



Rotavirus infections in a community based cohort in Vellore, India



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ABSTRACT

Introduction: The burden of infection in communities determines the spread of rotavirus infection and disease in susceptible populations. This study reports rotavirus infection and disease in a community based birth cohort in Vellore.

Methods: Bimonthly surveillance and diarrheal stool were collected from 452 children enrolled at birth, of whom 373 completed three years of follow up. Samples were screened for rotavirus by an ELISA and genotyped by reverse transcription polymerase chain reaction for VP7 and VP4 genes. Rotavirus incidence rates were calculated using Poisson regression equations. Risk factors associated with symptomatic and asymptomatic rotavirus infections were compared using multiple logistic regression.

Results: A total of 1149 episodes of rotavirus infections occurred in 94.4% children in the cohort. Incidence of rotavirus infection was 1.04 (0.97–1.1) per child-year with 0.75 asymptomatic and 0.29 symptomatic infections per child-year. About 18% of the children were infected in the first month, mainly with the G10P[11] strain. Rotavirus infections were more prevalent during October–March, but seasonality was not as marked in rotavirus disease. Rotavirus was associated with 15.1% of mild diarrhea, 38.9% of moderate/severe diarrhea and 66.7% of very severe diarrhea. Four common G types – G1 (26.8%), G2 (16%), G10 (11.2%) and G9 (9.6%) were seen, with high rates of mixed infections and untypable samples. Male gender, presence of siblings and low maternal education were associated with rotavirus disease.

Conclusion: This study demonstrates that rotavirus is the most common cause of gastroenteritis in the community, and indicates that since rotavirus caused the greatest proportion of moderate and severe disease, targeted interventions such as vaccines are needed for rotavirus, in addition to health education, sanitation and appropriate treatment to decrease diarrheal disease in communities.

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1. Introduction

Since 1973 when it was first described in humans [1], rotavirus has been widely investigated in many hospital based studies. With enteric pathogens that have a feco-oral route of transmission, it is the burden of infection in the community that determines spread of infection to susceptible populations and subsequent disease. A limited number of community based studies have been carried out, but most focused on disease and not infection [2]. Cohort studies on incidence and the natural history of rotaviral infection have been even fewer. [3].

Group A rotaviruses causes disease mainly in young children. Adults occasionally develop subclinical infection and rarely have symptoms. Asymptomatic infections occur at a higher rate among neonates particularly in developing countries [4], and disease is most common in children 4–24 months of age [5]. The epidemiology of rotavirus varies by setting [6]. Seasonality of infection is prominent in temperate climates while a low prevalence is maintained throughout the year in tropical countries [7]. The mode of transmission, though believed to be mainly feco-oral, is also pos-

sibly airborne and person-to-person because infection occurs in childhood irrespective of sanitary conditions [8]. Rotaviral gastroenteritis is usually accompanied by vomiting and fever and results in severe disease among infants [9]. Rotavirus is excreted in large numbers during diarrhea and the virus can remain infectious on inanimate surfaces, moist surfaces and hands. This report describes rotavirus infection detected by stool testing in children followed from birth to three years of age, with sampling during and in the absence of diarrhea.

2. Methods

This study was conducted from 2002 through 2006 in three contiguous slums in Vellore, India after approval by the institutional review board of the Christian Medical College, Vellore. The study conduct, recruitment, and sample collection methods have been published previously [10]. Briefly, a birth cohort of 452 children was followed from birth till three years of age, analysis was restricted to the 373 children who completed three years of follow-up. Surveillance of children for rotavirus infection was done by screening bimonthly stool samples and diarrheal stool samples, and clinical data were collected to record diarrheal severity using the Vesikari score with scores <5 considered mild, 6–10 moderate, 11–15 severe and 16–20 very severe [11]. In case of a surveillance sample, positive samples detected by ELISA (Dako Rota IDEIA, Ely,

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Table 1
Definitions used for rotavirus infection in a birth cohort in a South Indian urban slum.

