

# Trends of Diarrheal Cases and Mortality in under 5 Children in Ethiopia Pre and Post Vaccine Introduction (A 7 years Trend Analysis)

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**Abstract:** *Background:* Rotavirus is the most common cause of gastroenteritis in young children. Most children will experience at least one infection with rotavirus by the time they are five years old, with some requiring hospitalisation for dehydration with the highest incidence being in developing countries before the introduction of Rota virus vaccines which has been introduced into vaccination programme in Ethiopia since November 2013. *Objective:* This study assessed trends of diarrhea cases (morbidity and mortality) in under 5years' children in Ethiopia pre and post vaccine introduction. *Methods:* A retrospective population survey of all watery diarrhea cases (defined as 3 or more watery, non-bloody stools within 24 hours that has lasted for less than or =7 days) and mortality from national data (HMIS- health management information system) for the years 2011- 2013 and 2014-2017 was done. *Results:* There were 178,057diarrheal cases, male, 118,922(66.8%) and female, 59,135(33.2%) in prevaccine era (2011-2013) with 22, 025(13.2%) diarrheal related deaths. In the post vaccine era(2014-2017) 59,788 diarrheal cases with males, 36,154 (60.5%) and females, 23,634 (39.5%) with deaths, 3,079 (5.1%). *Conclusions:* This study clearly demonstrated that there is significant reduction in diarrheal prevalence, 178,057 VS 59, 788,(1.2% and 0.43%), diarrheal related mortality (13.2% VS 5.1 %,) in Ethiopia.

**Keywords:** Rota vaccine, diarrheal prevalence, diarrheal related mortality

## Abbreviations

- **HMIS-** health management information system
- **NIPs-**National Immunization Programs
- **GAVI-**Global Alliance for vaccines and immunization
- **IRB-**institutional review board

## Operational definition

- **Prevaccine era-** before the introduction of Rota vaccine in Ethiopia
- **Post vaccine era-** After the introduction of Rota vaccine in Ethiopia
- **Watery diarrhea-** passage of 3 or more stools per day with no blood or mucoid in it.
- **Seasonality-** the months at which largest diarrheal cases have been registered on HMIS book.
- **Not died-** children with acute watery diarrhea registered on HMIS, treated and cured.

## 1. Introduction

Rotavirus is a leading cause of watery diarrhoea in children, estimated to account for approximately 39% of diarrhoea hospitalizations in young children with 1.7 million diarrhoea deaths among children aged <5 years. It is estimated that rotavirus is responsible for 611 000 diarrhoea deaths annually (1). It is globally estimated that rotaviruses are annually responsible for more than 111 million cases of infantile gastroenteritis and approximately 600,000 deaths. Highest in the developing countries (3, 17)

Rotavirus vaccines represent an important preventive approach to reducing rotavirus infections and, along with therapeutic interventions such as oral rehydration solution and zinc supplementation, present an opportunity to decrease diarrhoea morbidity and mortality.

Rotavirus is the leading cause of severe acute gastroenteritis in the world, and vaccination is considered the most effective intervention to reduce its occurrence (7,8) Before the introduction of rotavirus vaccines, almost all children experienced at least one episode of rotavirus gastroenteritis before the age of 5 years(9) and was estimated to cause 215, 000 deaths and 2 million hospitalizations per year worldwide (10).After demonstrated studies of safety and efficacy among children and significant reduction of cases and severity, vaccines were adopted by the immunization schedules of different countries (11-13).Routine surveillance systems from North America and Europe have reported consistent evidence of Rotateq and Rotarix effectiveness through their routinely collected statistics (14.)

Rotavirus vaccination would be a highly cost-effective intervention .It was predicted to reduce deaths attributed to rotavirus diarrhea (15) lower-middle-income countries have introduced rotavirus vaccination in their National Immunization Programs (NIPs) as of June 2010-2013 including 10 GAVI-eligible countries: Armenia, Bolivia, Georgia, Ghana, Guyana, Honduras, Moldova, Nicaragua, Sudan, and Yemen (16, 17), Ethiopia introduced Rotarix vaccine since November, 2013.. In clinical trials, the efficacy of rotavirus vaccines varies by the level of income, immuneresponses, concomitant enteric infections, oral polio vaccine interference and under nutrition (18 -22).

