

Burden of Rotavirus Diarrhea in Under-five Indian Children

ASHOK KUMAR, SRIPARNA BASU, *VIPIN VASHISHTHA AND *PANNA CHOUDHURY

From the Department of Pediatrics, Institute of Medical Sciences, Banaras Hindu University, Varanasi, India and *Indian Academy of Pediatrics, Kailash Darshan, Kennedy Bridge, Mumbai, India. †Deceased.

Correspondence to: Professor Ashok Kumar, Department of Pediatrics, Institute of Medical Sciences, Banaras Hindu University, Varanasi 221 005, India. ashokkumar_bhu@hotmail.com

Need and purpose: Rotavirus is the most common cause of severe diarrhea in infants and young children worldwide. The burden of rotavirus diarrhea in Indian children is not well established. The present study reviewed the epidemiology of rotavirus diarrhea in hospitalized children and in the community, molecular serotyping and under-five mortality caused by rotavirus diarrhea. **Methods:** Publications, reporting rotavirus diarrhea in Indian children, were retrieved through a systematic search of databases including Medline, PubMed, IndMed, websites of WHO, UNICEF, National Family Health Survey, Ministry of Health and Family Welfare, and Government of India. 'Human' studies in 'English' language were included. Age group selected was 0 month to 5 years. No restrictions were applied in terms of study design and time frame. **Conclusions:** Stool sample positivity varied from 4.6% in Kolkata to 89.8% in Manipur, among hospitalized children, and from 4% in Delhi to 33.7% in Manipur in community. Most cases of rotavirus diarrhea in India are caused by G1, G2, and G untypeable strains with distinct regional variations. Rotavirus was identified as an etiological agent in 5.2 to 80.5% cases of nosocomial diarrhea. Data are lacking for rotavirus mortality.

Keywords: Burden, Community, Epidemiology, Gastroenteritis, Incidence, Prevalence, Systematic review.

Rotavirus is the most common cause of severe diarrhea in infants and young children worldwide. It is estimated to be responsible for 611,000 annual childhood deaths globally [1], and another 2 million hospitalizations every year [2]. More than 80% of these deaths occur in low-income countries [1-3]. It is estimated that India spends approximately Rs. 2.0-3.4 billion (US\$ 41-72 million) [4] annually for the treatment of rotavirus diarrhea in children <5 years of age.

Rotaviruses are double stranded RNA viruses within the family Reoviridae. The primary mode of transmission is via the fecal-oral route with symptoms typically developing after an incubation period of one to two days. Majority of children become infected with rotavirus within the first three years of life, with a peak incidence of rotavirus diarrhea between 6 to 24 months [5]. Previous infection offers protection from subsequent illnesses. However, re-infections are frequent but subsequent illnesses tend to be less severe [6].

Laboratory procedures for diagnosis of rotavirus include electron microscopy (EM), passive latex agglutination assays (LA), electrophoretotyping using polyacrylamide gel electrophoresis (PAGE), enzyme-linked immunosorbent assays (ELISA) and reverse transcription-polymerase chain reaction (RT-PCR) [7]. ELISA is the method of choice for routine screening. For genotyping, newer methods like multiplex RT-PCR based

genotyping, hybridization assays and nucleotide sequencing are used. Rotaviruses are classified into seven different groups (A-G), of which groups A, B and C are known to infect humans. Severe, life-threatening disease in children worldwide is caused predominantly by group A rotaviruses. Rotavirus strains are further subtyped based on the proteins of the outer capsid eliciting neutralizing antibodies, VP7 (G serotypes) and VP4 (P serotypes). Till date, at least 15 G genotypes and 25 P genotypes have been identified [8].

Considering the high burden of the disease, there is a need to summarize and critically evaluate all available information related to rotavirus diarrhea in India. The present review was done to estimate the burden of rotavirus diarrhea in under-five Indian children in the community and hospital settings.

METHODS

The primary research question was 'epidemiology of rotavirus diarrhea in under-five children of India' which was further subcategorized into (i) epidemiology of rotavirus diarrhea in hospitalized children from different parts of India; (ii) epidemiology of rotavirus diarrhea in community from different parts of India; (iii) demographic profile of rotavirus diarrhea (iv) identification of molecular epidemiology of rotavirus diarrhea from different parts of India; (v) incidence of rotavirus infection as a cause of nosocomial diarrhea; and (vi) mortality from rotavirus diarrhea.

The primary databases searched were Medline through PubMed (www.pubmed.com) and IndMed (<http://indmed.nic.in/>). Other sources included online reports from the websites of World Health Organization (WHO) (www.who.int), documents of the UNICEF (www.unicef.org/india/), National Family Health Survey (<http://www.nfhsindia.org/>), and documents of the Ministry of Health and Family Welfare, Government of India (www.mohfw.nic.in). The related articles and the reference lists of included publications were also searched to identify additional studies.

All types of publications available in scientific public domain and reporting on rotavirus infection in India were included. No particular time frame was set. Our search was limited to ‘humans’, children (0 month to 5 years) and articles published in ‘English’ language. For searching PubMed, we followed a standard search methodology [9]. A search string was devised by converting each research question into problem, intervention, comparison, outcome (PICO) format. MeSH headings were looked for the research theme in question and added to the PubMed search builder. Salient keywords were included during search. A search for MeSH headings for ‘rotavirus’, revealed ‘rotavirus, infections’, which was relevant and yielded 31 subheadings from which we selected ‘rotavirus diarrhea’, ‘rotavirus gastroenteritis’, and ‘rotavirus disease’. For assessing the epidemiology of rotavirus diarrhea in India, we searched PubMed using the search string: “(epidemiology* OR burden OR morbidity OR mortality or incidence OR prevalence OR profile) AND (rotavirus OR rotavirus diarrhea OR rotavirus gastroenteritis OR rotavirus disease) AND India. For the subcategories, an additional search was made by combining keywords/MeSH terms using the search string “(*) AND (rotavirus, infections) AND India”, where the asterisk represented the MeSH term/keywords for the subcategories. To search IndMed, the search string was kept simple using search keywords. The search date, search terms, search string and search output were recorded and saved. In the next step, we scrutinized all titles and excluded the titles which were not relevant; the remaining articles were studied further. The next step involved examination of the abstract or the introduction (where the abstract was not published) of the short-listed titles; the ones which were not found relevant were excluded and the remaining articles were processed further. In the next step examination of full-text articles was done. Related articles and cross-references in identified articles were also reviewed and similar steps were performed before short listing the cross-references.

