ROTAVIRUS SURVEILLANCE REPORT, SOUTH AFRICA, 2014-2015: A COMPARISON WITH PREVIOUS ROTAVIRUS SEASONS

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Executive summary

Since the introduction of the rotavirus vaccine into the national immunization program in August 2009, there has been a sustained reduction in both rotavirus and all-cause diarrhoeal disease in children <5 years in South Africa. Diarrhoeal surveillance at selected sentinel sites in 2014 and 2015 showed lower rotavirus prevalence and reduced absolute numbers of hospitalized diarrhoea cases in children <5 years compared to 2013. The genotypes circulating in 2014 included G1P[8] and G2P [4] and in 2015, G9P[8] and G3P[8] with no strain replacement evident. Surveillance also showed that genotypes circulating in the Western Cape consistently differed from the predominant types in the rest of the country. Despite the success of the rotavirus vaccine, protection is not complete and annual rotavirus seasons from May-September, affecting mostly children <2 years, should be expected. Health care providers are encouraged to prepare for the annual rotavirus season by ensuring adequate supplies of oral rehydration solution and intravenous fluids, and educating mothers on vaccination and signs of dehydration.

Introduction

Since South Africa introduced the rotavirus vaccine into the national immunization program in August 2009, the Centre for Enteric Diseases (CED) at the National Institute for Communicable Diseases (NICD) has been monitoring the impact of the vaccine at selected sentinel sites. In addition to describing the annual rotavirus season and prevalence of rotavirus disease, the surveillance system reports on the circulating genotypes each year.

Early rotavirus vaccine impact studies conducted at three of the sentinel sites between 2009 and 2011 indicated that the vaccine reduced rotavirus hospitalizations in children <5 years by 54% - 58% and lowered all-cause diarrhoea hospitalization by one-third.[1] Data from a vaccine effectiveness case-control study conducted between 2010 and 2012 showed that the vaccine was 40% effective after one dose and 57% effective after two doses in preventing rotavirus diarrhoea.[2] The study also revealed that vaccine effectiveness was similar in HIV-exposed versus HIV-unexposed children.[2] A further study looking at the temporal association of the introduction of the rotavirus vaccine and all-cause childhood diarrhoea hospitalizations at Chris Hani Baragwanath Academic Hospital revealed a 45-66% reduction in diarrhoea incidence in children <1 year and a 40-50% reduction in diarrhoea incidence in children in their second year of life.[3] This study also showed that reductions were observed in both HIV-infected and HIV-uninfected children.[3]

This report describes the timing, age distribution and circulating genotypes for the 2014 and 2015 rotavirus seasons in South Africa. The report compares the 2014 and 2015 seasons to the 2013 season to assess rotavirus prevalence per site, magnitude of the season and age distribution of cases. In addition, the timing of the rotavirus seasons and the genotypes circulating in each sentinel site were assessed between 2009 and 2015 to examine any potential changes that may have occurred since the introduction of the rotavirus vaccine.

Methods

During the period 2013 to 2015, the programme enrolled children <5 years of age admitted to sentinel hospitals with symptoms of three or more loose stools within a 24 hour period, following informed consent. The sentinel hospitals included Chris Hani Baragwanath Academic Hospital, Mapulaneng Hospital, Matikwane Hospital, Dr George Mukhari Hospital, Edendale Hospital and Red Cross Children's Hospital. Kimberley Hospital was included as a sentinel site in September 2014 and Pelonomi Hospital was established in April 2015. Case investigation forms including patient demographic, socioeconomic and clinical information, were completed by surveillance officers. A stool specimen was collected from each case for rotavirus screening.

Testing of stool samples was performed at the Centre for Enteric Diseases (CED), NICD, and at the MRC - Diarrhoeal Pathogens Research Unit (MRC-DPRU), Sefako Makgatho Health Sciences University. The stool samples were screened with the ProSpecT™ Rotavirus Microplate Assay (Oxoid, Basingstoke, UK).

