ROTAVIRUS SURVEILLANCE REPORT, SOUTH AFRICA, 2013

Nicola Page[1,2], Francinah Mapuroma[1], Mapaseka Seheri[3], Tersia Kruger[1], Ina Peenze[3], Sibongile Walaza[4], Cheryl Cohen[4], Michelle Groome[5,6], Shabir Madhi[5,7]

[1]Centre for Enteric Diseases, NICD
[2]South African Field Epidemiology and Laboratory Training Programme, NICD
[3]Diarrhoeal Pathogens Research Unit, University of Limpopo Medunsa Campus
[4]Centre for Respiratory Diseases and Meningitis, NICD
[5]Department of Science and Technology/National Research Foundation: Vaccine Preventable Diseases, University of the Witwatersrand
[6]Medical Research Council: Respiratory and Meningeal Pathogens Research Unit, University of the Witwatersrand
[7]National Institute for Communicable Diseases

Introduction

South Africa introduced the rotavirus vaccine into the national immunization program in August 2009. Since then, monitoring of the rotavirus vaccine has continued at six sentinel surveillance sites in four provinces. The main objectives of the surveillance programme are to describe the epidemiology of rotavirus infection and to monitor the impact of the rotavirus vaccine since introduction on the incidence of diarrhoeal disease.

Between 2009 and 2011, analysis from three of the six sites indicated that the vaccine reduced rotavirus hospitalizations in children under five years by 54%-58% and lowered all-cause diarrhoea hospitalization by a 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, an encouraging result for the introduction of the vaccine in high-HIV prevalent countries in Africa. Results from the rotavirus surveillance for 2013 are reported below.

Methods

The programme enrolled children under five years of age who were admitted to the 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 Hospital, Mapulaneng Hospital, Matikwane Hospital, Dr George Mukhari Hospital, Edendale Hospital and Red Cross Children's Hospital. Case investigation forms including patient demographic, socioeconomic and clinical information were completed by surveillance officers. A stool sample was collected from each case for rotavirus screening.

Testing of stool samples was performed at the Virology Division, Centre for Enteric Diseases (CED), NICD, and at the Diarrhoeal Pathogens Research Unit (DPRU), University of Limpopo Medunsa Campus. 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 real-time polymerase chain reaction (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.[3]

Results

A total of 1,224 stool samples was collected in 2013 (table 1). Laboratory screening could not be performed in 15% (183/1,224) of diarrhoea cases owing to insufficient collection of stool. Rotavirus was detected in 28% (292/1,041) of cases, ranging from 19% (26/134) at Dr George Mukhari Hospital to 31% at Edendale (21/68) and Red Cross Children's Hospitals (131/417).

Table 1: Total stools from diarrhoea cases collected for rotavirus detection (children under five years), number of stools insufficient for testing and rotavirus results for 2011–2013 by sentinel hospital.

Site	Total	Insufficient (%)	Rotavirus positive		
			2013 (%)	2012 (%)	2011 (%)
Chris Hani Baragwanath	311	72 (23)	71/239 (30)	39/213 (18)	45/288 (16)
Mapumaleng	84	10 (12)	16/74 (22)	16/70 (23)	12/48 (25)
Matikwane	120	11 (9)	27/109 (25)	25/139 (18)	20/99 (20)
Dr George Mukhari	161	27 (17)	26/134 (19)	27/156 (17)	45/198 (23)
Edendale	76	8 (11)	21/68 (31)	13/57 (23)	28/93 (30)
Red Cross Children's	472	55 (12)	131/417 (31)	70/359 (19)	152/497 (31)
Total	1,224	183 (15)	292/1,041 (28)	190/994 (19)	302/1,223 (25)

The start of a rotavirus season is defined as a rotavirus detection rate of above 20% for two consecutive weeks. The end of a season is defined as a rotavirus detection rate of below 20% for two consecutive weeks. The 2013 rotavirus season started in week 12 (18th March 2013) and ended in week 39 (23rd September 2013), with the peak in week 30 (22nd July 2013) during which 61% (22/36) of stools collected were positive for rotavirus (figure 1). A higher proportion of rotavirus cases was detected in the 2013 season (30%; 292/1,041) compared to 2012 (19%; 190/994).