RESULTS

Initial search in PubMed (initially accessed on 19th

August 2013 and updated on 1st March 2014) using ‘rotavirus’ yielded 4173 articles. While searching, filters activated were: Humans, English, Newborn: 0-1 month, Infant: 1-23 months, Preschool Child: 2-5 years. Search with ‘rotavirus diarrhea’ yielded 2241 articles and search with ‘rotavirus gastroenteritis’ yielded 2013 articles. Details of search strings and yield of articles have been summarized in **Web Table I**.

Burden of Rotavirus Diarrhea in Hospitalized Children

A total of 54 studies [8,10-62], carried out using samples obtained from under-five Indian children hospitalized with rotavirus diarrhea were included (**Table I**). There was large variability in sample size ranging from 39 [33] to 3064 [31]. Maximum number of studies (19) was carried in Northern India. The range of stool positivity for rotavirus was widely distributed, varying from 4.6% in Kolkata [38] to 89.8% in Manipur [35]. Most of the studies used ELISA/PAGE for the screening of rotavirus although latex agglutination assay, immunoblot and electron microscopy were also used in a limited number of studies.

Kelkar, *et al.* [33] investigated an epidemic of diarrhea in Jawhar, a tribal area of Thane district, Maharashtra. Within a period of approximately 2 months, 490 cases of acute diarrhea were reported among children under-five years of age, with a case fatality rate of 0.40%. Twenty-seven out of 39 (69.2%) rectal swabs/fecal specimens obtained from hospitalized children up to 2 years of age were positive by ELISA for rotavirus.

Burden of Rotavirus Diarrhea in the Community

A total of 16 studies [3,10,54,63-75], carried out using samples obtained from under-five Indian children in community with rotavirus diarrhea were included (**Table II**). Stool sample positivity varied from 4% in Delhi [64] to 33.7% in Manipur [73].

Demographic profile of Rotavirus Diarrhea

Demographic profile of rotavirus diarrhea has been summarized in **Table III**. A total of 27 studies [10,11,13,18,24,31,33-37,44,47,48,50-55,61,64-70] could be identified which described signs and symptoms of rotavirus diarrhea both in hospitalized children and in children from the community. Rotavirus infection is most common below 2 years of age, 7-12 months being the most commonly affected age group. Maximum infection occurs in winter months, from October-February.

Rotavirus Serotypes

A total of 50 studies [3,19,22,23,25-30,32,40,41,44-48,76-95] could be identified which dealt with serotyping

TABLE I ROTAVIRUS POSITIVITY IN CHILDREN HOSPITALIZED WITH DIARRHEA FROM DIFFERENT PARTS OF INDIA

<i>Reference</i>	<i>Place of study</i>	<i>Study period (year)</i>	<i>Age group (year)</i>	<i>Detection method</i>	<i>Stool samples collected</i>	<i>Positive, n (%)</i>
<i>Northern India</i>						
Samantaray, <i>et al.</i> [10]	Delhi	1980-1981	<5	ELISA	99	32 (32.3)
Broor, <i>et al.</i> [11]	Chandigarh	1982-1983	<5	ELISA	242	44 (18.2)
Singh, <i>et al.</i> [12]	Chandigarh	1982 - 1985	<5	ELISA	694	111 (15.9)
Ram, <i>et al.</i> [13]	Chandigarh	1984-1987	<3	ELISA	1024	120 (11.72)
Aggarwal, <i>et al.</i> [14]	Delhi	1985	<5	ELISA	256	19(7.4)
Chakravarthi, <i>et al.</i> [15]	Delhi	1987 - 1989	<5	ELISA	978	176 (18.0)
Chakravarti, <i>et al.</i> [16]	Delhi	1987 - 1988	<5	ELISA	288	44 (15.3)
Broor, <i>et al.</i> [17]	Delhi	1988 - 1990	<5	ELISA	990	104 (10.5)
Patwari, <i>et al.</i> [18]	Delhi	1989 - 1990	<3	Immunodot	400	23 (6.0)
Chatterjee, <i>et al.</i> [8]	Delhi	1990	<5	ELISA	157	71 (45.0)
Husain, <i>et al.</i> [19]	Delhi	1990 - 1991	<5	ELISA/PAGE	450	60 (13.3)
Sharma, <i>et al.</i> [20]	Northern India	Not mentioned	Not mentioned	ELISA	172	32 (19.0)
Chakravarti, <i>et al.</i> [21]	Delhi	1998 - 2000	<5	ELISA/PAGE	1172	158 (13.5)
Chakravarti, <i>et al.</i> [22]	Delhi	1998 - 2000	<3	ELISA/PAGE	560	100 (17.8)
Bahl, <i>et al.</i> [23]	Delhi	2000 - 2001	<5	ELISA	584	137 (23.5)
Nag, <i>et al.</i> [24]	Lucknow	2003-2004	<2	ELISA/PAGE	90	14(15.6)
Chakravarti, <i>et al.</i> [25]	Delhi	2005 - 2007	<2	ELISA	862	318(36.9)
Mishra, <i>et al.</i> [26]	Lucknow	2004 - 2008	<3	ELISA	412	79 (19.2)
Gazal, <i>et al.</i> [27]	Jammu & Kashmir	Not mentioned	<5	PAGE	210	88 (41.9)
<i>Western India</i>						
Desai, <i>et al.</i> [28]	Mumbai	1984 - 1986	Not mentioned	LA /EM / ELISA	273	63 (21.0)
Kelkar, <i>et al.</i> [29]	Pune	1990 - 1993	Not mentioned	ELISA	722	188 (26.0)
Kelkar, <i>et al.</i> [30]	Pune	1992 - 1996	<5	ELISA	945	266 (28.2)
Kelkar, <i>et al.</i> [31]	Pune	1990-1997	<5	ELISA	3064	432 (14.1)
Kelkar, <i>et al.</i> [32]	Pune	1993-1996	<5	ELISA	628	177 (28.3)
Kelkar, <i>et al.</i> [33]	Thane	2000-2001	<5	ELISA	39	27 (69.2)
Borade, <i>et al.</i> [34]	Pune	2009-2010 (?)	<5	ELISA	246	88 (35.8)
<i>Eastern India</i>						
Sengupta, <i>et al.</i> [35]	Manipur	1979	Not mentioned	ELISA	59	53 (89.8)
Saha, <i>et al.</i> [36]	Kolkata	1979-1981	<12	ELISA	245	55 (22.4)
Sen, <i>et al.</i> [37]	Kolkata	1979-1981	Not mentioned	ELISA	356	27 (7.6)
Ghosh, <i>et al.</i> [38]	Kolkata	1986-1988	<6 months	ELISA	218	10 (4.6)
Phukan, <i>et al.</i> [39]	Dibrugarh	1999 - 2000	<5	ELISA	202	47 (23.3)
Samajdar, <i>et al.</i> [40]	Kolkata & Berhampur	2003-2005	<4	ELISA	545	198 (36.3)
Samajdar, <i>et al.</i> [41]	Kolkata	2005 - 2006	<4	ELISA	668	249 (37.3)
Nair, <i>et al.</i> [42]	Kolkata	2007-2009	<5	Not mentioned	648	312 (48.1)
Mukherjee, <i>et al.</i> [43]	Manipur	2005 - 2008	<5	ELISA	489	244 (49.9)
<i>Southern India</i>						
Paniker, <i>et al.</i> [44]	Calicut	1976-1978	<5	EM	3355	368 (70.7)
Mathew, <i>et al.</i> [45]	Kerala	Not mentioned	<5	ELISA	1827	648 (35.9)

