

## Original Research Article

# A study of efficacy of 'rota virus vaccination' on morbidity due to rotavirus diarrhoea in children aged 6 months to 5 years

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### ABSTRACT

**Background:** Rotavirus diarrhoea was the most common cause of mortality due to diarrhoea among children under 5 years of age. Deaths due to diarrhoea is one of important health issue that needs to be addressed due to high morbidity and mortality associated with it. Rotavirus is recognized as the major cause of hospitalizations among children and it is clear that improvements in hygiene and sanitation alone are not sufficient to decrease the cases. This study was conducted to assess the efficacy of rotavirus vaccine on morbidity amongst vaccinated and unvaccinated children.

**Methods:** Our study include 40 patients diagnosed with diarrhoea, with stool report positive for rotavirus, with varying degree of dehydration coming to Lilavati Hospital in outpatient department, pediatric ward or pediatric intensive care unit.

**Results:** Out of 40 children, 77.5% of the children vaccinated. We observed the rate of hospitalization was higher 77.8% i.e. 7/9 in the group of unvaccinated children than 45.2% i.e. 14/31 in group of vaccinated children. We found significant difference in the degree of dehydration in vaccinated and unvaccinated children. We found that nearly half of the children in vaccinated group did not have signs of dehydration (belongs to no dehydration category as per World Health Organization scale), while more than 88% of the children in unvaccinated group had some (66.7%) to severe (22.2%) degree of dehydration.

**Conclusions:** Our study concludes that vaccination against rotavirus significantly reduce the morbidity associated with rotavirus diarrhoea as compared to unvaccinated children.

**Keywords:** Diarrhoea, Rotavirus, Rotavirus vaccine, Morbidity

### INTRODUCTION

Rotavirus infects every child by the age of 3–5 years and are globally the leading cause of severe, dehydrating diarrhoea in children aged <5 years. In low income countries the median age at the primary rotavirus infection ranges from 6 to 9 months (80% occur among infants <1 year old) whereas in high income countries, the first episode may occasionally be delayed until the age of 2–5 years, though the majority still occur in infancy (65% occur among infants <1 year old).<sup>1</sup> Each year, rotavirus causes approximately 111 million episodes of gastroenteritis requiring only home care, 25 million clinic

visits, 2 million hospitalizations, and 352,000–592,000 deaths (median, 440,000 deaths) in children <5 years of age. Rotavirus vaccines represent an important preventive approach to reducing rotavirus infections.<sup>2</sup> In children aged less than one year, monovalent (RV1), compared to placebo, probably prevents 70% of all cases of rotavirus diarrhoea (RR 0.30, 95% CI 0.18 to 0.50; seven trials, 12,130 participants; moderate-quality evidence), and 80% of severe rotavirus diarrhoea cases (RR 0.20, 95% CI 0.11 to 0.35; seven trials, 35,004 participants; moderate-quality evidence). Similarly, pentavalent (RV5) prevents 73% of all rotavirus diarrhoea cases (RR 0.27, 95% CI 0.22 to 0.33; four trials, 7614 participants; high-quality evidence),

and 77% of severe rotavirus diarrhoea cases (RR0.23, 95% CI 0.08 to 0.71; three trials, 6953 participants; high-quality evidence). Both vaccines prevent over 80% of rotavirus diarrhoea cases that require hospitalization.<sup>1</sup> At present, 2 live oral vaccines are available for the prevention of rotavirus diarrhoea. RV5 vaccine (containing G1, G2, G3, G4 attachment protein VP7 and G6 attachment protein P1A8) and RV1 (containing G1P8).

At present RV1 and RV5 are reported equally efficacious vaccines in preventing rotavirus diarrhoea; both have comparable safety and efficacy profiles.<sup>3</sup>

Objective of the research was to study the correlation of vaccination status on morbidity due to rotavirus diarrhoea amongst children aged 6 months–5 years.

## **METHODS**

### ***Study area***

The study was conducted at the Lilavati Hospital and Research Centre, Mumbai.

