

RESEARCH ARTICLE

INCIDENCE OF ROTAVIRUS IN THE NATIONAL CAPITAL REGION, INDIA: A RETROSPECTIVE STUDY BASED ON MULTICENTRIC DIAGNOSTIC LABORATORY

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ABSTRACT: Background: Throughout India, severe watery dehydrating diarrhea is the major cause of morbidity and mortality in children. Rotavirus is the leading cause of severe diarrhea in children under five years of age. **Objective:** To examine the epidemiology of rotavirus disease across age and gender in the National Capital Region (NCR), India. **Method:** It is a retrospective observational study based on diagnostic laboratory data of multiple tertiary care hospital located in Delhi and NCR. The samples which were tested for rotavirus from April 2014 to July 2017 in tertiary healthcare centers; were included in the study. The overall sample size was 1942. Data analysis has been done by using MS Excel, and R. Monthly positive rates were calculated as the proportion of positive cases out of total laboratory test done for rotavirus in that month. **Results:** The study reported that the high-risk population groups like pediatric (0-5 years) and elderly (>64 years) were most affected with the rotavirus infection, 226 (52%) and 70 (16%) respectively. Season-wise trends of rotavirus disease showed the highest positivity during the post-monsoon and winters while decreasing trends towards summers and monsoons of the year for 2014 to 2017. The study also reported a significantly higher positivity rate among inpatient population (22.8%) in comparison to outpatients (12.4%). **Conclusion:** This study outlines how laboratory data analytics can be critical in understanding the epidemiology of rotavirus disease, its seasonal trend, for preventive strategies.

KEY WORDS: Rotavirus, Diarrhea, Pediatric population, Surveillance, Laboratory data

INTRODUCTION:

India has a high under-5 years mortality rate, in which diarrhea is a significant contributor. Rotavirus is one of the most critical diarrhea-causing etiological agents among children. Rotavirus is a wheel-shaped, non-envelope virus, with a genome composed of 11 segments of double-stranded RNA. Its primary mode of transmission is fecal-oral route. The clinical

manifestation of rotavirus infection varies from asymptomatic, self-limited watery diarrhea to severe dehydrating diarrhea. Rotavirus is a leading cause of severe diarrhea among infants and young children. A nationally representative survey^[1] found that rotavirus is the reason for 34% of all diarrheal deaths in children under-5 years of age in India. This survey

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reveals that approximately 1 in 242 children will die because of rotavirus disease before their fifth birthday. Tate *et al.*,^[2] estimated that worldwide, 37% (215000) of all diarrheal deaths (578,000) in children under-5 years of age in 2013 was contributed by rotavirus disease. India contributed 22% (47,100) of total mortality because of rotavirus in 2013.

According to J Johnnet *al.*,^[3] the burden of rotavirus disease is 11.37 million episodes of rotavirus gastroenteritis requiring 3.27 million outpatient visits, 0.87 million hospital admissions and causing 78,000 deaths in India. This study estimated that the overall cost incurred by the country as INR 4.9 billion (3.3-6.9 billion) in hospital admissions and INR 5.38 (3.6-7.6) billion on outpatient visits. Other studies estimated annual mortality because of rotavirus in India to be between 90,000-1,53000.^[1,4,5]

Rotavirus disease is not only a problem associated with infants and young children, but other populations like pregnant, geriatric, and immunocompromised individuals are also at high risk. Though multiple studies highlighted the burden of rotavirus disease among infants and children, more research is required to understand the epidemiology among other age groups like adults and elderly. A hospital-based study^[6] in southern India has shown 3.8% positivity rate for rotavirus disease in individuals older than 12 years. As rotavirus disease is mainly regarded as a health issue of children only. In fact, most of the epidemiological studies in India has included only children in their studies. Further research on rotavirus disease among adults and elderly will help in understanding the broader implication of rotavirus infections.

Cook *et al.*,^[7] found that seasonality of rotavirus is less distinct in tropical areas and a low level of infection maintains throughout the year. A meta-analysis^[8] has estimated that for 1° centigrade increase in mean temperature, 1 cm increase in mean monthly rainfall, and 1% increase in relative humidity showed a reduction in rotavirus incidence by 10%, 1%, and 3% respectively. India is a vast country where weather varies from sub-tropical and tropical to temperate. The climate of Delhi varies from humid subtropical to semi-arid associated with high-temperature differences between winter and summer. Our study has assessed the epidemiological patterns of rotavirus disease among patients

(outpatients and inpatients) of tertiary healthcare centers in the National Capital Region (NCR) of India. We have analyzed diagnostic data of patients who got tested for rotavirus disease in laboratories attached to tertiary care centers located in the NCR. This study would help in understanding the epidemiological patterns of rotavirus disease across age, sex, and season. Seasonality is an essential aspect as better understanding will be helpful for better planning of preventive strategies including immunization.

