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REVIEW ARTICLE

Rota virus infections: prevalence, diagnosis and prevention

Padmanabhan Vidhya[1], Ponnambalam Arun[1], Palani Gunasekeran[2], Kavitha Arunagiri[2], Mohana Sambasivam[2], Kaveri Krishnasami[2]

[1]Bharathiyar University, Coimbatore; India

[2]King Institute of Preventive Medicine and Research, Guindy,Chennai,India

Abstract:

Background: *Diarrhoea is one of the leading causes of infant mortality. Various diagnostic methods are available and there is a need to select an ideal one. The use of Vaccines, its efficacy needs to be studied.* ***Methods:*** *A pubmed search, pubchem assay journal of epidemiology and infection, Google search generated results were included for review, out of 900 articles generated 111 articles are studied and were included for review.* ***Conclusion:*** *Molecular typing methods for viruses should aim to provide clinically and biologically useful information about field viruses, particularly with regard to virulence, viral epidemiology, and virus serotype identification. These data may be important for assessing the need for introducing rotavirus surveillance and vaccines into immunization programs in India particularly Tamilnadu.*

Keywords: *Rota virus, Gastroenteritis, RNA viruses, Vaccines, Rotatrix.*

Corresponding author: *Arun Ponnambalam; Department of Virology, King Institute of Preventive Medicine and Research, Guindy, Chennai , India; e-mail: arunpatchai@yahoo.co.in*

Introduction

Rotavirus is the most common cause of severe gastroenteritis in infants and young children worldwide. Nearly every US child who is not vaccinated against rotavirus as an infant is expected to be infected with rotavirus within the first years of life, and the majority will have symptomatic gastroenteritis. The clinical spectrum of rotavirus illness ranges from mild, watery diarrhea of limited duration to severe diarrhea with vomiting and fever that can result in dehydration with shock, electrolyte imbalance, and death. Following an incubation period of 1–3 days, the illness often begins abruptly, and vomiting often precedes the onset of diarrhea. Gastrointestinal symptoms generally resolve in 3–7 days. Up to one-third of patients have a temperature of >102°F (>39°C). Severe, dehydrating rotavirus infection occurs primarily among unvaccinated children aged 3–35 months [1-6]. Adults can also be infected, though disease tends to be mild [7].

Rota viruses are shed in high concentration from stool of infected children's through oral-faecal route. Rotavirus is highly communicable, with a small infectious dose of < 100 virus particles [8] by the age of five; nearly every child in the world has been infected with rotavirus at least once [9]. There are five species of this virus, referred to as A, B, C, D, and E [10]. In addition to its impact

on human health, rotavirus also infects animals, and is a pathogen of livestock [11].

The incidence and severity of rotavirus infections has declined significantly in countries that have added rotavirus vaccine to their routine childhood immunization policies [12, 13].

Since the widespread use of rotavirus vaccines, this seasonality has shifted and this trend in rotavirus peak activity is no longer consistently observed [14-17].

Additionally no indication of waning vaccine-induced immunity has yet been observed during the rotavirus vaccine post-licensure period [18-19]. Rotavirus also is an important cause of Nosocomial gastroenteritis [3,20-25].

Outbreaks of RV gastroenteritis in day-care centers and hospitals can spread rapidly among no immune children, presumably through person-to-person contacts, airborne droplets, or contact with contaminated toys [26]. Children from low socioeconomic background and low birth weight infants have an increased risk for hospitalization [27].

Mortality still is the greatest in south and south-eastern Asia and sub-Saharan Africa, with almost 100,000 deaths each year in India alone and more than 200 000 in African countries [28]. The Asian Rotavirus Surveillance Network, which involves 14 countries working in collaboration with the WHO, PATH and the Centers for Disease Control and Prevention (CDC) in Atlanta, GA (USA) estimated that 73% of hospital admissions of children for diarrhea in South Korea were RV positive, 58% in Japan, 55% in Vietnam, 53% in Myanmar, 46% in China, 43% in Thailand and 30% in HongKong [29].