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Reference	Place of study	Study period (year)	Age group (year)	Detection method	Stool samples collected	Positive, n (%)
Aijaz, <i>et al.</i> [46]	Bangalore	1988 - 1994	Not mentioned	PAGE	694	150 (21.6)
Aijaz, <i>et al.</i> [46]	Mysore	1993 - 1994	Not mentioned	PAGE	447	50 (11.2)
Ananthan, <i>et al.</i> [47]	Chennai	1997 - 1999	0 - 2, >2	ELISA	245	51 (20.8)
Saravanan, <i>et al.</i> [48]	Chennai	1995 - 1999	<3	ELISA/PAGE	745	168 (22.6)
Anand, <i>et al.</i> [49]	Hyderabad	1998 - 1999	<2	PAGE	352	57 (16.2)
Shetty, <i>et al.</i> [50]	Karnataka	Not mentioned	<5	LA	106	19 (18)
Ballal, <i>et al.</i> [51]	Karnataka	1995-2000	<5	LA	780	40 (19.9)
Anand, <i>et al.</i> [52]	Tirupati	1991	<2	ELISA	170	40 (23.5)
Kang, <i>et al.</i> [53]	Vellore	1995 - 1998	<5	ELISA / LA	602	126 (20.9)
Banerjee, <i>et al.</i> [54]	Vellore	2002 - 2004	<5	ELISA/LA	343	94 (27.1)
Sowmyanarayanan, <i>et al.</i> [55]	Vellore	2005-2008	<5	EIA/PCR	1001	354 (35.4)
<i>Multiple locations</i>						
Ramachandran, <i>et al.</i> [56]	Multiple 1	1993	6 mo to <5 yr	ELISA	458	63 (13.7)
Jain, <i>et al.</i> [57]	Multiple 2	1996 - 1998	<5	ELISA	1502	313 (20.8)
Kang, <i>et al.</i> [58]	Multiple 3	1998 - 1999	<5	LA /EM/ ELISA	365	82 (22.5)
Das, <i>et al.</i> [59]	Multiple 4 ^a	1998 - 2000	<4	PAGE	406	141 (34.7)
Das, <i>et al.</i> [60]	Multiple 5	2001	<4/all ^b	PAGE	454	161 (35.4)
Kang, <i>et al.</i> [61]	Multiple 6	2005 - 2007	<5	RT-PCR	4243	1405 (39.2)
Kang, <i>et al.</i> [62]	Multiple 7	2005 - 2009	<5	RT-PCR	7285	2899 (40)

LA, latex agglutination; EM, electron microscopy; PAGE, polyacrylamide gel electrophoresis; ELISA, enzyme linked immunosorbent assay; Multiple 1: Shimla, Lucknow, Bhopal, Nagpur, Davengere; Multiple 2: Shimla, Lucknow, Bhopal, Nagpur, Davengere, Delhi, Hyderabad; Multiple 3: Vellore, Mysore, Jalandhar, Yamunagar; Multiple 4: Kolkata, Imphal, ^aData on disease burden from Kolkata only; Multiple 5: Kolkata, Dibrugarh, Bhuvaneshwar, Chandigarh; ^b<4/all: Samples collected from two groups: children <4 yr, patients of all age groups.

of rotavirus, of which G and P typing were done in 44 studies. Details of studies have been summarized in **Web Tables II, III and IV**.

Overall, G1 was the most common serotype isolated in Indian studies, followed by G2 and G-untypable. On regional distribution, in Northern India, G1 was the most common serotype isolated, followed by G2, G-untypable and G9. In Western India, G2 was predominant, closely followed by G-untypable and G1. In Eastern India, G1 was commonest followed by G2. In Southern India, G1 was predominant, followed by G2 and G-untypable. In P serotyping, P[4] was most prevalent all over India, followed by P[6] and P Untypable/others. In Northern India, P[6] was most common, followed by P[4].

In the study of Kelkar, *et al.* [95], about 10% of stool specimen showed multireactivity in enzyme immunoassay with monoclonal antibodies specific for serotypes G1-4, 6, 8, and 10. The isolates were more close to G6 RF strain, which is a bovine rotavirus and is the first report of isolation of bovine serotype, G6 from India. Tran, *et al.* [96]

provided evidence for the formation of the G3P[4] strain through genetic reassortment in which a G2P[4] strain with a typical DS-1 genogroup background acquired the VP7 gene from a co-circulating G3 human rotavirus strain.

Nosocomial Rotavirus Infections

Five studies were identified which dealt with nosocomial rotavirus infection, one in Delhi [97], two studies in Kolkata [98,99], and two in Vellore [100,101]. Details of the studies have been discussed in **Table IV**. Stool positivity for Rotavirus varied from 5.2% in Vellore [101] to 80.5% in Kolkata [98].