OBJECTIVE:

To understand the epidemiology of rotavirus disease across age and gender in the NCR, India by using diagnostic laboratory-based data with special focus on seasonality of the disease.

METHODS:

A diagnostic laboratory-based data of multiple tertiary care hospital located in New Delhi and surrounding cities of NCR, from April 2014 to July 2017, was analyzed to understand the epidemiology of rotavirus disease in the NCR India. It's a retrospective observational study based on diagnostic laboratory data.

Sampling and sample size

All those samples who were tested for rotavirus from April 2014 to July 2017 in these tertiary healthcare centers were included in the analysis. The overall sample size was 1942 with maximum number from New Delhi (1542), as shown in Table 1.

Data analysis

We have used big data technologies to extract and transform data and finally to create a master data repository. The data analysis has been done by using MS excel and R. The monthly positive rates were

Table 1: Overall sample population distribution with positivity

| NCR cities | Test done | Positivity (%) |
|---------------|-------------|-------------------|
| Ghaziabad | 155 | 34 (21.9) |
| Greater Noida | 13 | 4 (30.8) |
| Gurgaon | 136 | 32 (23.5) |
| New Delhi | 1542 | 333 (21.6) |
| Noida | 96 | 29 (30.2) |
| Total | 1942 | 432 (22.2) |

Table 2: Rotavirus positivity across categories (age, gender, inpatients/outpatients)

| Category | Number of tests | Positivity (%) | Statistical significance |
|--------------------|-----------------|----------------|---|
| Sex | | | |
| Male | 1081 | 247 (22.8%) | Chi-square test p value: 0.47 |
| Female | 861 | 185(21.5%) | |
| Age (years) | | | |
| 0-1 | 394 | 97 (24.6%) | Chi-square test p value: <0.05 (0.007) (Categories are 0-5, 5-14, 14-44, 44-64 and >64 years) |
| >1-2 | 316 | 94 (29.7%) | |
| >2-3 | 98 | 18 (18.4%) | |
| >3-4 | 40 | 10 (25.0%) | |
| >4-5 | 31 | 7 (22.6%) | |
| >5-14 | 172 | 28 (16.3%) | |
| >14-44 | 271 | 47 (17.3%) | |
| >44-64 | 283 | 61(21.6%) | |
| >64 | 337 | 70 (20.8%) | |

calculated as proportion of positive cases out of total laboratory test done for rotavirus in that month. The positivity rates were plotted across age, sex, and states. Overall burden in different categories has been estimated by calculating percentage contribution in total cases. The Chi square test has been conducted to compare categories.

Laboratory methods

All diagnostic laboratories of Max healthcare have been using latex agglutination test (LAT) for the diagnosis of rotavirus. The LAT is highly efficient test for screening of rotavirus disease. The sensitivity and specificity of LAT were found to be 85.7% and 100% respectively in a study.⁹ Another research¹⁰ showed sensitivity and specificity as 98.2% and 94.2% respectively in comparison to electron microscopy as gold standard.

Ethical approval

The confidentiality of subjects has been maintained by de-identifying personal information and only anonymized data has been used. The ethical approval for the study has been taken from the Max Healthcare Ethics Committee (MHEC), New Delhi.

RESULTS:

A total sample of 1942 was analyzed which showed positivity rate of 22.2%. The proportion of out patients in samples was 5%, with a positivity rate of 12.4%, while the inpatient proportion was 95% with a positivity rate of 22.8%. The positivity rate among inpatients was significantly high (chi-square statistics: 5.7 and p value< 0.05) than outpatients (Table 2).

Among under-5 years, children age between 1-2 years showed the highest detection rate for rotavirus. Population age > 50 years showed detection rate in the range of 20%, higher than other adult populations (Fig 1).

Out of total rotavirus disease burden, 0-5 years contributed more than half of the burden (52 %), while population older than 44 years, 30% (Fig 1).

Among age group 0-5 years, 85% burden of the disease is in 0-2 years age category (Fig 2). The age group 1-2 years showed the highest positivity rate (29.7%).