Before the introduction of vaccination, RV gastroenteritis was estimated in the USA to account for over 50 000 hospitalizations, 200 000 emergency department visits, 410 000 physician office visits, and 20 to 40 deaths per year. In 2006 in the region of the Americas there were more than 10 million episodes of RV diarrhoea requiring domiciliary visits, 2 million requiring a clinic consultation, and 75,000 requiring hospitalization, leading to considerable medical costs (more than US$ 17 million in Mexico alone). In Asia, universal RV immunization would avert about 110 000 deaths, 1.4 million hospitalizations and 7.7 million outpatient visits [30]

Rotavirus (RV) infections are a major cause of acute gastroenteritis in children and domestic animals, infecting virtually all children within their first 5 years of life [31]. Rota viral gastrointestinal disease is particularly prevalent in third-world and developing countries Therefore, the development of potential inhibitors of this virus is of great interest [32].

The development of potential inhibitors of this virus is of great interest. Hence evaluation of a number of N-acetylneuraminic acid-based compounds as potential rotavirus inhibitors are studied and this inhibition is carbohydrate based molecules and does appear to be strain dependent [32].

In a study conducted using hot watrer extracts of Stevia rebaudiana (SE) against HRV-infected MA104 cells suggest that SE may bind to 37 kD VP7 and interfere with the binding of VP7 to the cellular receptors by steric hindrance, which results in the blockade of the virus attachment to cell [33].

The ability of six polyphenols isolated from the roots of Glycyrrhiza uralensis to inactivate rotaviruses specially G5P[7] and G8P[7] was evaluated. The CPE inhibition assay showed that five compounds inhibited viral replication with EC (50) values of 12.1-24.0 μM against G5P[7] and 12.0-42.0 μM against G8P[7], respectively. Compounds isolated from the roots of G. uralensis may be potent anti-rotavirus agents in vivo, acting by inhibiting both viral absorption and viral replication [34].

Synthesis of the unsaturated keto and exomethylene pyranonucleoside analogues, were evaluated for their anticancer and antiviral activities using several tumor cell lines and gastrointestinal rotavirus. All of the compounds showed direct antiviral effect against rotavirus

infectivity in Caco-2 cell line [35]. In and another study it has been found that synthesis of 3-fluoro-5-thio-xylofuranosyl nucleosides of thymine has been found to be biologically active against rota viral infection and growth of tumor cells [36].

Interest in the use of innate immune modulating agents recently has increased in the context of developing effective biodefense strategies. Increasing natural disease resistance by administration of agonists that stimulate pathogen recognition receptors and gene expression pathways is an approach that would provide broad protection from infection without need for pathogen-specific vaccines [37]

Some traditional herbal medicines have been tested for the infectivity of Rota virus. Among the 34 kinds of herbal medicines tested, the fruit of Citrus aurantium had the most potent inhibitory activity on rotavirus infection. The active components of the fruit of Citrus aurantium were neohesperidin and hesperidin [38].

Virus infectivity was assessed in MA-104 cells using a focus forming unit assay. The modulation of SBIF isoflavone composition and concentration represents novel nutritional approaches to potentially reduce the severity of RV infection in human and production animals [31].

Rotaviruses are 70 nm icosahedral, non-enveloped, double-stranded RNA viruses that belong to the family Reoviridae. The virus is characterized by its three-layer capsid, an outer and an inner capsid and an internal shell that surrounds the 11-segment double-stranded RNA genome. The outer capsid is made of two proteins, VP4, also named "P protein", and VP7, also known as the "G protein", which define the "P" and "G" serotypes of the virus, respectively. Both are key neutralization determinants on the surface of the virion. The inner capsid is made of the VP6 protein, the most abundant and immunogenic protein in the virion.