Rotavirus Diarrhea in Neonates

In hospitalized neonates, the prevalence of neonatal infection varies from 22-73% in India [102-106], though the infection remains asymptomatic in 69-95% [102,105-107]. Viral excretion begins as early as 2 days of age, peaking around 3-6 days and resolves by 2 weeks. The chance of acquiring an infection is inversely proportional to the length of hospital stay [102,105,107]. In two

TABLE II BURDEN OF ROTAVIRUS DIARRHEA IN THE COMMUNITY FROM DIFFERENT PARTS OF INDIA

Reference	Place of study	Community	Study period	Age (y)	Detection method	Diarrhea	Sample size (n)	Positive, n (%)
<i>Northern India</i>								
Samantaray, <i>et al</i> [10]	Delhi	Semi urban	1980-1981	<5	ELISA	Yes No	212 82	45 (21.2) 2 (2.4)
Panigrahi, <i>et al</i> [66]	Northern India	Urban/rural	1982 - 1983	<5	ELISA	Yes No	105 350	44 (29.3) 43 (12.3)
Malik, <i>et al</i> [67]	Aligarh	Semi urban	1982-1983	<5	ELISA	Yes No	216 216	40 (18.5) 1 (0.05)
Bhan, <i>et al</i> [63]	Delhi	Semi urban	1985-1986	<5	ELISA	Yes No	204 98	42 (20.6) 2 (2.0)
Raj, <i>et al</i> [64]	Delhi	Semi urban	1985-1986	<3	ELISA	Yes No	346 211	14 (4.0) 14 (6.6)
Bhan, <i>et al</i> [65]	Delhi	Urban/rural	1985	<5	ELISA	Urban Yes No Rural Yes No	Urban 330 319 Rural 340 315	6 (1.9) 50 (15.2) 6 (1.9) 56 (16.5) 9 (2.9)
Yachha, <i>et al</i> [68]	Chandigarh	Urban/ peri-urban/ rural	1988 - 1991	<5	ELISA	Yes	218	25 (11.5) rural-14 periurban-7; urban -4
Nath, <i>et al</i> [69]	Varanasi	Urban	1988 - 1989	<5	LA	Yes No	376 299	67 (17.7) 12 (4)
Nath, <i>et al</i> [70]	Varanasi	Urban	1988 - 1989	<5	LA	Yes	607	100 (16.4)
<i>Western India</i>								
Desai, <i>et al</i> [71]	Mumbai	Urban	1984-1986	<5	EM/LA /ELISA	Yes No	273 273	63 (23) 3 (1.1)
Kelkar, <i>et al</i> [72]	Pune		1993 - 1996	<5	ELISA	Yes	489	76 (15.5)
<i>Eastern India</i>								
Krishnan, <i>et al</i> [73]	Manipur	Urban/Semi urban	1989-1992	<5	ELISA	Yes No	787 457	265 (33.7) 22 (4.8)
<i>Southern India</i>								
Maiya, <i>et al</i> [74]	Vellore*	Urban	1974-1975	<2	EM	Yes No	50 30	13 (26) 0 (0)
Mathew, <i>et al</i> [75]	Vellore	Urban, periurban, rural	1983-1985	<3	EM	Yes No	916 587	95 (10.4) 5 (0.9)
Banerjee, <i>et al</i> [54]	Vellore	Urban	2002 - 2004	<5	ELISA	Yes	1152	82 (7.1)
Gladstone, <i>et al</i> . [3]	Vellore	Urban	2002 - 2004	<5	ELISA/ PCR	Yes	1103	535 (48.5)

*Both hospital and community; NK, not known; EM, electron microscopy; LA, latex agglutination; ELISA, enzyme linked immunosorbent assay.

reports, neonatal infections are found to confer protection against future rotavirus diarrhea. Bhan, *et al.* [105] reported 46% fewer episodes of rotavirus diarrhea and 22% fewer episodes of all-cause diarrhea in the first year of life following neonatal rotavirus infections, whereas

Vethanayagam, *et al.* [104] documented 37% less chance of infection after neonatal rotavirus diarrhea. However, a larger study from Vellore [106] did not find any association between neonatal infection and subsequent rotavirus diarrhea.

TABLE III DEMOGRAPHIC PROFILE OF ROTAVIRUS DIARRHEA

<i>Reference</i>	<i>Study location</i>	<i>Place of study</i>	<i>Peak age incidence (%)</i>	<i>Gender affected</i>	<i>Peak season</i>
Samantaray, <i>et al.</i> [10]	Delhi	Hospital	0-6 mo	M:F=26:19	October - June
Broor, <i>et al.</i> [11]	Chandigarh	Hospital	7-12 mo	Not mentioned	Not mentioned
Ram, <i>et al.</i> [13]	Chandigarh	Hospital	10-12 mo	M:F=3:1	November
Patwari, <i>et al.</i> [18]	Delhi	Hospital	7-12 mo	M:F=256:144	February-April
Yachha, <i>et al.</i> [68]	Chandigarh	Community	6-11 mo	Not mentioned	November-February
Panigrahi, <i>et al.</i> [66]	North India	Community	37-60 mo	Not mentioned	April-June
Malik, <i>et al.</i> [67]	Aligarh	Community	<1 yr	M=F	January-March
Bhan, <i>et al.</i> .[65]	Delhi	Community	0-6 mo	Not mentioned	Not mentioned
Raj, <i>et al.</i> [64]	Delhi	Community	13-24 mo	Not mentioned	October - December
Nag, <i>et al.</i> [24]	Lucknow	Hospital	6-12 mo	M:F=2.5:1	Not mentioned
Nath, <i>et al.</i> [69]	Varanasi	Community	<2 yr	F>M	November - February
Kelkar, <i>et al.</i> [31]	Pune	Hospital	6-12 mo (64.7)	M>F	Winter
Borade, <i>et al.</i> [34]	Pune	Hospital	11-20 mo	M=F	December - January
Kelkar, <i>et al.</i> [33]	Thane	Hospital	6-12 mo	M>F	Not mentioned
Saha, <i>et al.</i> [36]	Kolkata	Hospital	6-12 mo	M=F	January
Sen, <i>et al.</i> [37]	Kolkata	Hospital	<2 yr (25)	Not mentioned	Not mentioned
Sengupta, <i>et al.</i> [35]	Manipur	Hospital	Not mentioned	M:F=1.9:1	November
Ananthan, <i>et al.</i> [47]	Chennai	Hospital	7-12 mo (28.7)	Not mentioned	Not mentioned
Saravanan, <i>et al.</i> [48]	Chennai	Hospital	7-12 mo (62.5)	M:F=93:75	Sept-Feb
Shetty, <i>et al.</i> [50]	Karnataka	Hospital	<2 yr-59(56)	Not mentioned	Winter (Dec-Feb)
Ballal, <i>et al.</i> [51]	Karnataka	Hospital	7-12 (65)	Not mentioned	Not mentioned
Anand, <i>et al.</i> [52]	Tirupati	Hospital	7-12 mo	M>F	Not mentioned
Kang, <i>et al.</i> [53]	Vellore	Hospital	Mean age 19.5 mo	Not mentioned	Not mentioned
Banerjee, <i>et al.</i> [54]	Vellore	Hospital	Not mentioned	Not mentioned	December-January
Sowmyanarayanan, <i>et al.</i> [55]	Vellore	Hospital	6-12 mo	M:F=75:51	January-February
Paniker, <i>et al.</i> [44]	Calicut	Hospital	6-23 mo	M=F	November -January
Kang, <i>et al.</i> [61]	Multiple locations	Hospital	Mean age 12.9±9.0mo	M>F	Not mentioned

Strains responsible for neonatal infections included G9P[11], G10P[11], and G12P[6] in most studies [102-104,108,109]. Some of these strains were found to have genetic homology with non-human rotavirus, suggesting a role of human and animal reassortant viruses in neonatal infections [40,102,104,108].