Term	Definition
Diarrhea	Diarrhea was defined as 3 or more loose or watery stools in a 24-h period or a change in consistency and number of stools reported as diarrhea by the mother in children less than 6 months of age
Symptomatic rotavirus infection	Detection of rotavirus in any stool samples collected within seven days after or before the diarrheal episode by enzyme-linked immunosorbent assay (ELISA) or reverse transcription polymerase chain reaction (RT-PCR)
Asymptomatic rotavirus infection	Detection of rotavirus in a surveillance sample (out of range of the symptomatic rotavirus infection definition) by ELISA
Asymptomatic rotavirus re-infection	Detection of the same/different genotype detected in a non-consecutive surveillance sample Detection of a different genotype in a consecutive surveillance sample Detection of rotavirus of a same genotype in a consecutive surveillance sample which was 28 or more days after the previous positive sample

UK) were genotyped by reverse-transcription polymerase chain reaction (RT-PCR) for VP7 and VP4 amplification while for a diarrheal sample, irrespective of the ELISA result, one sample per episode was screened using RT-PCR for VP6 before genotyping [12]. The definitions for symptomatic and asymptomatic rotavirus infections used in this study are given in Table 1.

2.1. Statistical methods

Age-specific incidence and seasonality of symptomatic and asymptomatic infections were studied. The incidence rates were obtained by Poisson regression equations and frailty models adjusted for clustering of disease/infection within a child. For cumulative incidence of rotavirus infection, Kaplan–Meier estimates of median time to infection were calculated and compared between children infected with rotavirus overall and with specific genotypes. Factors influencing rotavirus infection as well as disease rates were studied using Poisson regression. To study the risk factors for rotavirus infection, children who experienced rotavirus infection in the first year were compared to children who did not experience rotavirus infection in the first year using multiple unconditional logistic regression. Covariates included age, gender, social class, mother's education, age of the mother, occupation of the head of the household, family size, birth weight, birth order, duration of exclusive and any breastfeeding, weaning, hygiene status, nutritional status at the age of 1 month. Similarly, factors associated with risk of developing symptomatic rotavirus were explored by comparing children who ever had a rotavirus diarrhea with children who had rotavirus infection, but never developed rotavirus diarrhea.

3. Results

3.1. Burden of disease

Of 1149 rotavirus infections identified on stool testing in 352 (94.4%) of children followed from birth to three years, 324 symptomatic infections occurred in 193 (52%) children, and led to 250 hospital/clinic visits. Of 352 primary rotavirus infections, 124 (35%) were symptomatic. The incidence rate of rotavirus infection was 1.04 (0.97–1.1) infection per child year including a rate of 0.75 (0.69–0.82) asymptomatic infections and 0.29 (0.25–0.33) symp-

Table 2
Distribution of the proportion of asymptomatic and symptomatic rotavirus infections by order of infection.

Order of infection (nth infection)	Asymptomatic infection	Symptomatic infection	Overall
1	228 (64.8)	124 (35.2)	352 (100)
2	200 (68.3)	93 (31.7)	293 (100)
3	150 (74.6)	51 (25.4)	201 (100)
4	92 (80.0)	23 (20.0)	115 (100)
5	59 (84.3)	11 (15.7)	70 (100)
≥6	96 (81.4)	22 (18.6)	118 (100)
Total	825 (71.8)	324 (28.2)	1149 (100)

tomatic infections per child year. A steady fall in the proportion of symptomatic rotavirus infections was seen with the increase in the order of infection (Table 2).