This study determined the prevalence ofdiarrheal disease before and after rotavirus vaccine, assess temporal trend and age group distribution of acute gastroenteritis and identify proportion of diarrheal cases.

## 2. Materials and Method

All-causes of diarrheal cases, and data for children under 5 years in Ethiopia from 2011to2017 were reviewed. The

proportion of acute diarrhea (defined as 3 or more watery, non-bloody stools within 24 hours that has lasted for less than or =7 days) was determined. Temporal trend and age group distribution of all-causes of diarrhea and / or gastroenteritis before and after introduction of the vaccines was compared. The study period was from 2011 to 2013 for pre vaccination and from 2014 – 2017 for post vaccination by using HMIS (National data). Data was collected by pediatricians in the surveillance sites, and trained general practitioners working in the Ethiopian federal minister of health, and checked and cleansed by the principal investigator.

Children coming from different corners of Ethiopia and served in different health facilities were the source of population for the study. All children aged 0 - 59 months with the diagnosis of dehydrating diarrhea during the study periods (2011-2017) on HMIS data were included and were our study samples.

**Ethical Clearance**

Ethical clearance was obtained from department research ethical committee, Addis Ababa University medical faculty college of health sciences institutional review board (IRB). A letter was written from the department of pediatrics and

child health to Ethiopian federal ministry of health to get permission for the HMIS data and agreement was signed.

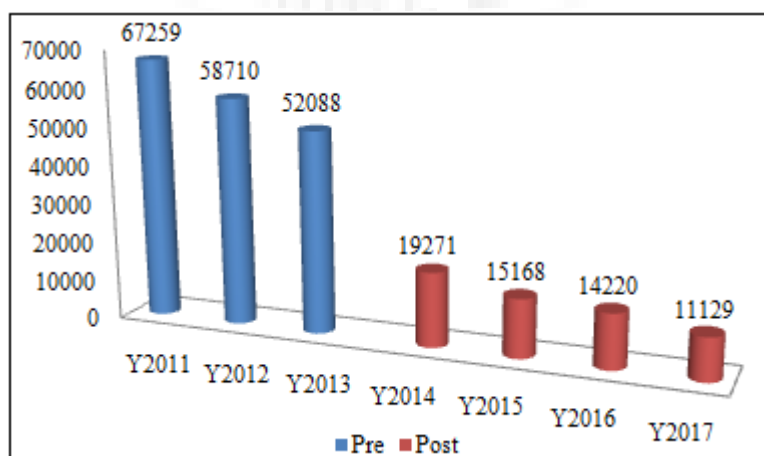
**3. Result**

There were 178,057 diarrheal cases, male, 118,922( 66.8%) and female, 59,135( 33.2%) in prevaccine era ( 2011-2013) with 22, 025( 13.2%) diarrheal related deaths, most deaths occurring in age groups < 11months and most diarrheal episodes in infants age 9-12 months. Among the 178,057 diarrheal cases, 138,896(78%) were with some dehydration and 39,161(22%) were cases of severe dehydration. Great majority of the occurrences were in April.-August. The prevalence of diarrheal disease in the general population, taking population mean of the risks or under fives is  $178,057/15,349,673 = 1.2%$  before the vaccine and  $59,788/13,769,874 = 0.43%$  after the vaccine (Table 1)

In the post vaccine era, there were a total of 59,788 diarrheal cases with males, 36,154(60.5%) and females, 23,634(39.5%). Regarding deaths, 3,079 (5.1%). Among the 59,788 diarrheal cases, some dehydration, 49,489(82.3%) and severe dehydration, 10,299( 17.7%)(Table 1.) Seasonality is the same with the pre vaccine episodes (Fig. 2.)

**Table 1:** Diarrheal disease during pre and post vaccination era (2011-2017), in Ethiopia

Variables	Pre vaccination		Post vaccination	
	Frequency (N=178,057)	Percentage	Frequency (N=59788)	Percentage
<b>Sex</b>				
Male	118,922	66.8	36154	60.5
Female	59,135	33.2	23634	39.5
<b>Age</b>				
0 – 3 Months	85817,473	0.5	493	0.7
3 – 6 Months	24,264	9.8	6,07312,843	10.2
6 – 9 Months	86,234	13.6	23,670	21.5
9 – 12 Months	49,228	48.4	16,709	39.627.9
>12 Months		27.7		
<b>Degree of dehydration</b>				
Some dehydration	138,896	78	49489	82.3
Sever dehydration	39,161	22	10,299	17.7
<b>Patient outcome</b>				
Death	22,025	13.0	3,079	5.1
<b>Cured and discharged( Not died)</b>	156,032	87.0	56709	94.9