NSP4 is a viral enterotoxin to induce diarrhoea and was the first viral enterotoxin discovered [39] NSP6 is a nucleic acid binding protein, [40] and is encoded by gene 11 from an out of phase open reading frame [41]

Anti-VP6 antibodies do not neutralize virus infectivity but VP6-specific IgAs appear to confer protection in vivo, perhaps through inhibition of virus transcytosis through the intestinal epithelium barrier [42] In fact, G serotypes G1-G4 and G9, and P genotypes P[4] and P[8] are predominant worldwide, causing aver 90% infections in industrialized countries and about 68% infections in South American and Asian countries [43]

P[8]-G1 is the globally predominant strain, followed by P[8]-G3, P[4]-G2, and P[8]-G4 [44]. G9 strains have emerged in the early 2000s and have become predominant in some regions of the world, including Europe, Thailand and parts of Eastern Asia.

Less usual strains may also be found, such as P[6]-G8 in Africa, P[8]-G5 in Brazil and novel P[11]-G10 and P[6]-G12 in India [45].

Even if vaccination early in life may not prevent all subsequent disease episodes, it should prevent most cases of severe RV disease and their complications such as dehydration, physician visit, hospitalizations and deaths [46].

The G9 genotype, which is emerging worldwide, was identified in 12% of all Danish samples, and the uncommon G1P[4] genotype was identified in 4.3% of the Danish samples Other uncommon genotypes identified were G9P[8] (7%), G1P[4] (4%), and G2P[8] (3%) [47].

Group C rotaviruses were detected by reverse transcription-PCR in 14 (2.3%) of 611 group A rotavirus negative stool specimens from the patients admitted to the International Centre for Diarrhoeal Disease Research, Bangladesh hospital, Dhaka, Bangladesh, during July to December 2003 [48].

It was found that 117 fecal specimens (19.4%) were positive for group A rotavirus. Rotavirus infection was detected continuously from November to June, with the highest prevalence in April The predominant genotype was G1P[8]

(70.1%), followed by G3P[8] (17.9%), G9P[8] (6.8%), and G2P[4] (2.6%) [49].

Of 731 stool specimens collected from children with diarrhea in Kathmandu, Nepal, from August 2004 through July 2005, 170 (23.3%) tested positive for rotavirus [50].

The majority of strains were demonstrated to belong to genotype G1 (54.5%) or P[8] (77.8%) on the basis of nucleotide sequencing of fragments from their VP7 and VP4 genes. The other genotypes detected included G2, G8, G9, G12, and P[4]. A G8P[6] strain, strain DS108, was detected for the first time in northern India [51].

Fourteen cases of G12 infection were identified between June and September 2005. G12 was seen in combination with P[6], P[8], or nontypeable P type. Significant temporal and time-space clustering of eight of these cases represents a possible recent introduction of a new rotavirus VP7 genotype during a birth cohort study between June and July 2005 [52].

Group B rotavirus was detected in 12 of 220 (5.5%) adult patient stool samples and 2 of 67 (3.0%) child stool samples. Group A rotavirus was detected in 9 (4.1%) adults and 7 (10.4%) children, and group C rotavirus was detected in 2 (0.9%) adults [53].

Two unusual rotavirus strains not previously reported in India, G11P [25] (CRI 10795) and G3P[3] (CRI33594) were isolated from faecal samples of asymptomatic children in India [54].

Rotavirus group A G12 genotypes were detected in 3 (1.5%) of 198 stool samples positive for human rotavirus.G12P [6] was present in 2 samples, and a mixed G3G12P[8] was found in 1 sample [55].

Of the 435 stool samples from children with acute gastroenteritis, 27.6% were positive for rotavirus A. The predominant G type was G1 (37.5%), followed by G3 (25%), G2 (17.5%), G4 (12.5%), G9 (2.5%) and three mixed-G infections G3G4 (2.5%) were identified. Only P[8] (80.8%), P[4] (16.7%) and P[9] (0.8%) genotypes were found [56].

G9 strains belonged to P[8]G9, subgroup II, and long electropherotype, except one belonged to P[4]G9, subgroup II, and short electropherotype from 4 cases and constituted 33.8% and 54.8% of the rotavirus-positive samples in 2001 and 2002 [57].