Rotavirus Mortality

As per current global estimate, worldwide, each year, rotavirus related diarrhea results in 453 000 deaths (95% CI 420 000,494 000) in children younger than 5 years, accounting for 37% of diarrhea-related deaths and 5% of all deaths in this age group. The greatest proportion of these deaths is estimated to be contributed by India (98621, 22%) [110]. Child Health Epidemiology

Reference Group of WHO and UNICEF documented an overall decline in the mortality of under-five children by only 14%, from 527,000 in 2004 to 453,000 in 2008 [111,112].

DISCUSSION

In this review, we have examined the epidemiology of rotavirus diarrhea in under-five children of India both in hospitalized children and in children from the community. Overall, stool positivity for rotavirus was higher in hospitalized children than in community. Highest percentage of stool positivity was reported from North-Eastern India, both in hospital and community setting. This shows greater geographical burden of rotavirus diarrhea in this part of India.

TABLE IV NOSOCOMIAL ROTAVIRUS INFECTIONS

<i>Reference</i>	<i>Place of study</i>	<i>Study period (year)</i>	<i>Age group (years)</i>	<i>No. of hospitalized children (n)</i>	<i>Nosocomial diarrhea (n)</i>	<i>Rotavirus positive, n(%)</i>
Uppal, <i>et al.</i> [97]	Delhi	Not mentioned	Children	75	30	5 (16.7)
Dutta, <i>et al.</i> [98]	Kolkata	1985 - 1986	<12	189	36	29 (80.5)
Dutta, <i>et al.</i> [99]	Kolkata	1987	<5	3138	320	15 (8.4)
Desikan, <i>et al.</i> [100]	Vellore	1990 - 1991	<3	194	39	13 (6.7)
Kamalaratnam, <i>et al.</i> [101]	Vellore	1990 - 1991	<3	214	41	13 (5.2)

In the present review, the average incidence of stool positivity for rotavirus in hospitalized children with diarrhea is found to be higher than previous ones. Earlier, Jain, *et al.* [89] reviewed the epidemiology of rotavirus in India from 30 studies conducted between 1976 and 1997 from a total patient population of 12,164 children. Rotavirus was detected in 15-23% of patients hospitalized for severe diarrhea. In a later report, the proportion of diarrhea hospitalizations attributable to rotavirus appeared to have increased between 2000 and 2004, from 22% (range 17%-28%) to 39% (range 29%-45%) [113]. In the review of Ramani, *et al.* [114], a total of 29 studies carried out using samples obtained from 22 Indian cities in hospitalized children with diarrhea. A total of 15,476 samples were tested. Rates of rotavirus positivity ranged from 6-45%. The possible reasons could be either true increase in the incidence of rotavirus diarrhea compared to other etiological agents or an increase in the awareness of parents seeking early hospitalization. It can also be secondary to better diagnostic facilities in health care set ups. The authors explained this phenomenon by a relatively slower rate of decrease in hospitalizations for rotavirus compared with other causes of severe childhood diarrhea.

Two studies from Delhi reported 0-6 months as the most common age group [13,63]. On the other hand, Panigrahi, *et al.* [66], from Northern India reported a higher age group of 37-60 months. Some studies in India have found no association between rotavirus infection and time of year [8,18], though most have observed an increase in rotavirus-associated diarrhea during the winter months, October to February. Jain, *et al.* [89] found that rotavirus was most prevalent (31%) in children between 7 and 12 months of age, followed by children between the ages of 1 to 2 years (20%), and children <7 months of age (13%).

G1 was the most commonly isolated serotype in Indian studies, followed by G2 and G-untypeable. On regional distribution, in northern India, G1 was the most common serotype isolated, followed by G2, G-untypeable and G9. In Western India, G2 was predominant, closely followed by G-untypeable and G1. In Eastern India, G1 was

detected most commonly, followed by G2. In Southern India, G1 was predominant, followed by G2 and G-untypeable. Children infected with G1 strains had a greater risk of developing more-severe cases of diarrhea than did children infected with other rotavirus strains [23].

In P serotyping, P[6] was most common in northern India, followed by P[4]. In western and eastern India, prevalence of P[4] was higher than other P serotypes. In southern India, untypeable P type was most commonly documented, closely followed by P[8]. P[4] was documented in lesser number of children. Several studies have also reported different G-P combinations [19,21,26,40,78]. Presence of nontypeable strains also posed a significant diagnostic challenge [29]. Emergence of G9 and G12 as important strains of rotavirus has been reported by several authors [40,43,57,59].

Very few studies examined the impact of rotavirus diarrhea in under-five mortality in India. Most of the data of rotavirus mortality are not direct; only estimated figures have been projected. World Health Organization estimates that globally 453000 (420 000 - 494 000) child deaths occurred during 2008 due to rotavirus infection [115].

The major limitation of this review was that we did not evaluate the quality of included studies, and a formal meta-analysis was not carried out. Moreover, studies had marked heterogeneity in terms of selection of patients/samples, method of diagnosis for rotavirus positivity, and molecular characterization. Moreover, some other studies may have been published since the last date of search of this review.

In conclusion, rotavirus diarrhea is a significant health problem in under-five children of India both in hospital and community setting. The prevalence of infection is not uniform, varying widely from region-to-region and state-to-state. Most of the studies are confined to few places, and sample size differed widely in individual studies. Different methodologies are employed for virus detection in different studies. Moreover, there is lack of data from many geographical locations, especially Central India, where the burden of diarrheal disease is particularly heavy.