**Figure 1:** Prevalence of diarrhea during pre and post vaccination eras(2011- 2017) in Ethiopia

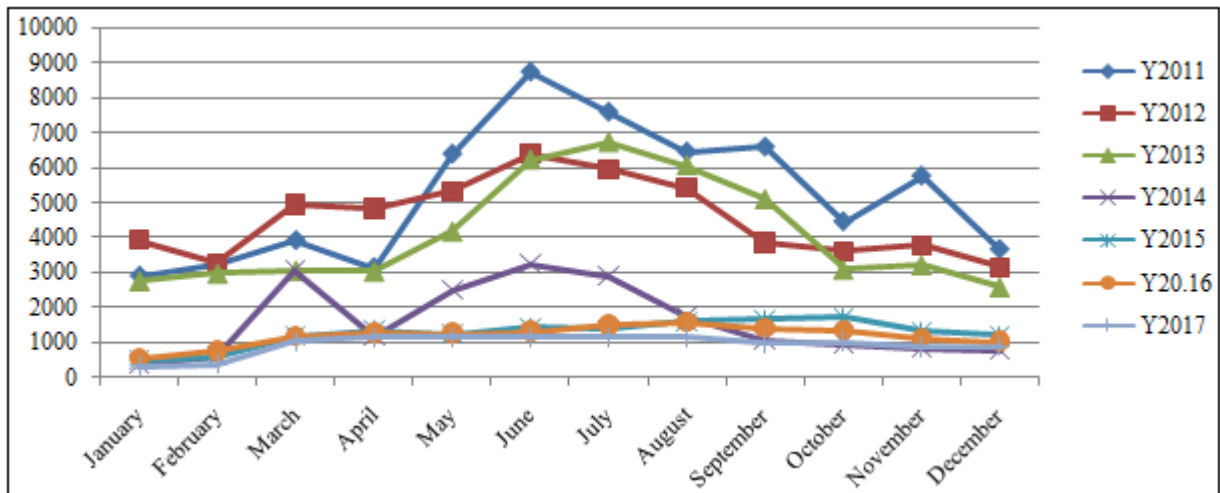


Figure 2: Peak months of diarrhea distribution during pre vaccination (2011-2013) and post vaccination (2014-2017) era

Table 2: Monthly frequency of diarrhea during pre vaccine era (2011-2013)

Variables	(Year 2011) (N=67259)	(Year 2012) N=58710	(Year 2013) (N=52088)	Frequency (N=178,057)	Percentage
January	3249	4284	3013	10546	5.9
February	3598	3622	3231	10451	5.9
March	4264	5294	3315	12873	7.2
April	3648	5182	3293	12123	6.8
May	6749	5679	4433	16861	9.5
June	9103	6752	6491	22346	12.6
July	7954	6322	6989	21265	11.9
August	6809	5791	6323	18923	10.6
September	6952	4212	5352	16516	9.3
October	4808	3946	3343	12097	6.8
November	6118	4118	3467	13703	7.7
December	4007	3508	2838	10353	5.8

Table 3: Monthly frequency of diarrhea during post vaccine (2014-2017) era

Variables	Y2014	Y2015	Y2016	Y2017	Frequency (N=59,788)	Percentage
	N=19,271	N=15,168	N=14,220	N= 11,129	Total	
January	372	490	548	318	1728	2.9
February	591	627	749	372	2339	3.9
March	3083	1174	1185	1027	6469	10.8
April	1171	1352	1264	1141	4928	8.2
May	2519	1233	1253	1123	6228	10.4
June	3251	1415	1307	1127	7100	11.9
July	2893	1381	1492	1145	6911	12.6
August	1761	1619	1564	1132	6076	10.2
September	1053	1643	1407	978	5081	8.5
October	973	1718	1324	1003	5018	8.4
November	841	1313	1103	879	4136	6.9
December	763	1203	1024	884	3874	6.5

#### 4. Discussions

In developing countries, diarrhea is a major cause of disease among under-5-years, with an estimated 600,000 deaths each year. This study suggests majority of cases involving severe diarrhea is caused by rotavirus infection. Rotavirus vaccines have shown a potential to prevent more than 20% of all diarrhea-related hospitalizations in children. Vaccine has been proven to be one of the most significant interventions in reducing childhood mortality.