From a collection of 333 positive stool samples of Rota virus revealed G1P[8] (32.1%), G2P[4] (28.5%),G4P[8] (11.2%) and six G8 and 5G9 were identified as part of mixed infections from an Ireland study between 1997-1999 [58].

Out of 533 patients 202 tested positive samples for rota virus had a higher incidence of vomiting (185/202 vs. 212/331, 92% vs. 64%, $P < 0.001$), lethargy (67/202 vs. 51/331, 33% vs. 15%, $P < 0.001$), and dehydration (81/202 vs. 78/331, 40% vs. 24%, $P < 0.001$) [59].

Out of 500 patients diagnosed for acute watery diarrhea 147 (29.4%) were positive for group A rotavirus. Majority of positive patients 116/147 (78.9%) were in the age group 2 months to 12 months [60].

The globally common genotypes G1P[8] and G2P[4] constituted 58% of the total positive strains, while 3% and 8% strains were emerging genotypes, G9P[6] and G12P[6]. This is the first report of genotype G12 in Manipur the VP7 genes of G4 and G10 strains clustered with porcine and bovine strains, indicating possible zoonotic transmission [61].

In a systematic surveillance undertaken in two government-run rural health facilities, 457 children, aged less than five years, having acute watery diarrhoea, were studied between August 2005 and July 2007 to determine the prevalence of rotavirus. Rotavirus infection was detected in 114 (25%) and Vibrio cholerae in 63 (14%) children [62].

NSP4 has been recognized as the rotavirus-encoded enterotoxin. However, a few studies failed to support its diarrheagenic activity [63].

Out of 4,634 (2,533 male) children aged less than 5 years admitted to hospitals in Australia identified G serotypes of rotaviruses were

identified in 81.9% (3,793 of 4,634) children. They included 67.8% (from 3,143 children) serotype G1 isolates, 11.5% (from 531 children) serotype G2 isolates), 0.8% (from 39 children) serotype G3 isolates, and 1.6% (from 76 children) serotype G4 isolates. G6 (two strains) and G8 (two strains) isolates were identified during the same period. G1 was predominant. In all temperate climates rotavirus incidence peaked during the colder months [64].

In an study comprising 110 human faecal samples resulted [P8]G1 was predominant, and 5.5% belonged to the G9 genotype by reverse transcriptase PCR. Rotavirus-positive fecal samples from 28 calf herds were genotyped by DNA sequencing. Genotypes G6 and G10 predominated; G6 and G10 were detected in 22 (78.6%) and 16 (57.1%) of the rotavirus-positive calf herds, respectively. In 12 (42.9%) calf herds, we found mixed infections [65].

Stool specimen molecularly characterized revealed G10P[11] from a 14 year old giraffe sequence analysis of VP4 and VP7 revealed significant identity at the amino acid sequence level to Bovine RV (BoRV) which suggest that surveillance of RV strains in various animal populations, which will facilitate the identification of rotavirus hosts not previously reported and timely identification of new emerging strain types [66].

Rotavirus diarrhea in 453 pediatric patients (29.8% of 1,518) was studied in greater Bangkok during 1985 to 1987. The disease persisted all year, increasing in incidence from August to January (30 to 50%) [67].

The prevalence of "common" G/P combinations, G1P[8], G3P[8], G4P[8], and G2P[4], ranged between 50 and 85%. The G9 genotype, which is emerging worldwide, was identified in 2 to 35% of all samples depending on the country. Unusual combinations, such as G1 or G4 associated with P[4] or G2 with P[8], which may have arisen by reassortment between human strains, were found in samples from 3 to 20% of patients from a study conducted in central and south eastern Europe during the period 2004 to 2006 [68].

Characterization of a genotype G5P[7] human rotavirus (HRV) from a child in Cameroon who had diarrhea was studied. This G5P[7] strain exemplifies the importance of heterologous animal rotaviruses in generating HRV genetic diversity through reassortment [69].