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WEB TABLE I RESULTS OF LITERATURE SEARCH

Q. No.	Research Question	Search engine	Total	After title screening	After abstract screening	After reading full text	From cross reference	Additional search	Finally included
1	Epidemiology of rotavirus diarrhea in under-5 hospitalized children from different parts of India	(epidemiology* OR burden OR morbidity OR mortality or incidence OR prevalence OR profile OR hospital) AND (rotavirus OR rotavirus diarrhea OR rotavirus gastroenteritis OR rotavirus disease) AND India	171	97	87	48	4	0	54
2	Epidemiology of rotavirus diarrhea in under-5 children in community from different parts of India	(epidemiology* OR burden OR morbidity OR mortality or incidence OR prevalence OR profile OR community) AND (rotavirus OR rotavirus diarrhea OR rotavirus gastroenteritis OR rotavirus disease) AND India	152	82	27	15	0	0	16
3	Demographic profile of rotavirus diarrhea in under-5 Indian children	(epidemiology* OR demography OR profile OR hospital OR community) AND (rotavirus OR rotavirus diarrhea OR rotavirus gastroenteritis OR rotavirus disease) AND India	138	95	46	35	0	0	35
4	Molecular epidemiology of rotavirus diarrhea in under-five children of India	(classification* OR genetics OR phylogeny OR virology OR genotype OR polymerase chain reaction OR classification OR genetic variation OR molecular epidemiology) AND (rotavirus OR rotavirus diarrhea OR rotavirus gastroenteritis OR rotavirus disease) AND India	137	100	54	47	2	1	49
5	Incidence of rotavirus infection as a cause of nosocomial diarrhea	(epidemiology* OR burden OR morbidity OR mortality or incidence OR prevalence OR profile OR hospital OR nosocomial) AND (rotavirus OR rotavirus diarrhea OR rotavirus gastroenteritis OR rotavirus disease) AND India	122	18	9	5	0	0	5
6	Mortality from rotavirus infection in under-5 children from different parts of India	(epidemiology* OR burden OR morbidity OR mortality or incidence OR prevalence OR profile OR hospital OR community OR case fatality) AND (rotavirus OR rotavirus diarrhea OR rotavirus gastroenteritis OR rotavirus disease) AND India	168	38	22	14	0	1	15

WEB TABLE II ROTAVIRUS SEROTYPES DETECTED FROM VARIOUS PARTS OF INDIA

<i>Reference</i>	<i>Place of study</i>	<i>Study period (year)</i>	<i>Age group (yr)</i>	<i>Detection method</i>	<i>Total stool samples tested for G strains (n)</i>	<i>Total stool samples positive for G strains (n)</i>	<i>G strains not tested</i>	<i>Total stool samples tested for P strains (n)</i>	<i>Total stool samples tested positive for P strains(n)</i>
<i>Northern India</i>									
Husain, <i>et al.</i> [19]	Delhi	1990-1991	<5	RT-PCR	51	44	G9, G12	57	45
Chakravarti, <i>et al.</i> [77]	Delhi	1998 -2000	<3	RT-PCR	100	66	G9, G12	134	84
Sharma, <i>et al.</i> [78]	Delhi	2000 - 2001	<5	RT-PCR	465	437	None	457	428
Bahl, <i>et al.</i> [23]	Delhi	2000 - 2004	<5	RT-PCR	135	89	G12	NT	0
Chakravarti, <i>et al.</i> [22]	Delhi	2005-2007	<2	RT-PCR	100	100	None	100	100
Mishra, <i>et al.</i> [26]	Lucknow	2004 - 2008	<3	ELISA,PAGE	79	75	G12	79	75
<i>Western India</i>									
Awachat, <i>et al.</i> [81]	Pune	1993-1994	<2	RT-PCR	Examined 35 nontypeable specimens of Rotavirus. 10 (28.57%) were identified as rotavirus serotype G9. The results indicate that serotype G9 may represent significant proportion of specimens, which were previously nontypeable.				
Kelkar, <i>et al.</i> [29]	Pune	1992-1996	<5	ELISA	205	107	G9, G12	NT	NT
Kelkar, <i>et al.</i> [30]	Pune	1990-1997	<5	PAGE	111	111	G12	None	None
Desai, <i>et al.</i> [28]	Thane	2000-2001	<5	RT-PCR	7	7	-	-	-
Zade, <i>et al.</i> [79]	Pune	1990- 1994, 2000-2002	Children	RT-PCR	90	90	G9, G12	89	89
Awachat, <i>et al.</i> [81]	Thane	2000-2001	Children	RT-PCR	Simian G3, SA11 like strains are isolated for the first time as etiological agents of diarrhea in humans				
Chitambar, <i>et al.</i> [82]	Surat	2004	NK	RT-PCR	Group B Rotavirus (<i>NSP2</i> gene) was detected in 295 (100%) cases				
Chitambar, <i>et al.</i> [82]	Sangli, Maharashtra	2009	NK	RT-PCR	RT-PCR Group B Rotavirus (<i>NSP2</i> gene) was detected in 5 (17.2%) cases				
<i>Eastern India</i>									
Samajdar, <i>et al.</i> [83]	Kolkata	2000 - 2004	<4	RT-PCR	147	147	None	140	140
Khetawat, <i>et al.</i> [84]	Kolkata	2000 - 2004	<4	RT-PCR	140	124	G12	NT	0
Barman, <i>et al.</i> [85]	Kolkata	2002-2004	<3	RT- PCR	37 (18.5%) sporadic cases of human group B rotavirus infection was detected of which 15 (7.5%) showed mixed infection with group A rotaviruses				
Mukherjee, <i>et al.</i> [86]	Kolkata	2004-2006	<4	RT- PCR	60	31	None	60	31
Samajdar, <i>et al.</i> [97]	Kolkata and Orissa	2004-2006	<4	RT-PCR	P[8] strains were isolated in 317 (43.2%) children. Phylogenetic analysis of VP8* amino acid sequences of 16 of these strains with other P[8] strains revealed four distinct lineages, clustered within rare OP354-like and Hun9-like lineages, pointing towards co-prevalence of divergent P[8] strains.				
Samajdar, <i>et al.</i> [40]	Kolkata	2005 - 2006	Children	RT- PCR	249	197	None	249	204