3.2. Age and infection

When rotavirus infections in the cohort were distributed according to age, the highest incidence was during the first month, followed by lower rates. Sixty-eight children were infected by one month of age, accounting for 18.2% of the cohort and 6% of the total rotavirus infections. The first three months of infancy were different from the rest of the first year because 74% ($p = 0.01$) of infections were asymptomatic. A Kaplan–Meier estimate of the median (interquartile range, IQR) age to rotavirus infection was 8.3 (2.2–17.3) months. In the first two months of life, about 25% of the children were infected followed by the next 6 months where the next quartile of children were infected. The third quartile took longer, about 9 months. By six months, 43% of the children were infected and 21% had rotavirus diarrhea, 63% were infected and 37% had diarrhea at the end of one year, 84% were infected and 45% had diarrhea by two years and 94% were infected and 52% had diarrhea by three years.

3.3. Re-infections

Fifty-nine (16%) children had only one documented infection, 92 (24%) had two, 86 (23%) had three, 45 (12%) had four, and 70 (20%) had five or more infections each. A total of 112 (30%) children had one symptomatic rotavirus infection, 54 (15%) had two, 27 (7%) had three or more symptomatic infections each. Survival analysis of each order of infection showed that each subsequent infection took longer than the previous one. Half the children had at least one rotavirus infection by 8.3 months, two by 20.3 months and three by 34.4 months.

3.4. Seasonality

As the data on incidence were obtained from a closed cohort, the rates of infection were adjusted for the effect of age. A significant rise in rotavirus infections ($p < 0.05$) was observed during the cooler months of October–March with incidence rates between 1.05 and 1.25, when compared to incidence rates of between 0.86 and 0.96, in April–September. The cooler months had 34% more infections, but the peaks were more prominent for asymptomatic infections than for diarrhea.

3.5. Rotavirus and disease

The proportion of rotavirus positives among surveillance stool samples was 3.1% (825/27,008) and among diarrheal samples was 17.5% (324/1856). Rotavirus was associated with 15.1% of mild diarrhea, 38.9% of moderate/severe diarrhea and 66.7% of very severe diarrhea. Of all rotavirus diarrheal episodes, 18.6% were moderate/severe and 4% of affected children were hospitalized. Of the

Table 3
Clinical features of diarrhea experienced by the birth cohort ($n = 373$) from birth to three years of age.

Characteristics	Diarrheal episodes associated with		<i>p</i> -Value ^a
	Rotavirus ($n = 324$)	No rotavirus ($n = 1522$)	
Median (iqr) age in months	10.4 (5–18)	10.8 (5.4–21.1)	0.08
Male - <i>n</i> (%)	830 (54.1)	186 (57.4)	0.30
Mean (sd) duration in days	4.1 (3)	3.4 (2.7)	<0.001
<i>Accompanying symptoms present – n (%)</i>			
Vomiting	88 (27.2)	209 (13.6)	<0.001
Fever	80 (24.7)	237 (15.5)	<0.001
<i>Treatment required – n (%)</i>			
Intravenous fluids	4 (1.2)	7 (0.5)	0.17
Hospitalization	12 (3.7)	31 (2.1)	0.26
<i>Severity – n (%)</i>			
Mild	249 (76.9)	1396 (91)	
Moderate	54 (16.7)	85 (5.5)	
Severe	6 (1.9)	3 (0.2)	0.002

^a Wald statistic after adjustment for clustering.

diarrheal episodes which resulted in hospitalizations, 28% were associated with rotavirus compared to 13% of diarrheal episodes treated at home.

Rotavirus diarrhea presented more often with vomiting (27% vs 14%, $p < 0.001$) and fever (25% vs 16%, $p < 0.001$) than non-rotaviral diarrhea (Table 3). Children with rotaviral diarrhea were taken to hospital, needed intravenous rehydration and hospitalization more frequently than children with non-rotaviral diarrhea, but these differences were not statistically significant. Rotaviral diarrhea lasted a little longer, 3 (2–5) days ($p < 0.001$), and the proportion that was severe was greater in rotaviral diarrhea than non-rotaviral diarrhea ($p = 0.002$). Vesikari score was 6 (5–9) for rotaviral diarrhea and 5 (4–7) for non-rotaviral diarrhea.