A rare G8P[4] rotavirus, designated GER1H-09, was detected in a stool sample from an infant suffering from repeated episodes of emesis for 2 days without diarrhea. The genotype composition of GER1H-09 (G8-P[4]-I2-R2-C2-M2-A2-N2-T2-E2-H2) suggests the occurrence of reassortment events between G8 genotypes and human DS-1-like G2P[4] rotaviruses [70].

In an population based retrospective study in Akita province an 3 year follow up of birth cohorts revealed 9.7% in Akita and Honjo city 16 hospitalizations per 1,000 children and 1.9% and 3.3% of children's from Akita and Honjo respectively resulted in hospitalizations [71]

WHO is working with the Global Reference Laboratory, based at the U.S. Centers for Disease Control and Prevention (CDC), and the Regional Reference Laboratories (RRLs) to launch an EQA programme in 2011.Highest by WHO region: South-East Asia Region (46%), Highest by country: Democratic Republic of the Congo (65%), Highest by age group: 6-11 months old, [72].

Diagnosis

Detection of rotavirus by electron microscopy was found to be more sensitive than by counter immune electrophoresis (C. J. Birch et.al.,) [73]. Latex agglutination was found to be more sensitive compared to ELISA as it detected rotavirus in 48 samples compared to 46 by ELISA (Hani O. Ghazi et.al.,) [74]. Among 170 children of the study group tested rota virus infection was detected among 40 (23.5%) [75]. The increased use of molecular methods for the characterization of

rotavirus strains provides not only increased sensitivity for typing but, also, allows accurate and more-complete characterization of strains, as

well as identification of putative reassortant strains [76]. Of the 586 samples tested, 131 (22.39%) and 468 (79.86%) were positive for coronavirus and group A rotavirus, respectively, using qRT-PCR. The sensitivity and specificity of the commercial ELISA and LAT assays evaluated in this study were low compared with qRT-PCR. The low positive and negative predictive values of the assays suggests that they were of limited diagnostic benefit in the population sampled [77].

Prevalence

In a 12 month survey of infants and children with gastroenteritis admitted to Fairfield Hospital, Melbourne, rotavirus was found in approximately 42% of patients [73]. Infection was documented in 43 to 78% of hospitalized infants between 4 and 6 days of life born at five of the six hospitals [78]. The reported prevalence of rotavirus diarrhea from global surveillance networks and hospital based studies ranges from 6% to 56% in Ghana,Uganda [79]. Rotaviruses was detected in 23.4% of patients with diarrhea who presented to the hospital. The incidence of rota virus diarrhea is highly variable in India being 22% in Vellore (8), 33.3% in Delhi (9) and 66% in Calicut (4) Rota virus diarrhea is known to occur predominantly among male children. This could be due to more exposure, more care for the male child or lack of immunity is not clearly understood. Similarly diarrheal diseases among children are related to low socio-economic status, illiteracy, overcrowding, lack of health consciousness and poor sanitary conditions. Such factors are common in rural areas in India. This might be the reason for rota viral 170 children in SVRR Hospital, Tirupati in 1991 [75]. The complex epidemiological profile of rotaviruses in India highlights the need for a unified protocol for surveillance of circulating strains by Indian laboratories.

In a prospective hospital-based surveillance for rotavirus in 20,780 children hospitalized with diarrhea in three Central Asian countries (Kazakhstan, Uzbekistan, and Kyrgyzstan) during 2005-2009 26% (95% confidence interval (CI) 25-27) were positive for rotavirus antigen by ELISA. On an annual basis, 2.6 per 1000 child-years in Kazakhstan, 2.1 per 1000 child-years in Uzbekistan, and 6.8 per 1000 child-years in Kyrgyzstan [80].

Strain types

Infection with116E like were the most common. In addition a shift in genotype was observed among specimens collected from two of these hospitals during a 2-year period in Delhi in 1994 [74]. The virus genotype G1P[8] was identified in 60% of 190 characterized samples from 2005 to 2006 Kyrgyzstan [81].