Rotavirus positive samples were further characterized to determine the G and P genotype of each strain. Rotavirus dsRNA was extracted from each stool sample using the QIAamp Viral RNA Mini kit (Qiagen, Hilden, Germany) and genotyped using standardized RT-PCR methods and primers for G-specific (G1, G2, G3, G4, G8, G9, G10, G12) and P-specific (P[4], P[6], P[8], P[9], P[10], P[11], P[14]) genotypes.[4]

The start of the rotavirus season was defined as a rotavirus detection rate of above 20% for two consecutive weeks. The end of the season was defined as a rotavirus detection rate of below 20% for two consecutive weeks. The rotavirus prevalence per site, magnitude of the season and age distribution of the cases was determined for the 2014 and 2015 rotavirus seasons. The 2013 season was also included in this analysis for comparison. The timing and duration of the rotavirus seasons as well as the predominant genotypes per site were compared between 2009 and 2015 to determine changes (if any) since the introduction of the rotavirus vaccine in August 2009.

Results

A total of 954 stool specimens was collected in 2014 with a further 838 collected in 2015 (Table 1). There was insufficient stool collected from 12% (256/2048) of diarrhoea cases preventing laboratory screening of them. Rotavirus was detected in 23% (217/954) of cases in 2014 and in 20% (170/838) of cases in 2015.

The start of the rotavirus season is usually in May although the season can start as early as March (Table 2, Figure 1). The end of the rotavirus season is usually in September although the season may terminate as early as August and as late as October (Table 2, Figure 1). The median duration of the rotavirus season is 20 weeks and ranges from 28 weeks in 2013 to 15 weeks in 2012 (Table 2). The maximum detection rate has decreased from 82% in 2009 to 53% in 2015 with the peak week of detection in June. The peak week of detection (week 35, 24 Aug) was late in 2015 compared to previous years (Table 2).

Table 1: Total numbers of stools collected and rotavirus results per surveillance site, South Africa, 2014 and 2015. (The 2013 rotavirus season has been included for comparison.)

Site	Rotavirus positive (%)		
	2015	2014	2013
Chris Hani Baragwanath	57/256 (22)	94/337 (28)	87/267 (33)
Mapumaleng	9/41 (22)	19/68 (28)	16/77 (21)
Matikwane	19/65 (29)	1/46 (2)*	29/114 (25)
Dr George Mukhari	22/108 (20)	28/115 (24)	26/134 (19)
Edendale	12/40 (30)	22/56 (39)	23/73 (32)
Red Cross Children's	19/128 (19)	51/304 (17)	149/434 (34)
Kimberley	13/55 (24)	2/28 (7)§	N/A
Polokwane	2/32 (6)#	N/A	N/A
Pelonomi	17/113 (15)#	N/A	N/A
Total	170/838 (20)	217/954 (23)	330/1099 (30)

* No surveillance officer between June and December 2014
§ Surveillance from September to December 2014
# Surveillance started in April/May 2015

Table 2: Characteristics of rotavirus seasons in South Africa between 2009 and 2015.

Year	Start week	End Week	Duration	Maximum detection rate	Peak week	Prevalence
2009	16 (14 Apr)	40 (4 Oct)	25	82% (37/45)	21 (18 May)	47% (428/917)
2010	20 (17 May)	36 (12 Sep)	17	60% (18/30)	24 (14 Jun)	25% (323/1317)
2011	19 (9 May)	39 (2 Oct)	21	72% (18/25)	25 (20 Jun)	27% (339/1246)
2012	21 (21May)	35 (2 Sep)	15	63% (15/24)	25 (18 Jun)	21% (202/963)
2013	12 (18 Mar)	39 (23 Sep)	28	61% (22/36)	30 (22 Jul)	30% (330/1099)
2014	16 (14 Apr)	34 (24 Aug)	19	65% (30/44)	24 (30 Jun)	23% (217/954)
2015	20 (11 May)	39 (27 Sep)	20	53% (9/16)	35 (24 Aug)	20% (170/838)