3.6. Risk factors for rotavirus infection and diarrhea

Of the 373 children in the cohort, 237 (63.5%) children experienced at least one rotavirus infection in the first year. A comparison of the infected children with the non-infected children demonstrated that developing rotavirus infection in the first year was associated with the mother's educational status, religion and birth order (Table 4). Month of birth was not associated with risk of developing rotavirus infection.

Factors associated with risk of developing symptomatic rotavirus were explored by comparing children who ever had a rotavirus diarrhea with children who had a rotavirus infection but never developed rotavirus diarrhea (Table 5). Of the 352 children who were eligible for the analysis, 193 children developed rotavirus diarrhea at least once while the remaining 159 did not

develop rotavirus diarrhea but had one or more rotavirus infections. The final model showed that a child was more likely to develop rotavirus diarrhea if male (odds ratio 1.6, $p = 0.03$), or had an illiterate mother (odds ratio 1.8, $p = 0.04$), and less likely if first-born (odds ratio 0.6, $p = 0.09$).

3.7. Molecular epidemiology

Genotyping results were available for 582 samples, 309 (53%) from children who had an asymptomatic infection whereas the other 243 (47%) were from children who had diarrhea. The most common G:P combinations observed were G1P[8] (14%), G2P[4] (11.5%), G10P[11] (7.4%), G9P[8] (6.5%), G1P[4] (4.6%), G1P[6] (1.2%), G10P[4] (1.2%), and G9P[4] (1.0%). Other genotypes identified were G3, G4, G8, G11 and G12 and P[3], P[9], P[10] and P[25]. Mixed infections were identified in about 39 (6%) of samples. Both G and P were untypable in samples from 88 (15.1%) infections. Of the samples for which genotyping results could not be obtained, the majority (80/88) were VP6 negative, indicating the ELISA result was false positive.

The earliest infections were G10P[11] strains, which infected neonates and were asymptomatic in about 60% of infections. G10P[11] infections were higher in hospital born children, but were also seen in neonates who were born in community clinics. Serotype-specific median age at primary infection and median severity scores are presented in Table 6. Infections with G9 presented with more severe diarrhea (Vesikari median score of 7) and these were usually followed by mixed infections, but the numbers of symptomatic infections was low and the association with severity not statistically significant.

Table 4
Multivariate logistic regression analysis of risk factors for rotavirus infection in the first year of life ($n = 373$).

Covariates	Total no. of children	Children with rotavirus infection in the first year <i>n</i> (%)	Unadjusted odds ratio	Adjusted odds ratio	<i>p</i> -Value
<i>Religion</i>					
Muslim	180	100 (56)	1	1	
Hindu	176	125 (71)	1.96 (1.26–3.04)	2.33 (1.44–3.75)	0.001
Christian	17	12 (71)	1.92 (0.65–5.68)	2.52 (0.81–7.82)	0.11
<i>Education of mother</i>					
High school/college	158	100 (63)	1	1	
Primary/middle school	109	66 (61)	0.89 (0.54–1.47)	1.19 (0.69–2.03)	0.54
Nil	106	71 (67)	1.18 (0.70–1.98)	1.81 (1.02–3.23)	0.04
<i>Birth order</i>					
First born	118	82 (70)	1	1	
Later born	255	155 (61)	0.68 (0.43–1.08)	0.64 (0.40–1.03)	0.07

Table 5
Multivariate logistic regression analysis of risk factors for developing diarrhea when infected with rotavirus ($n = 344$).