23.4% of patients with diarrhea who presented to the hospital were detected for RV during 1996-2001 from 18 Indian cities. G1 being the single most common G type identified in all parts of India, except for western India. Human infections with strains G6, G8, G10, and G9P[19], which may have occured as a result of zoonotic transmission of bovine and porcine rotaviruses, were reported from western, southern, and eastern IndiaEastern india had the highest percentage of G1 strains (41 %). G2 was the single G type most often identified in Northern india (29 %). A peculiar feature of infections with G9 rotavirus strains was noted in eastern India: these strains had 97%–99% homology to G9 strains isolated in Brazil, Malawi, Thailand, and the United States. G8 strains that cause diarrhea in children have been reported from Vellore and Mysore, India. A high incidence of asymptomatic rotavirus infection in neonates G10P[11] strains reported in southern India. Findings indicate that, in Vellore, at least, G10P[11] strains are not exclusive to neonatal or asymptomatic infections.

Three rotaviruses in children <8 months of age were identified as G12 strains by sequencing in Kolkata, India. These rotaviruses had high (i.e., 97%–99%) sequence homology to strains identified in the United States (strain Se585) and Thailand (strain T152) and had 90% sequence homology to strain L26, the G12 prototype [76].

VP7 genotypes G1 and G2 were most commonly isolated although significant heterogeneity of

serotypes was observed. P[11], G9 strains were most frequently isolated among neonates [82].

A novel neonatal strain P type 11 human rotavirus (116 E) was isolated from neonates in Delhi, the VP4 of which was closely related to the bovine serotype G10P[11] strain B223 and VP7 was closely related to the human serotype G9 strain.Another neonatal strain G10P[11] was reported from Bangalore. [83].

6-month period from December 2008 to May 2009 ethiopia study revealed G3P[6] (48%), G1P[8] (27%) and G2P[4] (7%) being the strains most commonly identified. A globally uncommon strain type, G3P[6], predominated within the rotavirus strains detected [84].

Daman, Union territory of India in 2000, GBR infections were detected. A total of 295 cases including 22 hospitalized and 273 visiting OPD of municipal corporation hospital, Muglisara, Surat were recorded. All three specimens were tested positive for GBR in RT-PCR of NSP2 gene carried out by the protocol described earlier and negative for group A rotavirus by antigen capture ELISA (Generic Assay, Germany). A total of 229 patients were reported from primary health centres of the respective villages. Faecal specimens (n=23) and rectal swabs (n=6) collected from a total of 29 (22 from Kalambi and 7 from Khanderajuri) cases who visited public health centres for the medical treatment were examined for identification of viral aetiological agents GBR was detected in 5 (17.2%) (4 faecal and 1 rectal swab) specimens by RT-PCR performed using NSP2 gene specific primers [85].

Among 656 stool samples, 39.5% samples were positive for rotavirus antigen. G2 was identified as the most dominant genotype (45.5%) followed by G1 (24.8%), G12 (9.6%), G9 (8.5%) and G4 (2.1%) genotypes in the Institute of Child and Mother Health, Matuail, Dhaka, Bangladesh during 2006-2007 [86].

Data collected during on the expenditure on Rota viral diarrhea from April 1, 2001 to March 31, 2003 was US $13.3 million and US $10.4 million, respectively. On average, families spent US $294 when their child's admission was associated with rotavirus infection; this cost represents ~40% of the monthly salary of an unskilled or service worker. In conclusion, these data emphasize the potential for a safe and effective rotavirus vaccine to reduce the economic burden associated with rotavirus disease [87]. India spends Rs 2.0–3.4 billion (US$ 41–72 million) annually in medical costs to treat rotavirus diarrhoea [88].

Despite the ARSN's comprehensive data from a mix of developed and developing countries, Asia has lagged the Americas in terms of the introduction of rotavirus vaccines into National Immunization Programmes (NIPs) [89].

