and testing patterns across pre-and post-vaccination periods [9,18,22–26]. No previous study has comprehensively examined this. The objective of this study was to assess the validity of routine hospital discharge diagnosis coding to estimate the relative and absolute burden of hospitalisations due to rotavirus gastroenteritis both before and after vaccine introduction. The study also compared estimates of rotavirus-attributable hospitalisations using unadjusted routine hospital data with those after adjustment for miscoding and under testing.

2. Methods

The study was conducted at the Children's Hospital at Westmead (CHW), a 275 bed tertiary referral paediatric hospital in Sydney, Australia, with approximately 49,800 emergency presentations and 28,900 inpatient admissions annually. It is the largest paediatric hospital in Australia's most populace state, NSW. Approximately 220,000 children less than 5 years of age reside in the catchment area of CHW. The study retrospectively reviewed data for AGE hospitalisations (obtained from the hospital inpatients' data collection) and hospital diagnostic laboratory data on all rotavirus tests performed (obtained from the hospital clinical laboratory database for all patient episodes; hospitalisation or emergency department) in children aged less than 5 years in the 10-year period from 1st January 2000 to 31st December 2009. All hospital inpatient episodes (hospitalisations) that had one of the ICD 10 AM acute gastroenteritis codes (Table 1) as their primary discharge diagnosis were defined as AGE hospitalisations. Patient medical record number (MRN), date of birth, date of admission and sex were obtained for records from both data sources.

During the study period stool testing for rotavirus was recommended on all patients who were admitted with symptoms and signs of AGE to CHW for routine clinical care and infection control purposes. Stools were tested for rotavirus antigen using enzyme immunoassay (EIA [Vidas, BioMerieux France, Craponne, France]) up to June 2006 and RIDA Quick rotavirus/adenovirus immunochromatographic (ICG) assay thereafter [18]. When evaluated against polymerase chain reaction method sensitivity of EIA was 96% and that of ICG was 99%. Both tests had a specificity of 96% [27]. ICD 10 AM was the only method used to code hospital discharge diagnoses at CHW during the entire study period.

The combination of MRN and admission date was used to identify and link the same hospital episode in the two data sets. When an AGE hospitalisation record did not have a matching record in the laboratory dataset that hospitalisation was considered to not have had a stool test for rotavirus performed. When there were multiple stool tests in the same hospital episode a composite record was constructed comprising of all tests for that episode; if at least one test was positive it was designated as a rotavirus test positive episode. When a laboratory record did not have a matching AGE hospitalisation record, it was presumed to be a non-inpatient episode or to be a hospitalisation not assigned any AGE code as the primary diagnosis. The diagnosis codes in those with positive rotavirus tests in the latter group were actively extracted.

The peak rotavirus season (winter/spring) in the study setting is June–November. Pre-and post-vaccine introduction periods were designated as 2000–2007 and 2008–2009 respectively.

2.1. Statistical analysis

Hospitalisation (inpatient stay episode) was the unit of analysis in the study. Sensitivity, specificity and positive predictive value (PPV) of the rotavirus specific diagnosis code among AGE hospitalisations (i.e. hospitalisations with a primary diagnosis of AGE) were assessed using linked data. The estimated number of rotavirus test positives among AGE hospitalisations that did not have stools tested was derived by extrapolation of rotavirus detection rates among those tested. It was assumed that such an extrapolation would be acceptable provided that any differences between hospitalisations with testing and those without are accounted for. For this purpose, first, AGE hospitalisations that were tested were compared to those not tested by demographic factors, seasonality and vaccination period. As AGE hospitalisations that had testing differed significantly from those not tested by age and pre/post vaccination periods, age and vaccination period specific rates for test positivity in those tested were then applied to those not tested to derive expected additional rotavirus positive hospitalisations. The Chi-square test was used for comparing differences in proportions in the study.