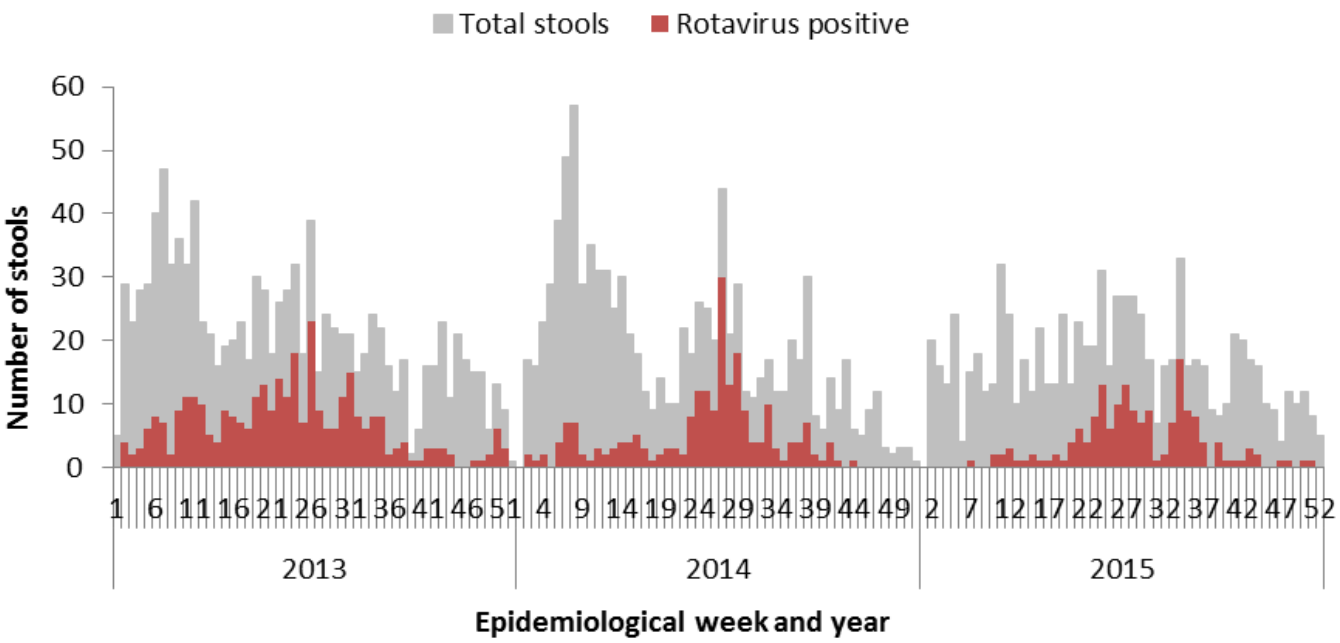

Figure 1: Numbers of stool specimens screened and rotavirus cases by epidemiological week between 2013 and 2015, South Africa.

The ages of children infected by rotavirus have remained relatively constant with children in the 7-9 month age group primarily affected (Table 3). The genotyping of the rotavirus strains revealed that G1P[8] (29%, 64/217) and G2P[4] (24%, 51/217) strains were predominant (Table 4) in 2014. In 2015, these strains were replaced by G9P[8] (67%, 99/148) and G3P[8] (16%, 24/148; Table 5). Analyses of genotype distribution by site between 2009 and 2015 showed that genotypes circulating in the Western Cape sentinel site differed from the rest of the country (Table 6). Similar observations were noted for sites in the Northern Cape and Free State provinces for 2015 (Table 6).

Table 3: Age distribution of children with rotavirus infections in 2014 and 2015, South Africa. The 2013 season has been included for comparison.