### ***Study duration***

The duration of the study was from August 2018 till October 2019.

### ***Study population***

The study was conducted in a tertiary care hospital. We prospectively include 40 patients diagnosed with diarrhoea, with stool report positive for rotavirus, with varying degree of dehydration coming to Lilavati Hospital in outpatient department, pediatric ward or pediatric intensive care unit.

### ***Inclusion criteria***

The following criteria was included in the study: children with diarrhoea and stool report positive for rotavirus, both genders (male and female), children from 6 months to 5 years of age, diarrhoea with varying degree of dehydration (no, some, severe as per WHO scale of dehydration), rotavirus vaccine received/not received, and parents willing to consent for the study.

### ***Exclusion criteria***

The following criteria was excluded from the study: antibiotic induced diarrhoea, radiation induced diarrhoea, blood in stools, and children having diarrhoea due to causes other than rotavirus.

### ***Sample size***

The size of the sample was 40.

### ***Study design***

The study was a prospective observational study.

### ***Consent***

After due counselling, the informed consent shall be documented from the legal caretaker of the study subjects.

### ***Methodology***

After obtaining approval from scientific and institutional ethics committee, all patients satisfying the inclusion criteria were enrolled in the study; no objection certificate (NOC) was taken from all the consultants for the enrolment of the patients; informed written consent was obtained from the parents of the study subjects; children diagnosed with stool positive for rotavirus were enrolled in the study with varying degree of dehydration; stool routine examination was done to rule out bacterial infection/ presence of blood in stools to meet the inclusion criteria; CerTest method for detection of rotavirus in stool was performed, it's a one-step card test, color chromatographic immunoassay for qualitative detection of rotavirus in a given stool sample; degree of dehydration was decided based on WHO scale of dehydration (no, some, severe dehydration); children were categorized in no, some, and severe dehydration categories and were managed as per plan A, B and C (WHO scale for dehydration management in diarrhea patient); detailed history was elicited from the parents/guardians with relevance to the case and detailed clinical examination was done; the baseline demographic characteristics and clinical characteristics were obtained from all the children who were enrolled in the study; and different parameters like patient's total duration of hospital stay in days, requirement of normal saline boluses in numbers, duration of IV fluids, their vaccination status (monovalent, pentavalent or not vaccinated), zinc and oral rehydration salts (ORS) administration were recorded and analyzed.

### ***Ethical justification***

The study was conducted after obtaining ethical clearance from the research advisory as well as the institutional ethics committee; patients were enrolled only after obtaining informed written consent from the parents/guardians; the parents/guardians were made aware that they will have full right to enrol or withdraw the child from the study and their decision of refusal was equally regarded and it was informed that it would not affect the future care and treatment given to the child in our hospital; there was no extra cost burden for participants as the investigations done for thesis purpose during the study were sanctioned by the hospital; and confidentiality of the records was maintained.

Sample size was calculated by following formula.

$$n = \frac{\sigma_d^2(Z_\beta + ZZ_{\alpha/2})}{\text{Difference}}$$

Where n is sample size,  $\sigma$  is standard deviation of the within pair difference=30%, difference=clinically meaningful difference=14%,  $Z_\beta$  corresponds to power (0.84=80% power), and  $Z_{\alpha/2}$  corresponds to two-tailed significance level (1.96 for  $\alpha=0.05$ ).

## RESULTS

Our study included 40 children with rotavirus positive diarrhea between the ages of 6 months to 5 years. We studied the occurrence of various morbidity parameters that are found to be associated with diarrhea like hospitalization rate, need of intravenous (IV) fluids and boluses, duration of hospital stay, degree of dehydration in patients with rotavirus positive diarrhea. 60% (n=24) were males and 40% (n=16) were females and 77.5% (n=31) of the total population was vaccinated. In our study amongst total vaccinated group (n=31) maximum patient i.e. 51.6% (n=16) belongs to no dehydration, followed by 45.2% (n=14) belongs to some dehydration and 3.2% (n=1) belongs to severe dehydration. However amongst total unvaccinated group (n=9) maximum patient i.e. 66.7% (n=6) belongs to some dehydration, followed by 22.2% (n=2) belongs to severe dehydration and 11.1% (n=1) belongs to no dehydration. These results are statistically significant.