The prevalence of diarrheal disease in the general population, taking population mean of the risks or under-fives is  $178,057/15,349,673 = 1.2\%$  before the vaccine and  $59,788/13,769,874 = 0.43\%$  after the vaccine. As compared to the pre vaccine era, severity of diarrhea decreases by

4.3% in post vaccination era, and death due to diarrhea decreases by 8.1%.

According to the age group, high prevalence was observed in the age groups of 9-12 months as compared to other age groups. But it decreases markedly as compared to the pre vaccination era by 10%.

There is no difference in seasonality in pre and post vaccination eras, the prevalence was peak during winter (April, May and June) and starts to decline during summer. This may be associated with shortage of water supply that predisposes to poor sanitation and may aggravate the occurrence of diarrhea.

Prevalence of diarrhea, degree of severity and death rate decreases uniformly in post vaccination era in Ethiopia.

This retrospective survey clearly showed that there is almost 40% reduction in diarrheal deaths after the introduction of Rota vaccine in Ethiopia. The result is similar to studies done in different countries, Rural Kenya ( 21, July, 2010) , Brazil ( Sempt.,2011,V. 16,pp 1180-1184) and April, 2011,) Mexico( Nov. 28, 2012) and many other countries.

In general, strong suggestive evidences on beneficiary effects of Rota virus vaccine against fatal deaths due to Rota dehydrating diarrhea is demonstrated in this study.

## 5. Conclusions

After the introduction of rotavirus vaccination for infants, significant reduction was observed in under-5-years diarrhea-related mortality and prevalence of diarrhea in Ethiopia.

The largest reductions in diarrhea-related mortality and prevalence for diarrhea were among children younger than 1 year, indicating that the reduced diarrhea burden in this age group was associated with introduction of the rotavirus vaccine (other factors which can contribute for the reduction of diarrhea in Ethiopia like personal and environmental sanitations, controlling other infections, preventing malnutrition etc, had been there even before the introduction of the Rotavirus vaccine but the diarrheal morbidity was higher before the introduction of the vaccine and declines after the vaccine).

These national data are consistent with evidences from other countries and strengthen the evidence base for the continuation of rotavirus vaccination as an effective measure for controlling severe and fatal childhood diarrhea.