Covariates	Total no. of children	Children with rotavirus diarrhea n (%)	Unadjusted odds ratio	Adjusted odds ratio	p -Value
<i>Education of mother</i>					
High school/college	149	73 (49)	1	1	
Primary/middle school	102	57 (56)	1.32 (0.80–2.18)	1.30 (0.78–2.17)	0.31
Nil	101	63 (62)	1.73 (1.03–2.89)	1.82 (1.08–3.07)	0.4
<i>Gender</i>					
Female	181	89 (49)	1	1	
Male	171	104 (61)	1.61 (1.05–2.45)	1.59 (1.03–2.44)	0.03
<i>Birth order</i>					
First born	113	69 (61)	1	1	
Later born	239	124 (52)	0.69 (0.44–1.05)	0.66 (0.42–1.06)	0.09

A predominance of G1 rotavirus strains was observed throughout 2003, G2 seemed to emerge next with its peak in January–March 2004 and G9 infections predominated in 2005. Rare genotypes such as G4, G8, G11, G12 and G3 appeared throughout the study period. Mixed rotavirus infections were also observed throughout, with more frequent occurrence as the age of the cohort increased.

4. Discussion

A birth cohort of 373 children, with follow-up from birth till three years of age, experienced 1149 rotavirus infections by stool testing, an incidence of one rotavirus infection per child per year. These data are similar to the Mexican cohort [13] of 200 children followed from birth till two years, which found an incidence of one rotavirus infection and 0.3 rotavirus disease per child-year. A similar study in Guinea-Bissau [14] estimates an incidence of 0.6 infections and 0.2 rotavirus diarrhea per child year. The Guinea-Bissau study used ELISA testing of stool samples alone for surveillance which would not have picked up low levels of viral shedding, while the incidence in the Mexican cohort was calculated based on rotavirus infection detected using both stool as well as serum samples.

In this cohort, rotavirus was associated with 17.5% of the diarrheal episodes, as the most common pathogen found in diarrheal stool samples. Rotavirus was associated with 67% of the severe diarrheal episodes experienced by the cohort children, making it the most important cause of severe diarrhea. Systematic reviews based on studies from Africa [15] and Latin America [16] and WHO burden of disease reports from different time-periods and countries [17] have estimated the proportion of rotavirus among gastroenteritis but mainly from hospitals. Studies in various community settings globally have shown a proportion of 8.1% (4.0–12.2%) rotavirus among diarrhea, lower than in this community [2]. This may be because of the increased sensitivity of screening diarrheal samples by RT-PCR which would detect low viral loads. A review of

the burden of disease of Group-A rotavirus infections in India [18] found few studies in a community setting in India. These studies were mainly before 1992, used older testing strategies, and determined the rotavirus positivity rate to be 4–29% among diarrheal disease and 2.4–12.3% among asymptomatic children.

The estimate of pathogenicity of rotavirus, represented by number of diarrheal episodes among all rotavirus infections, was 0.28 in this study. The Guinea-Bissau cohort [14] reported a proportion of 0.40 and it was one in three infections for the Mexican cohort [13]. The measure of pathogenicity is very sensitive to the accuracy of detection of asymptomatic infections which usually have low viral excretion and thus the estimate of Guinea-Bissau where neither serology nor molecular techniques were used could possibly be overestimated.

Though rotavirus infects children throughout the first three years of life, in some developing country settings it displays an affinity toward neonates. In this study, 18% of the children were infected in the first month. This phenomenon has been reported earlier in various studies [19–22] and in hospitalized settings [23,24]. One explanation could be that a newborn, exposed to an environment saturated with the virus, is more likely to get infected or that neonates might be infected with specific strains that could bind to receptors not expressed in the post-neonatal period [25].

While rotavirus infections occurred throughout follow up, disease was seen mainly between the ages of 4–12 months. During early infancy, the child seemed to be protected from developing diarrhea due to rotavirus, as evident from the proportionately higher asymptomatic infections in the first three months. Beyond three months, rotavirus produced symptoms more often. As the child crossed the age of one year, the proportion of rotavirus infections developing into disease decreased and stayed low until the end of the follow-up. This was also demonstrated by Velazquez et al. [26] where rotavirus associated diarrhea was found to peak between 4 and 6 months and asymptomatic infections were more frequent in the first three months and beyond 10 months.