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Reference	Place of study	Study period (year)	Age group (yr)	Detection method	Total stool samples tested for G strains (n)	Total stool samples positive for G strains (n)	G strains not tested	Total stool samples tested for P strains (n)	Total stool samples tested positive for P strains(n)
Mukherjee, <i>et al.</i> [88]	Manipur	2005-2006	<5	RT-PCR	244	244	None	244	244
<i>Southern India</i>									
Jain, <i>et al.</i> [89]	Vellore	1984	Children	PAGE/ELISA	46	32	G9, G12	NT	NT
Aijaz, <i>et al.</i> [46]	Mysore	1988-1994	Children	PAGE/ELISA	200	130	G9, G12	NT	NT
Jain, <i>et al.</i> [89]	Chennai	1995 - 1999	Children	PAGE/ELISA	90	70	G9, G12	NT	NT
Saravanan, <i>et al.</i> [48]	Chennai (21)	1995 - 1999	<3	PAGE/ELISA	118	118	G9, G12	NT	NT
Ananthan, <i>et al.</i> [47]	Chennai	1995 - 1999	Children	NK	48	48	G12	NT	NT
Kang, <i>et al.</i> [53]	Vellore	1995 - 1999	<5	RT-PCR	126	101	G12	126	78
Anand, <i>et al.</i> [90]	Hyd	1995 - 1999	Children	PAGE	46	29	G9, G12	NT	0
Mukhopadhyaya, <i>et al.</i> [92]	Vellore ²	1999-2000	<10	RT-PCR	20	20	None	20	20
Ramani, <i>et al.</i> [91]	Vellore	2002 - 2006	Children	RT-PCR	452	282	None	NT	0
Banerjee, <i>et al.</i> [54]	Vellore (26) ¹	2000 - 2004	Children	RT-PCR	161	129	G12	166	100
Gladstone, <i>et al.</i> [3]	Vellore	2002-2004	<5	RT-PCR	472	472	None	472	472
Banerjee, <i>et al.</i> [93]	Vellore	2005	<5	RT-PCR	13	13	Only G12 strains were taken for sequencing and phylogenetic analysis		
Sowmyanarayanan, <i>et al.</i> [55]	Vellore	2005-2008	<5	RT-PCR	354	341	None	354	296
<i>Multiple locations</i>									
Ramachandran, <i>et al.</i> [94]	Multiple	1993	Children	RT-PCR	63	56	G12	62	55
Jain, <i>et al.</i> [89]	Multiple	1995	Children	PAGE/ELISA	93	74	G9, G12	91	72
Jain, <i>et al.</i> [57]	Multiple	1995 - 1999	Children	RT-PCR	287	265	G12	277	253
Das, <i>et al.</i> [59]	Multiple	1995 - 1999	Children	RT-PCR	159	130	None	139	120
Kang, <i>et al.</i> [58]	Multiple	1998 - 1999	Children	RT-PCR	82	68	G12	82	52
Das, <i>et al.</i> [60]	Multiple	2001	<4	RT-PCR	161	126	G12	126	109
Kang, <i>et al.</i> [61]	Multiple	2005 - 2009	<4	RT-PCR	1375	1177	None	1375	1166

NT: not typeable.

¹ Rotavirus was detected in 82/1,152 (7.1%) episodes of diarrhea in the community and 94/343 (27.4%) cases in the hospital. In the community, the genotypes identified in symptomatic patients, in order of frequency, were G1 (36.5%), G10 (17.1%), G2 (15.9%), and G9 (7.3%) and mixed infections (7.3%). The most common G-P combinations were G1P[8], G2P[4], G1P[4], and G10P[11]. The distribution of G types from hospitalized children was G1 (46.8%), G9 (19.1%), G2 (8.5%), G10 (1.1%), and 4.3% mixed infections. The most common G-P combinations were G1P[8] and G9P[8].

² Anti-group C VP6 antibodies were detected in 237 of 936 samples with a seroprevalence for group C of 16.79% in children aged <10 years.

WEB TABLE III G SEROTYPES ISOLATED FROM DIFFERENT PARTS OF INDIA

<i>Reference</i>	<i>Place of study</i>	<i>G1</i>	<i>G2</i>	<i>G3</i>	<i>G4</i>	<i>G9</i>	<i>G12</i>	<i>G-mixed</i>	<i>G UT/</i>	<i>G Novel(n) Other</i>
<i>Northern India</i>										
Husain, <i>et al.</i> [19]	Delhi	17	13	5	4	NT	NT	5	7	G6(3)
Chakravarti, <i>et al.</i> [77]	Delhi	31	12	18	5	NT	NT	NR	34	-
Sharma, <i>et al.</i> [78]	Delhi	120	116	11	2	67	67	54G2P[11], G3P[11]	28	-
Bahl, <i>et al.</i> [23]	Delhi	32	18	8	0	21	NT	10P[8]G1,P[4]G2, P[8]G9, P[6]G1, P[6]G9, P[6]G3	46	-
Chakravarti, <i>et al.</i> [25]	Delhi	60	16	3	-	8	2	G1P[8], G1P[4], G1P[6]	-	-
Mishra, <i>et al.</i> [26]	Lucknow	30	12	13	4	8	NT	8G1P[8], G3P[6], G1P[6], G2P[8]	4	-
<i>Western India</i>										
Desai, <i>et al.</i> [28]	Thane	-	-	7	-	-	-	-	-	-
Kelkar, <i>et al.</i> [30]	Pune	15	49	1	9	NT	NT	33	98	-
Zade, <i>et al.</i> [79]	Pune	43	32	7	6	2	NT	(G1P[8], G2P[4], G3P[8], G4P[8]) -79.2% in 1990-1994 and 92.3% in 2000- 2002. G9P[8] -1.3% in 1990-1994 and 7.7% in 2000-2002. Unusual strains (G1P[6],G1P[4], G1P[19], G2P[8], G3P[4], G4P[6]) detected in 19.5%	0	-
Kelkar, <i>et al.</i> [32]	Pune	35	34	16	12	NT	NT	0	0	G6(6), G8(4), G10(4)
Kelkar, <i>et al</i> [95]	Pune	Isolated nucleotide sequences of cDNA derived from the gene encoding VP7 of two strains indicating >94% identity with G6, the serotype, generally associated with cattle. The isolates were more close to G6 RF strain, which is a bovine rotavirus, reported from France.								
<i>Eastern India</i>										
Samajdar, <i>et al.</i> [83]	Kolkata	79	33	0	0	3	25	7	NR	-
Khetawat, <i>et al.</i> [84]	Kolkata	49	27	0	30	0	NT	18	16	-
Samajdar, <i>et al.</i> [41]	Kolkata ^a	82	65	0	0	20	28	G1P[8], G2P[4], G9P[8], G12P[8], G12P[6]	-	-
Mukherjee, <i>et al.</i> [86]	Kolkata	0	0	0	0	0	0	G9P[4](8), G12P8, G1P[8](6), G10P[4](6), G2P[4](3)	-	G10(6)