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*The author*

## 8. Computing interest

None declared

## References

- [1] Wellcome Research Training Fellow, Viral Gastroenteritis Section, Division of Viral and Rickettsial Diseases, National Center for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, GA, USA. Current address: Malaria Project and Wellcome Trust Centre; and Department of Paediatrics, College of Medicine, Blantyre, Malawi.
- [2] Medical Officer, Child Vaccine-Preventable Diseases Branch, National Immunization Program, Centers for Disease Control and Prevention, Atlanta, GA, USA.
- [3] WHO (2009) World health statistics 2009. In: World Health Statistics Series (ed. WHO) World Health Organization, Geneva, pp. 35–45.
- [4] Suwantika AA, Tu HT, Postma MJ. Cost-effectiveness of rotavirus immunization in Indonesia: taking breastfeeding patterns into account. *Vaccine* 31(32), 3300-3307 (2013).
- [5] Boom JA, Tate JE, Sahni LC, Rench MA, Hull JJ, et al. (2010) Effectiveness of pentavalent rotavirus vaccine in a large urban population in the United States. *Pediatrics* 125: e199–e207.
- [6] World Health Organization: Meeting of the Immunization Strategic Advisory Group of Experts, April 2009—conclusions and recommendations. *Wkly Epidemiol Rec.* 2009, 84: 220-236.
- [7] Greice Madeleine Ikeda do Carmo<sup>1</sup>, Catherine Yen<sup>2,3</sup>, Jennifer Cortes<sup>2,3</sup>, Alessandra Araujo Siqueira<sup>1</sup>, Wanderson Kleber de Oliveira<sup>1</sup>, Juan Jose Cortez-Escalante<sup>4</sup>, Ben Lopman<sup>2</sup>, Brendan Flannery<sup>5</sup>, Lucia Helena de Oliveira<sup>6</sup>, Eduardo Hage Carmo<sup>1</sup>, Manish Patel<sup>2\*</sup> Decline in Diarrhea Mortality and Admissions after Routine Childhood Rotavirus Immunization in Brazil: A Time-Series Analysis *PLoS Medicine* | www.plosmedicine.org April 2011 | Volume 8 | Issue 4 | e1001024
- [8] Parashar UD, Hummelman EG, Bresee JS, Miller MA & Glass RI (2003) Global illness and deaths caused by rotavirus disease in children. *Emerging Infectious Diseases* 9, 565–572.
- [9] Valencia-Mendoza A, Bertozzi SM, Gutierrez JP & Itzler R (2008) Cost-effectiveness of introducing a rotavirus vaccine in developing countries: the case of Mexico. *BMC Infectious Diseases* 8, 103.
- [10] Parashar UD, Burton A, Lanata C et al. (2009) Global mortality associated with rotavirus disease among children in 2004. *Journal of Infectious Diseases* 200(Suppl 1), S9–S15, and (Tate et al *CID*, 2016).
- [11] de Oliveira LH, Danovaro-Holliday MC, Matus CR & Andrus JK (2008) Rotavirus vaccine introduction in the Americas: progress and lessons learned. *Expert Review of Vaccines* 7, 345–353.
- [12] Ruiz-Palacios GM, Perez-Schael I, Velazquez FR et al. (2006) Safety and efficacy of an attenuated vaccine against severe rotavirus gastroenteritis. *New England Journal of Medicine* 354, 11–22.
- [13] Safadi MA, Berezin EN, Munford V et al. (2010) Hospital-based surveillance to evaluate the impact of rotavirus vaccination in Sao Paulo, Brazil. *Pediatric Infectious Disease Journal* 29, 1019–1022.
- [14] Tate JE, Panozzo CA, Payne DC et al. (2009) Decline and change in seasonality of US rotavirus activity after



- the introduction of rotavirus vaccine. *Pediatrics* 124, 465–471.
- [15] Nelson EAS, de Quadros CA, Santosham M, Parashar UD, Steele D. Overcoming perceptions of financial barriers to rotavirus vaccine introduction in Asia. *Hum. Vaccin.* 9(11), 2418-2426 (2013).
- [16] PATH. Country national immunization program (NIP), introduction of rotavirus vaccine. Available at: <http://sites.path.org/rotavirusvaccine/rotavirus-advocacy-and-communications-toolkit/country-introduction-maps-and-list/>.
- [17] Liu L, Johnson HL, Cousens S, et al. Global, regional, and national causes of child mortality: an updated systematic analysis for 2010 with time trends since 2000. *Lancet* 2012; **379**(9832): 2151–61.
- [18] Madhi SA, Cunliffe NA, Steele D, Witte D, Kirsten M, et al. (2010) Effect of human rotavirus vaccine on severe diarrhea in African infants. *N Engl J Med* 362: 289–298.
- [19] Black RE, Cousens S, Johnson HL, Lawn JE, Rudan I, et al. (2010) Global, regional, and national causes of child mortality in 2008: a systematic analysis. *Lancet* 375: 1969–1987.
- [20] Parashar UD, Burton A, Lanata C, Boschi-Pinto C, Shibuya K, et al. (2009) Global mortality associated with rotavirus disease among children in 2004. *J Infect Dis* 200(Suppl 1): S9–S15.
- [21] Armah GE, Sow SO, Breiman RF, Dallas MJ, Tapia MD, et al. (2010) Efficacy of pentavalent rotavirus vaccine against severe rotavirus gastroenteritis in infants in developing countries in sub-Saharan Africa: a randomised, double-blind, placebo-controlled trial. *Lancet* 376: 606–614.
- [22] Patel MM, Parashar UD (2009) Assessing the effectiveness and public health impact of rotavirus vaccines after introduction in immunization programs. *J Infect Dis* 200(Suppl 1): S291–S299.
- [23] Linhares AC, Velazquez FR, Perez-Schael I, Saez-Llorens X, Abate H, et al. (2008) Efficacy and safety of an oral live attenuated human rotavirus vaccine against rotavirus gastroenteritis during the first 2 years of life in Latin American infants: a randomised, double-blind, placebo-controlled phase III study. *Lancet* 371: 1181–1189.