Age range (in months)	Rotavirus positive (%)		
	2015	2014	2013
0-3	11/83 (13)	36/153 (24)	35/150 (23)
4-6	30/ 133 (23)	27/134 (20)	70/198 (35)
7-9	37/125 (30)	51/154 (33)	69/185 (37)
10-12	26/103 (25)	40/133 (30)	57/172 (33)
13-18	26/132 (20)	30/156 (19)	61/183 (33)
19-24	8/50 (16)	20/101 (20)	20/95 (21)
>24	9/100 (9)	10/118 (8)	18/116 (16)
Unknown	23/112 (21)*	3/5 (60)	0 (0)
Total	170/838 (20)	217/954 (23)	330/1099 (30)
Predominant genotypes	G9P[8] G3P[8]	G1P[8] G2P[4]	G2P[4] G9P[8]

*Age data for Dr George Mukhari Hospital missing for 2015

Table 4: Rotavirus strains (G and P genotypes) detected at sentinel sites in South Africa in 2014. The predominant strains in each site are shaded grey.

Genotype	CHBAH		MP		DGM		EdH		RCCH		Total
	n	%	n	%	n	%	n	%	n	%	
Rotavirus strains covered by the monovalent vaccine											
G1P[8]	36	38	7	37	16	57	2	9	3	6	64
G3P[8]	10	11	3	16	0	0	1	5	5	10	19
G9P[8]	19	20	0	0	2	7	0	0	0	0	21
G12P[8]	1	1	0	0	0	0	1	5	0	0	2
Total	66	70	10	53	18	64	4	18	8	16	106
Rotavirus strains not covered by the monovalent vaccine											
G2P[4]	2	2	2	11	1	4	8	36	38	75	51
G2P[6]	17	18	6	32	4	14	6	27	1	2	34
G9P[4]	1	1	0	0	0	0	0	0	0	0	1
G9P[6]	0	0	1	5	3	11	0	0	0	0	4
Total	20	21	9	47	8	29	14	64	39	76	90
Mixed and non-typeable rotavirus strains											
Mixed	4	4	0	0	2	7	0	0	2	4	8
Not typed	4	4	1	5	0	0	4	18	2	4	11
Total	8	9	1	5	2	7	4	18	4	8	19
Grand total	94	43	20	9	28	13	22	10	51	24	215*

CHBAH = Chris Hani Baragwanath Academic Hospital, MP = Mapulaneng and Matikwane Hospitals, DGM = Dr. George Mukhari, EdH = Edendale Hospital and RCCH = Red Cross Children's Hospital.
*Two rotavirus-positive specimens from Kimberley Hospital were typed as G1P[8] and G2P[6].

Table 5: Rotavirus strains (G and P genotypes) detected at sentinel sites in South Africa in 2015. The predominant strains in each site are shaded grey.

Genotype	CHBAH		MP		EdH		RCCH		KBH		PLH		Total
	n	%	n	%	n	%	n	%	n	%	n	%	
Rotavirus strains covered by the monovalent vaccine													
G1P[8]	0	0	0	0	3	25	0	0	0	0	0	0	3
G3P[8]	0	0	1	4	0	0	7	37	8	62	8	47	24
G9P[8]	54	95	20	71	8	67	5	26	3	23	7	41	97
G12P[8]	1	2	6	21	0	0	0	0	0	0	0	0	7
Total	55	96	27	96	11	92	12	63	11	85	15	88	131
Rotavirus strains not covered by the monovalent vaccine													
G2P[4]	1	2	0	0	0	0	6	32	2	15	2	12	11
G2P[6]	0	0	1	4	0	0	1	5	0	0	0	0	2
Total	1	2	1	4	0	0	7	37	2	15	2	12	13
Mixed and non-typeable rotavirus strains													
Mixed	1	2	0	0	0	0	0	0	0	0	0	0	1
Not typed	0	0	0	0	1	8	0	0	0	0	0	0	1
Total	1	2	0	0	1	8	0	0	0	0	0		2
Grand total	57		28		12		19		13		17		146*

CHBAH = Chris Hani Baragwanath Academic Hospital, MP = Mapulaneng and Matikwana Hospitals, EdH = Edendale Hospital, RCCH = Red Cross Children's Hospital, KBH = Kimberley Hospital and Pelonomi Hospital.
*Genotyping data from Dr George Mukhari Hospital is missing for 2015 (n=22).
*Two rotavirus-positive specimens from Polokwane Hospital were genotyped G9P[8]

Table 6: Annual predominant rotavirus genotype compared to the predominant genotypes circulating in each site by year. The strains in each site that differ from the predominant genotype are shaded grey.