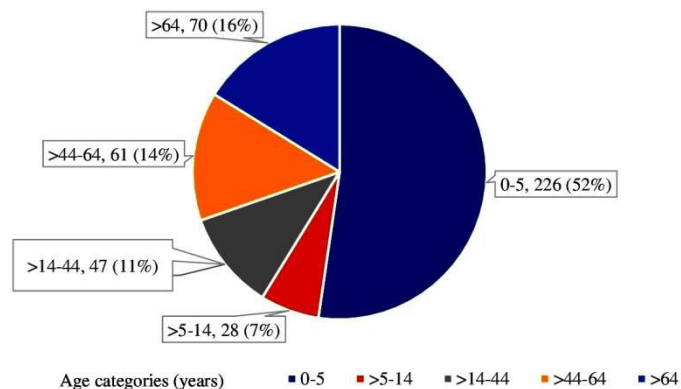


Fig. 1 Age categories

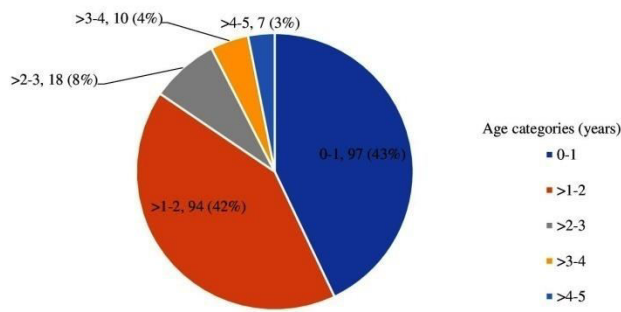


Fig.2

Season wise trends of rotavirus disease positivity rate

The analysis shows (Fig 3-5) the highest positivity rate during cooler months while decreasing rate during warmer months of summer and monsoon. A major proportion of the burden of rotavirus disease is limited to winter months in the NCR (December, January, and February).

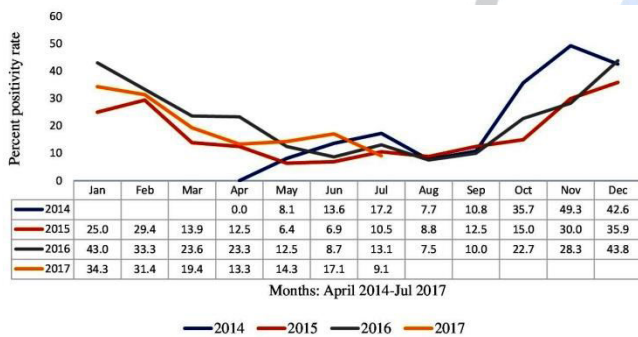


Fig. 3

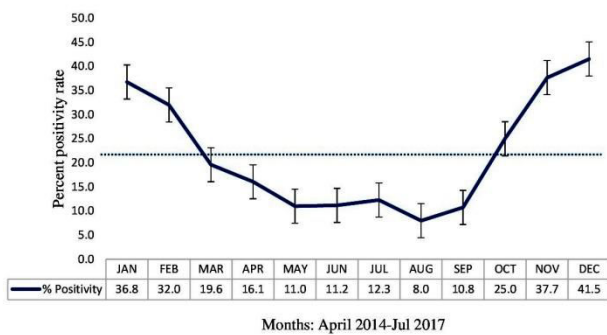


Fig. 4

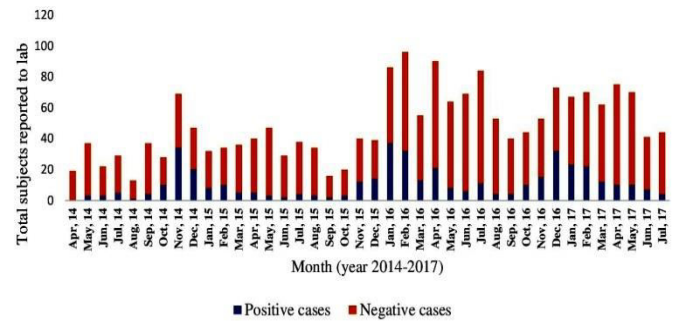


Fig. 5

Four months (November to February) bear ~60% of the total burden of rotavirus disease (Fig 6). Starting from October till March, positivity remains very high (>20%), while for other months of the year it remains less than 20%. The NCR shows a clearly well-marked seasonal trend for the infection. The trends are consistent over years from 2014 to 2017.