Table 6
Age at infection and severity of different G/P types in asymptomatic and symptomatic rotavirus infections in the birth cohort ($n = 373$).

Common G/P types	Asymptomatic infection		Symptomatic infection			
	N	Age at primary infection ^a	N	Age at primary infection ^a	n	Severity as Vesikari score ^a
G1	19	9.9 (5.6–17.1)	32	6.3 (3.9–9.8)	73	6 (5–9)
G2	10	13.9 (10.0–15.6)	20	7.8 (5.5–11.8)	49	6 (5–11)
G9	4	17.7 (12.3–27.6)	6	9.0 (4.9–12.7)	21	7 (5–9)
G10	33	0.3 (0.2–0.5)	18	0.8 (0.3–3.8)	24	6 (5–10.5)
P[4]	12	15.5 (11.6–19.3)	25	10.3 (7.0–13.9)	75	6 (5–11)
P[6]			3	3.1 (1.1–10.4)	9	5 (5–6)
P[8]	16	10.6 (7.4–23.9)	27	6.0 (2.9–11.5)	68	5 (5–8.5)
P[11]	28	0.3 (0.2–0.5)	12	0.4 (0.2–1.4)	17	6 (5–10)
Mixed G/P	3	32.2 (8.2–34.9)	6	11.2 (7.7–24)	14	6.5 (5–9)

^a Median (inter-quartile range).

Description of the natural history of rotavirus, especially of asymptomatic infections is limited. The Kaplan Meier estimates from the Mexican cohort [13] showed that 34% of the children were infected by six months, 67% by one year and 96% by the age of two years. The West African cohort found that 26% infected by six months, 46% by one year and 74% by the age of two years [14]. While the survival curves of these two cohorts were gradual and uniform, the Vellore cohort displayed a steeper curve initially with a high incidence rate and 43% infected by six months.

The late infancy window of a high rate of symptomatic rotavirus infection has been reported previously in many studies [27–29]. This may occur following the waning of the maternal antibodies known to be protective against disease and preceding the steady build-up of child's immune system, or corresponding to weaning, and increased levels of contamination. Overall, rotavirus was associated with more severe diarrhea, thus the proportional presentation increased with severity, low in community gastroenteritis, more in outpatients and highest in inpatients admitted with gastroenteritis [2].

Rotavirus may re-infect a child with or without producing disease. Of the 352 children who were ever infected, 293 (83%) had a re-infection at the end of three years. There was a higher rate of re-infection (234/334, 70%) at the end of two years than described in the other two cohort studies, 62% in Mexico [13] and 19% in Guinea-Bissau [14]. Re-infections occurred at a slower pace and developed lesser disease than primary infections. This finding is in line with the other two cohorts where there was a significant reduction in severity with increase in order of infection, although as demonstrated by analysis including serology, protection in the Indian cohort was much lower than reported in Mexico [10,13].

Unlike temperate climates, tropical countries display mild seasonality of rotavirus infections [30]. In this study, rotavirus was prevalent all through the year although there were small peaks during cooler months. A fallacious crude season specific incidence rate, possibly due to contamination by the age effect of the birth cohort may be unmasked to a certain extent by age adjusted estimates. With this adjustment, marked seasonality was found with higher incidence of rotavirus infections during October–March and less marked seasonality of rotavirus diarrhea in January–March, the relatively cooler months of the year. In a closed cohort design, it would not be appropriate to look for cyclical patterns due to the aging of the cohort as well as the lower number of children at the beginning and end of the study period.

With presence of any rotavirus infection in the first year as the dependent dichotomous outcome, religion, education of the mother and birth order were found to influence rotavirus infection. It is likely that more Hindu families had working mothers, with the children left with an elderly or very young caretaker, usually a sibling and were at higher risk of infection. Another possible explanation would be nutrition including micro-nutrients, where diet pattern of Muslims differ from that of Hindus.