Year	2009	2010	2011	2012	2013	2014	2015
Predominant genotype	G1P[8] 46%	G1P[8] 22%	G12P[8] 48%	G12P[8] 41%	G2P[4] 54%	G1P[8] 30%	G9P[8] 67%
Site							
CHBAH	G1P[8] 36%	G1P[8] 35%	G12P[8] 42%	G12P[8] 27%	G2P[4] 70%	G1P[8] 38%	G9P[8] 95%
MP+MK	G1P[8] 55%	G2P[4] 28%	G12P[8] 47%	G12P[8] 47%	G2P[4] 84%	G1P[8] 35%	G9P[8] 71%
DGM	G1P[8] 58%	G2P[4] 30%	G9P[8] 36%	G12P[8] 67%	G2P[4] 88%	G1P[8] 57%	ND
EDH	ND	G1P[8] 21%	G12P[8] 65%	G8P[4] 50%	G2P[4] 83%	G2P[4] 36%	G9P[8] 67%
RCCH	ND	G12P[8] 40%	G12P[8] 54%	G2P[4] 62%	G9P[8] 77%	G2P[4] 75%	G3P[8] 37%
KBH	ND	ND	ND	ND	ND	ND	G3P[8] 62%
PLH	ND	ND	ND	ND	ND	ND	G3P[8] 47%

CHBAH = Chris Hani Baragwanath Academic Hospital, MP = Mapulaneng and Matikwana Hospitals, EdH = Edendale Hospital, RCCH = Red Cross Children's Hospital, KBH = Kimberley Hospital and Pelonomi Hospital.

Discussion

The South African rotavirus seasons in 2014 and 2015 were lower than the comparatively high season of 2013. These annual fluctuations are considered normal after rotavirus vaccine introduction. In fact, the average rotavirus detection rates in the US vary between 10% in high years and 4% in low years.[5] In addition, certain regions in the US have reported differences in rotavirus prevalence between high and low years of up to 12%.[5] These increases are, however, substantially below pre-vaccine rotavirus levels and the absolute numbers of hospitalized rotaviruses cases has decreased.

Analyses of the timing of the rotavirus seasons suggest that the start of the season shifts later in four year cycles, returning to an earlier start during a comparatively high year. Furthermore, rotavirus seasons are shorter (15-21 weeks; 2010-2012, 2014, 2015) in low seasons compared to high seasons (25-28 weeks; 2009 and 2013).

The age group with the highest detection rate for rotavirus amongst diarrhoea patients <5 years remained in the children 7-9 months old age group, even in low years although the absolute numbers of cases tends to decrease. Children within this age group should have been vaccinated and factors including reduced vaccine effectiveness, incomplete protection against certain genotypes and the presence of concomitant enteric pathogens may contribute to the development of diarrhoeal disease. Despite the success of the rotavirus vaccine in reducing diarrhoea in children <2 years, protection is not complete and healthcare providers are encouraged to prepare for the annual rotavirus season by educating mothers with children < 2 years of age on the signs of dehydration in children with diarrhoea and ensuring adequate supplies of oral rehydration solution and intravenous fluids.

The current genotyping results continue to demonstrate that strain replacement after the introduction of the rotavirus vaccine is not present. Various rotavirus genotypes continue to circulate in an annual or biannual manner with an inability to predict the predominant genotype from one year to the next. An interesting observation was that the genotypes circulating in the

Western Cape site are often different from those circulating in the rest of the country. The season in the Western Cape also starts earlier (March/April) compared to the rest of the country (May). These results indicate that the predominant genotype may not always be circulating across South Africa and a proportion of rotavirus-positive specimens from a site without sentinel surveillance should be genotyped to detect any challenges associated with incomplete protection.

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