The study has evidenced the predominant occurrence of strains with short E-type, SGI and serotype G2 in 66.1% of the samples. The presence of strains representing 10 different E-types and mixed genotype specificities with G2 P[4,8] and G1-G2 P[4,8] [90].

A total of 287 strains were G and P genotyped by reverse transcription-PCR, and some were further characterized by electropherotyping and subgrouping. Of the four strains common globally, three were found in only 43% of samples (P[8], G1, 15%; P[4], G2, 22%; P[8], G4, 6%), whereas G9 strains made up 17% of the total. Of the 253 strains that were fully typed,

54 (21%) had a mixed G or P genotype. Serotype G2 strains were detected more often in infections caused by single strains than in mixed infections ($P < 0.05$), whereas serotype G1 strains were found more often in mixed infections than in infections caused by single strains ($P < 0.05$). [91].

A total of 1106 stool samples collected from diarrhea patients admitted to Dhaka hospital of the International Centre for Diarrhoeal Disease Research, Bangladesh, during January–December 2008 were analysed The group B-specific RNA migration pattern was detected in 26 patients (2.4%) and group A-specific pattern in 259 patients (23.4%).Sequence analyses of VP4, VP7 and NSP2 indicated that an Indian–Bangladeshi lineage of the virus, which is different from both

the prototype (Chinese) lineage and from the animal group B rotaviruses, has been circulating in Bangladesh. Continuous monitoring of group B rotaviruses both in hospitals and in the community will be helpful to determine the true burden of group B rotaviruses [92].

Faecal specimens collected from 2101 patients with acute gastroenteritis from three cities (Pune, Alappuzha, Belgaum) in India during 1994–1995 and 2004–2010 were tested for group B rotavirus (RVB) by amplification of the NSP2 gene using RT–PCR. Seventy-five (3.6%) specimens were shown to contain RVB RNA. The positivity rate in Pune, Alappuzha and Belgaum was 4.1%, 7.3% and 4.1%, respectively, The study confirmed the occurrence of RVB infections in western India and reported for the first time circulation of RVB strains in southern India, suggesting that an increased awareness and monitoring for RVB infections is necessary in India [93].

Vaccines

Cost-effectiveness was analyzed from the perspectives of the health care system and society. At US$80 per dose for the Rotarix vaccine, the program would cost US$32.7 million, provided an increasing cost offset of US$19.8 million to the health care system with $135 per case averted. Despite a higher burden of serious rotavirus disease than estimated previously, routine rotavirus vaccination would unlikely be cost-saving in Taiwan at present unless the price fell to US$41 (Rotarix) or US$29 (RotaTeq) per dose from societal perspective, respectively [94].

Democratic Republic of the Congo, Ethiopia, India, Nigeria, and Pakistan; India alone accounted for 22% of deaths (98 621 deaths). Introduction of effective and available rotavirus vaccines could substantially affect worldwide deaths attributable to diarrhea [95].

Health impact and the costs of treatment associated with rotavirus diarrhea in six yearly cohorts (2001–2006) of Mexican infants. Estimates of DALYS were 19,426 in 2001 and decreased by 28.9% for 2006 meanwhile costs of treatment were relatively constant, estimated at US$ 38.7 million and increased only by 5% [96].

Rotarix is a human, live attenuated rotavirus vaccine containing a rotavirus strain of G1P [8] specificity. ROTARIX is indicated for the prevention of rotavirus gastroenteritis caused by G1 and non-G1 types (G3, G4, and G9) when administered as a 2-dose series in infants and children [97].

In March 2010 FDA officials urged pediatricians to temporarily stop using GlaxoSmithKline's Rotarix because they found it contaminated with fragments of DNA from porcine circovirus-1. Although this contamination was thought to be benign, vaccines are supposed to be sterile. In May 2010 the suspension of the vaccine was lifted [98].