**Table 1: Association between vaccine status and degree of dehydration.**

Degree of dehydration	Vaccinated (%)	Unvaccinated (%)
No	16 (51.6)	1 (11.1)
Some	14 (45.2)	6 (66.7)
Severe	1 (3.2)	2 (22.2)
Total	31 (100)	9 (100)

P value: 0.033, conclusion: significant

In our study amongst total vaccinated group (n=31) maximum patient i.e. 51.6% (n=16) belongs to no dehydration, followed by 45.2% (n=14) belongs to some dehydration and 3.2% (n=1) belongs to severe dehydration.

However amongst total unvaccinated group (n=9) maximum patient i.e. 66.7% (n=6) belongs to some dehydration, followed by 22.2% (n=2) belongs to severe dehydration and 11.1% (n=1) belongs to no dehydration. These results are statistically significant.

In our study 77.8% (n=7) of the children from non-vaccinated group were hospitalized, as against 45.2% (n=14) of the children from the vaccinated group. Hence we conclude that rate of hospitalization among the vaccinated group is less as compared to the unvaccinated group, though statistically insignificant.

**Table 2: Association between hospitalization status and vaccination status among study participants.**

Hospitalization status	Vaccinated (%)	Unvaccinated (%)
Yes	14 (45.2)	7 (77.8)
No	17 (54.8)	2 (22.2)
Total	31 (100)	9 (100)

**Table 3: Percentage of hospitalized children requiring IV bolus according to the vaccination status.**

Vaccine status	Total hospitalized	Required bolus	%
Vaccinated	14	13	92.8
Unvaccinated	7	7	100

All unvaccinated hospitalized children and 92.8% of vaccinated hospitalized children required IV bolus.

**Table 4: Association between no. of days of IV fluids required in hospitalized children and vaccination status.**

No. of days of IV fluids	Vaccinated (%)		Total (%)
	No	Yes	
1	0 (0.0)	6 (42.85)	6 (28.57)
2	1 (14.28)	4 (28.57)	5 (23.80)
3	5 (71.42)	2 (14.28)	7 (33.33)
4	1 (14.28)	1 (7.14)	2 (9.52)
5	0 (0.0)	1 (7.14)	1 (4.76)
Total	7 (100.0)	14 (100.0)	21 (100.0)

In our study 42.85% (n=6/14) of the children in vaccinated group required IV fluids for one day followed by 28.57% (n=4/14) required for two days, 14.28% (n=2/14) for three days and 14.28% (n=2/14) for four days and more. 71.42% (n=5) of the children in unvaccinated group required IV fluids for three days, 14.28% (n=1) required for two and four days respectively.

## DISCUSSION

In our study amongst the vaccinated group (n=31) nearly half of the children i.e. 51.6% (n=16/31) did not have dehydration. Where as in unvaccinated group two third of the total population i.e. 66.7% (n=6/9) were in the category of some dehydration and only 11.1% (n=1/9) did not suffer from dehydration, remaining i.e. 22.2% (n=2/9) children had severe dehydration. These results are found to be statistically significant (p value=0.033). However no significant difference was found amongst vaccinated and unvaccinated population based on symptoms like fever, vomiting. Among the hospitalized children (n=21), all the children who belongs to unvaccinated group and 92.8% of the vaccinated group required IV bolus.

In our study amongst the hospitalized children we found that 64.28% (n=9/14) of the patients in the vaccinated

group could be managed with only one IV bolus as against only one child could be managed with only one bolus in unvaccinated group.