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<i>Reference</i>	<i>Place of study</i>	<i>G1</i>	<i>G2</i>	<i>G3</i>	<i>G4</i>	<i>G9</i>	<i>G12</i>	<i>G-mixed</i>	<i>G UT/</i>	<i>G Novel(n)</i>
Jain, <i>et al.</i> [89]	Manipur	126	57	0	2	11	20	23G10[4](36%), G2P[4](22%), G12P[6](8%), G9P[6](3%)	4	G10(1) G(1+2) P[6](4), G(1+2) P[8](5), G(2+9) P[4](8), G(2+9) P[6](4), G(1+12) P[4](1), G(1+12) P[6](1)
<i>Southern India</i>										
Aijaz, <i>et al.</i> [46]	Mysore	38	20	65	7	0	NT	NR	70	-
Ananthan, <i>et al.</i> [47]	Chennai	0	0	0	0	0	0	G[2,1], P[4,8](7). G2P[4]-P[8](12)	NR	-
Saravanan, <i>et al.</i> [48]	Chennai	11	78	2	16	0	NT	G2P[4,8], G1-G2P[4,8]	NR	-
Kang, <i>et al.</i> [53]	Chennai	7	33	1	0	0	NT	7	NR	-
Mathew, <i>et al.</i> [45]	Kerala	-	-	-	-	-	-	88G1P[8] (49.7%) G9P[8] (26.4%), G2P[4] (5.5%), G9P[4] (2.6%) G12P[6] (1.3%)		
Kang, <i>et al.</i> [58]	Vellore	50	24	1	30	5	NT	G1P1A[8], G1P1B[4], G2P1B[4], G4P1A[8]	25	-
Anand, <i>et al.</i> [90]	Hyderabad	16	0	0	8	NT	NT	5 17	-	
Ramani, <i>et al.</i> [91]	Vellore	155	91	1	2	59	9	31G12P[6](10), G12P[8](3)	101	G8 (1) and G10 (69)
Banerjee, <i>et al.</i> [54]	Vellore ¹	74	21	0	0	24	NT	10 32	-	
Sowmyanarayanan, <i>et al.</i> [55]	Vellore*	0	0	0	0	0	0	G2P [4] (30.8%), G1P [8] (17.8%) and G9P [8] (15.8%)	-	-
Mukhopadhy, <i>et al.</i> [92]	Vellore	0	0	0	0	0	0	G1P[8], G2P[4], G10P[11]	-	-
Banerjee, <i>et al.</i> [93]	Vellore	0	0	0	0	0	13	0 -	-	
Gladstone, <i>et al.</i> [3]	Vellore	The most common types were G1P[8] (15.9%), G2P[4] (13.6%), G10P[11](8.7%), G9P[8] (7.2%), G1P[4] (4.4%), G10P[4] (1.7%), G9P[4] (1.5%), G12P[6] (1.1%), and G1P[6] (0.6%).								
<i>Multiple locations</i>										
Ramachandran, <i>et al.</i> [94]	Multiple	7	14	7	6	15	NT	7 7	-	
Jain, <i>et al.</i> [89]	Multiple	15	3	2	12	NT	NT	NR 14	-	
Jain, <i>et al.</i> [57]	Multiple	51	99	2	32	50	NT	31 22	G8 (1)	
Das <i>et al.</i> [59]	Multiple	61	38	0	20	0	0	11 29	-	
Kang, <i>et al.</i> [58]	Multiple	33	7	9	12	7	NT	NR 14	-	

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<i>Reference</i>	<i>Place of study</i>	<i>G1</i>	<i>G2</i>	<i>G3</i>	<i>G4</i>	<i>G9</i>	<i>G12</i>	<i>G-mixed</i>	<i>G UT/</i>	<i>G Novel(n)</i>
Das <i>et al.</i> [60]	Multiple	62	17	0	6	0	NT	G1P[6],G2P[8], G2P[6],G4P[4], G4P[6]	15	-
Kang <i>et al.</i> [61]	Multiple*	G2P[4] (354 strains [25.7%]), G1P[8] (304 [22.1%]), and G9P[8] (117 [8.5%]), G1[P4](11), G1P[6](15), G2P[6](15), G2P[8](16), G9P[4](3), G9P[6](7), G3P[8], G4P[4](1), G10P[6](2), and G2P[10](1), G10P[11](1)								
Kang, <i>et al.</i> [62]	Multiple*	G1[P4] (14), G1[P6] (21), G1[P8] (545), G1[P untyped] (114), G1[P Mixed] (22), G2[P4] (489), G2[P6] (17), G2[P8] (26), G2[P untyped] (48), G2[P Mixed] (15), G9[P4] (25), G9[P6] (16), G9[P8] (176), G9[P untyped] (150), G9[P Mixed] (4), G12[P4] (2), G12[P6] (2), G12[P8] (4), G12[P untyped] (4)								

*Only detected combination of strains; NT - Not typed; NR - Not reported; UT - Untypeable; ^aPhylogenetic analysis of 13 G9 strains revealed clustering within G9 lineage III. Nine of 28 G12 strains were sequenced and exhibited phylogenetic clustering with previously reported G12 strains from Kolkata.

WEB TABLE IV P SEROTYPES ISOLATED FROM DIFFERENT PARTS OF INDIA

<i>StudyGroup [reference]</i>	<i>Place</i>	<i>P[4]</i>	<i>P[6]</i>	<i>P[8]</i>	<i>P mixed</i>	<i>P UT/Other</i>
<i>Northern India</i>						
Husain, <i>et al.</i> [19]	Delhi	14	4	23	2	14
Chakravarti, <i>et al.</i> [77]	Delhi	16	29	32	7	50
Sharma, <i>et al.</i> [78]	Delhi	90	104	162	72	29
Chakravarti, <i>et al.</i> [22]	Delhi	26	17	40	G1P[8] (26%), G1P[4] G1P[6]	0
Mishra, <i>et al.</i> [26]	Lucknow	11	24	35	5	4
<i>Western India</i>						
Zade, <i>et al.</i> [79]	Pune	38	11	40	0	0
<i>Eastern India</i>						
Samajdar, <i>et al.</i> [83]	Kolkata	45	14	31	50	0
Samajdar, <i>et al.</i> [40]	Kolkata	64	15	111	14	-
<i>Southern India</i>						
Kang, <i>et al.</i> [53]	Vellore	32	7	39	NR	-
Sowmyanarayanan, <i>et al.</i> [55]	Vellore	28	3	65	4	66
<i>Multiple locations</i>						
Ramachandran, <i>et al.</i> [108/94]	Multiple	13	27	8	7	7
Jain, <i>et al.</i> [57]	Multiple	63	88	69	33	24
Kang, <i>et al.</i> [58]	Multiple	19	2	31	NR	22
Das, <i>et al.</i> [59]	Multiple	35	8	51	26	19
Das <i>et al.</i> [60]	Multiple	19	61	19	-	27

NT: Not typed; *NR*: Not reported; *UT*: Untypeable.