RotaTeq is a live, oral pentavalent vaccine that contains five rotaviruses produced by reassortment. The rotavirus A parent strains of the reassortants were isolated from human and bovine hosts. Four reassortant rotaviruses express one of the outer capsid, VP7, proteins (serotypes G1, G2, G3, or G4) from the human rotavirus parent strain and the attachment protein VP4 (type P7) from the bovine rotavirus parent strain. The fifth reassortant virus expresses the attachment protein VP4, (type P1A), from the human rotavirus parent strain and the outer capsid protein VP7 (serotype G6) from the bovine rotavirus parent strain. In February 2006, the U.S. Food and Drug Administration approved RotaTeq for use in the United States. In August 2006, Health Canada approved RotaTeq for use in Canada [99].

Merck is working with a range of partners including governmental and non-governmental organizations to develop and implement mechanisms for providing access to this vaccine in the developing World [100].

Vaccine has been developed in India using the strains isolated from the country. The strain used was 116E which was isolated from Delhi. The vaccine has successfully passed the clinical trials and is in the process of getting approved by the

Drug Control for use in the public. Once this is released there will be an economical alternative for the current Rota viral vaccines in India.

Effectiveness

A 2009 review estimated that vaccination against rotavirus would prevent about 45% of deaths due to rotavirus gastroenteritis, or about 228,000 deaths annually worldwide. At $5 per dose the estimated cost per life saved was $3,015, $9,951 and $11,296 in low-, lower-middle-, and upper-middle-income countries, respectively [101].

Safety and efficacy trials of Rotarix and RotaTeq in Africa and Asia found that the vaccines dramatically reduced severe disease among infants in developing countries, where a majority of rotavirus-related deaths ocur [102]

A 2012 Cochrane review of 41 clinical trials that included 186,263 participants concluded Rotarix and RotaTeq are effective vaccines [103].

Additional rotavirus vaccines are under development [104].

Rotavirus vaccines are licensed in more than 100 countries, but only 31 (World Health Organization)105 countries have introduced routine rotavirus vaccination as of 2011 [106].

The incidence and severity of rotavirus infections has declined significantly in countries thathave acted on the recommendation to introduce the rotavirus vaccine [107].

In Mexico, which in 2006 was among the first countries in the world to introduce rotavirus vaccine, the diarrheal disease death rates from rotavirus dropped by more than 65% among children age two and under during the 2009 rotavirus season [108].

In Nicaragua, which in 2006 became the first developing country to introduce the rotavirus vaccine, investigators recorded a substantial impact, with rotavirus vaccine preventing 60% of cases against severe rotavirus and cutting emergency room visits in half [109].

In the United States, vaccination has reduced rotavirus-related hospitalizations by as much as 86% since 2006. The vaccines may also prevent illness in non-vaccinated children by limiting exposure through the number of circulating infections [110].

In September 2013, the vaccine will be offered to all children in the UK, aged between two and three months, and it is expected to halve the cases of severe infection and reduce the number of children admitted to hospital because of the infection by 70 percent [111].

Conclusion

Molecular diagnostic methods offer highly sensitive detection and also enable the genotyping of viruses, therefore they are the methods of choice for diagnosis of rotaviral infections. Zoonotic transmission are likely to be relatively common events in India. Other than G5 strains, all G types that have been reported in

association with infections in humans are now found in India. The complex epidemiological profile of rotaviruses in India highlights the need for a unified protocol for surveillance of circulating strains by Indian laboratories. Another important aspect is that vaccines in India should also target G9 strains. Longitudinal surveillance of GBR in paediatric and adult cases of gastroenteritis would help determine their contribution to overall disease burden of diarrhoea in India. Vaccination for rota viruses should be taken seriously as it will reduce the incidence and also save on the medical costs.

Similarly diarrheal diseases among children are related to low socio-economic status, illiteracy, overcrowding, lack of health consciousness and poor sanitary conditions. Henceforth health campaign by approved authorities could help reduce the life threatening rotaviral infection thus saving lot of paediatric populations in India.

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