Burnett et al in their study “estimated impact of rotavirus vaccine on hospitalizations and deaths from rotavirus diarrhea among children <5 in Asia” projected the reduction in rotavirus hospitalizations and deaths following a hypothetical national introduction of rotavirus vaccines in all countries in Asia using data on national-level rotavirus mortality, <5 population, rotavirus hospitalizations rates, routine vaccination coverage, and vaccine effectiveness. They found 710,000 fewer rotavirus hospitalizations, a 49% decrease from the 1,452,000 baseline hospitalizations and 35,000 fewer rotavirus deaths, a 40% decrease from the 88,000 baseline deaths if all 43 Asian countries had introduced rotavirus vaccine. Rotavirus vaccines will substantially reduce morbidity and mortality due to rotavirus infections in Asia.<sup>4</sup>

Burnett et al in their study “global impact of rotavirus vaccination on childhood hospitalizations and mortality from diarrhea found that hospitalizations and ED visits due to rotavirus age were reduced by a median of 67% overall and 71%, 59%, and 60% in low, medium and high child mortality countries, respectively. Implementation of rotavirus vaccines has substantially decreased hospitalizations from rotavirus and all cause age.<sup>5</sup>

Ngabo et al in their study “effect of pentavalent rotavirus vaccine introduction on hospital admissions for diarrhoea and rotavirus in children in Rwanda: a time-series analysis” concludes that after the introduction of rotavirus vaccine in May 2012, the annual peak in admittances to hospital because of rotavirus in eastern province was blunted in 2013 and 2014, with a 61% and 70% fall in the number of admissions because of rotavirus in 2013 and 2014, respectively, compared with the pre vaccine year of 2011 ( $p=0.04$ ). Above studies clearly concludes the reduction in hospitalization after the introduction of rotavirus vaccine, in accordance with our study maximum hospitalization occurred in unvaccinated group as compared to the vaccinated group. We could not establish a statistically significant relationship between vaccination status and hospitalization rate. This could most likely be attributed to less number of samples and we recommend further observation.<sup>6</sup>

Araki et al in their study “effectiveness of monovalent and pentavalent rotavirus vaccines in Japanese children” enrolled 1412 children, out of which 487 children were rotavirus positive, immunization status of the children were taken from the vaccination record in 98% of the children in 2% verbal record, RV vaccines were highly effective against SRVGE needing intravenous rehydration or hospitalization (VE was 97.3% [95% CI: 88.8–99.3]) VEs of RV1 and RV5 against G1P [8] and

G2P [4] were comparable, at RV1, 89.8% (95% CI, 78.2–95.5%) and 78.3% (95% CI, 23.6–93.8%); and RV5, 85.8% (95% CI, 72.8–92.6%) and 88.1% (95% CI, 10.1–98.4%), respectively, concluded that rotavirus vaccines were effective in preventing mild to severe RVGE, irrespective of vaccine type. These results are in accordance with our study.<sup>7</sup> Results of above two studies clearly imply the reduction in mortality and morbidity after introduction of rotavirus vaccination. These results are in accordance with our study, as less number of bolus required for stabilization of the hospitalized vaccinated patients as compared to unvaccinated children (IV bolus here is taken as one of the parameters of morbidity indicator as we could not find any direct correlation between number of bolus requirement and vaccination status of the children). These results could not be found statistically significant.

### Limitations

Sample size of our study was small to assess the significant difference between the efficacies of two different types of vaccines available, but can tell us about the importance of rotavirus vaccine as it significantly reduces the morbidity related to rotavirus diarrhea. The serological diagnosis to determine the prevalent strain of rotavirus amongst the study population children was not done in this study.

### CONCLUSION

The result of our study concludes that vaccination against rotavirus significantly reduce the morbidity associated with rotavirus diarrhea as compared to unvaccinated children. Amongst the vaccinated population the difference between morbidity caused by rotavirus diarrhea amongst children who received pentavalent vaccine and/or monovalent vaccine wasn't statistically significant. No significant difference in associated symptoms like fever and vomiting amongst vaccinated and unvaccinated group. More number of children in unvaccinated group required in-patient management, while in vaccinated group, majority of children could be managed at home.

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