It is established that education of the mother determines the well-being of the family and is also reflective of the literacy status of a society [31,32]. Nutrition and hygiene may be biological pathways linking education and health. Maternal education was found to be an important determinant of the risk of both rotavirus infection and diarrhea, with children of educated mothers less likely to be infected.

Another significant covariate was gender with male children at a higher risk for a symptomatic rotavirus infection. Some of these factors may be more reflective of the risk of developing diarrhea [33,34] in general rather than specifically rotavirus diarrhea. For example, male gender and mother's education were also found to be associated with general gastrointestinal symptoms during infancy [35].

Malnutrition has been previously described in a study in North-eastern Ghana [36] where wasting was one of the risk factors for rotavirus diarrhea. The association between infection and nutrition is considered to be synergistic [37]. We found that nutrition at one year was associated with the rate of rotavirus diarrhea while nutrition at one month did not, reflecting a possible effect of infection on nutrition but not vice versa. However, change in nutritional status over time is possible and the association between nutrition and infection needs in-depth analyses.

Lower socio-economic status and crowding have been described in studies done in UK [38], Pakistan [39] and Ghana [36] as factors affecting incidence of rotavirus diarrhea but were not found in this study. This study population was in a generally poor neighborhood, and may not have had a sufficient range of data to display these associations.

Duration of exclusive or partial breastfeeding did not seem to influence rotavirus disease in the Vellore cohort. It is known that breast milk contains high levels of anti-rotavirus secretory IgA and other rotavirus specific antibodies, particularly in Indian mothers [40]. In the UK, exclusive breastfeeding was highly protective against rotavirus diarrhea [41]. However, in Bangladeshi infants, breastfeeding protected from severe diarrhea in the first year but not in the overall two year duration suggesting that breastfeeding temporarily postponed, rather than prevented, rotavirus disease [42].

Diarrhea due to mixed infections and G9 was relatively more severe. Association of serotypes to severity seems to vary between different communities and settings. While a report from an Indian slum found G1 associated with more severe disease [43], Linhares et al. [44] reported from Latin America that G9 was associated with more severe disease. The increased pathogenicity of serotype G2 strains has been described [45,46], but other studies did not find any association of serotypes with severity [45,47]. Coinfection with other pathogens is reported to be associated with more severe disease [48], but dual infections with rotavirus have not been shown to influence severity [49]. G10P[11] was reported from India as a neonatal strain associated with asymptomatic infections [50]. However, we found that 40% of the G10 infections in our population were associated with symptoms. Inference of pathogenicity estimates has to be made with caution since they depend on the detection of asymptomatic infections, but it must also be pointed out that there are limited studies on asymptomatic infections in the community.

Median age at first infection was found to be earlier for symptomatic infections compared to the asymptomatic infections. Median age at first symptomatic infection of different genotypes revealed that there is a dominance of different genotypes at different ages. G10 was a neonatal infection, followed by G1 infection with its peak at 6 months, then G2 infection at 8 months and G9 infection at 9 months. This pattern was reflected in the G type specific temporal distribution which depicted consecutive dominance of different G types in the same order as described above along with the aging of the cohort. The temporal distribution, with each serotype predominating alternatively during each season, may also be seen as the cyclical nature of rotavirus infections [26]. However, the study period was not long enough to confirm these yearly or cyclical changes.

In conclusion, this cohort study demonstrates the importance of rotavirus as a cause of disease in young children in India, and its contribution to severe disease. Rotavirus infection in the neonatal period in the community is rarely reported, and the influence of such infections on subsequent vaccination with rotavirus vaccines needs to be elucidated. The roles of early infections, and high rates of re-infections outside of a rotavirus season, specific genotypes in infection and disease in different regions of the world also need further

investigation to better understand virus circulation, transmission and pathogenicity.

Conflict of interest

None declared.

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