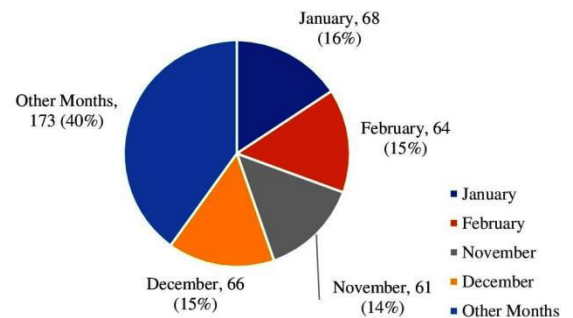


Fig. 6

Important factors associated with rotavirus disease positivity

On considering rotavirus positivity as dependent factor, binary logistic regression was conducted. Age, sex, and outpatient/inpatient were taken as independent variables. Males have slightly higher odds of getting infection but not found to be statistically significant. With increasing age, odds of infection decreases significantly. The samples from outpatients have significantly less odds of rotavirus isolation in comparison to samples from inpatient department. On binary logistic regression, age (p: 0.03) and hospitalization (0.01) was found to be significant factors associated with positive rotavirus disease.

DISCUSSION:

In patient population has significantly higher positivity rate (22.8%) in comparison to outpatients (12.4%). A higher positivity among inpatients has been reported by other studies as well.^[11] A study in South India which compared epidemiology of rotavirus in children from the community and hospital, found high detection in hospital cases (27.4%) than in the community (7.1%).^[12] A European multicenter study has suggested rotavirus as the major etiologic agent for severe diarrhea.¹³ Severe diarrhea put patients at higher risk of hospitalization, might be the reason of higher detection rate of rotavirus among hospitalized patients. Out of total positive outpatients^[12,11](91.7%) were in 0-10 years of age category and only one case was from the geriatric category (age: 71 years).

Our study estimated that 0-5 years of age group has a positivity rate of 25.7% and contributes 52.5% in the total burden of disease, while 0-2 years age group contributes 84.5% of total burden in 0-5 years age category. Indian rotavirus strain surveillance network^[14] reported rotavirus prevalence at all sites as 39% among 3580 patients (≤ 59 months), who were tested for rotavirus, while at Delhi, positivity was 36.7%. This study also reported the highest seasonal differences at Delhi with most distinct winter peaks. Rotavirus detection rates were the highest among 6-23 months of age. Jain *et al.*,^[15] reported that rotavirus had the highest prevalence (31%) in children of 7-12 months of age group, followed by children of 1-2 years age group. Two studies^{16,17} from Delhi suggested that 0-6 months is the most common affected group.

A tertiary care center-based study in south India reported a positivity rate of 25.6% among under-5 children hospitalized with diarrhea.¹⁸ Among other age categories, subjects more than 44 year of age contributes 30% of total rotavirus disease burden. However, the overall burden by age categories other than 0-5 years is less comparatively but not significantly different from older adults ($p > 0.05$) and geriatric ($p > 0.05$) population. Though, among population in age category of $> 5-14$ years and $15-44$ years, positivity is significantly less in comparison to 0-5 years age category ($p < 0.05$). There are few studies in India, which has estimated burden of rotavirus disease among adults. A hospital-based study in

Chicago estimated the prevalence of rotavirus among adults admitted to the hospital with diarrhea.^[19] Rotavirus was detected in 2.9% of all eligible bacterial stool cultures and rotavirus was 2.4 times more common than all bacterial pathogens from February-May. Adults in whom rotavirus was detected were older and immunosuppressed particularly with HIV. In Indian context, our study has highlighted a high burden among adults. Out of total 891 samples, (age > 14 years) were tested for rotavirus and 178 (20%) were found to be positive. Though, clinical profiles of these patients are not available for analysis as it is a laboratory-based study and it is not possible to assess other predisposing comorbidities.

Our study demonstrated peak in rotavirus disease prevalence during winter season (December to February). During the months of October, November, December, January, and February, positivity rate was more than 20%. The trend starts decreasing from March onwards till September.

The factors associated with positivity were ascertained by conducting binary logistic regression, shows age and inpatient/outpatients as the significant factors. The hospitalized patients have higher odds, while with increasing age odds of infection decreases.

Limitations

The limitation of the study includes non-availability of clinical profiles of cases, as study was based on diagnostic laboratory data. Other factors like demographic, clinical associated with rotavirus infection could not be ascertained also it is not possible to figure out whether admissions were because of the severe diarrhea or admitted patients got rotavirus infection during admission to the hospital because of some other clinical condition.

CONCLUSION:

Diagnostic laboratory-based studies can help in understanding the epidemiology of rotavirus disease, its seasonal trends, which can be useful in planning for preventive interventions like immunization. Our study revealed a very high rate of rotavirus disease among infants and 1-2 years of age group, and timely

targeted vaccination can help to reduce considerable morbidity and mortality. Our study also highlighted that rotavirus is not only a problem of children but affects adult inpatients as well and more research need to be done in this domain and existing surveillance networks should include high-risk population also, which include elderly and immunocompromised.

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