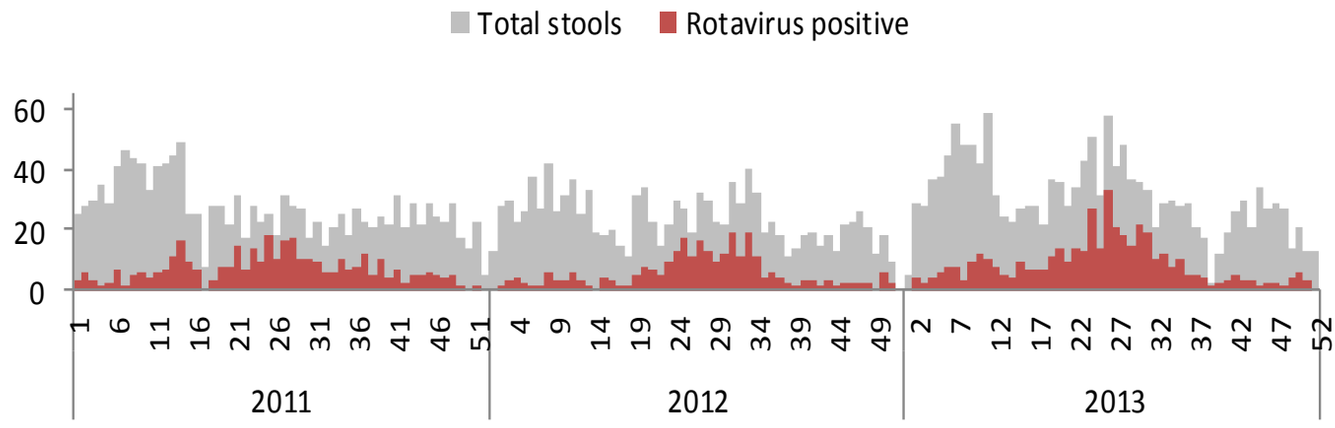

Figure 1: Total number of stool specimens screened for rotavirus and positive rotavirus cases by epidemiological week, 2011-2013.

The age of the children affected in 2013 ranged between 0 and 58 months with the majority of children affected between 4 and 9 months of age (table 2). The ages of children infected by rotavirus have remained relatively constant although differences are evident in the 0-3 age group in high rotavirus years (2011 and 2013). Preliminary analysis of the vaccination status of children with rotavirus detected in their stool revealed that 70% (203/292) had received two doses of vaccine prior to the diarrhoeal episode. Other enteric viruses were detected in 2% to 15% of rotavirus-positive cases (data not shown)

Table 2: Age distribution of children with rotavirus infections, 2011–2013, and predominant rotavirus genotypes by year.

Age range (in months)	Rotavirus positive (%)		
	2013	2012	2011
0-3	34 (12)	16 (8)	45 (15)
4-6	60 (21)	35 (18)	54 (18)
7-9	63 (22)	38 (20)	65 (22)
10-12	51 (17)	41 (22)	40 (13)
13-18	47 (16)	34 (18)	64 (21)
19-24	16 (5)	13 (7)	18 (6)
>24	17 (6)	12 (6)	13 (4)
Unknown	4 (1)	1 (1)	3 (1)
Total	292 (28)	190 (19)	302 (25)
Predominant genotypes	G2P[4] G9P[8]	G12P[8] G8P[4] G2P[4]	G12P[8] G9P[8]

The genotyping of the rotavirus strains revealed that the G2P[4] (47%; 137/292) and G9P[8] (39%; 115/292) strains were predominant (table 3). With the exception of Red Cross Children's Hospital, G2P[4] strains predominated in all sites in 2013.

Table 3: Rotavirus strains (G and P genotypes) detected at sentinel sites in South Africa, 2013. The predominant strains at each site are shaded grey. CHBH = Chris Hani Baragwanath Hospital, MP = Mapulaneng, MK = Matikwana, DGM = Dr. George Mukhari, EdH = Edendale Hospital and RCCH = Red Cross Children's Hospital.

Genotype	CHBH		MP		MK		DGM		EdH		RCCH		Total
	n	%	n	%	n	%	n	%	n	%	n	%	
Rotavirus strains covered by the monovalent vaccine													
G1P[4]	1	1	0	0	0	0	0	0	0	0	0	0	1
G3P[8]	0	0	0	0	0	0	0	0	0	0	7	5	7
G9P[8]	9	13	2	13	1	4	1	4	1	5	101	77	115
Total	10	14	2	13	1	4	1	4	1	5	108	82	123
Rotavirus strains not covered by the monovalent vaccine													
G2P[4]	49	69	14	88	22	81	22	85	19	90	11	8	137
G2P[6]	4	6	0	0	0	0	0	0	0	0	4	3	8
G3P[4]	1	1	0	0	0	0	0	0	0	0	0	0	1
G8P[4]	0	0	0	0	0	0	0	0	1	5	2	2	3
G9P[4]	0	0	0	0	0	0	0	0	0	0	1	1	1
G9P[6]	0	0	0	0	0	0	1	4	0	0	3	2	4
Total	54	76	14	88	22	81	23	88	20	95	21	16	154
Mixed and non-typeable rotavirus strains													
Mixed	3	4	0	0	0	0	1	4	0	0	0	0	4
Not typed	0	0	0	0	0	0	1	4	0	0	0	0	1
Negative	4	6	0	0	4	15	0	0	0	0	2	2	10
Total	7	10	0	0	4	15	2	8	0	0	2	2	15
Grand total	71		16		27		26		21		131		292

Discussion

The incidence of rotavirus cases recorded during the 2013 South African rotavirus season increased by 54% compared to the 2012 season (292 cases versus 190 cases) but was 3% less than the 2011 season (292 cases versus 302 cases). Most of the children affected were between 4 and 9 months of age (42%; 123/292) even though 70% of them had received two doses of the vaccine. Various factors including reduced vaccine effectiveness, the genotype of the circulating strain and the presence of concomitant enteric pathogens may have contributed to diarrhoeal disease in this age group. Initially, these results were a cause for concern. However, further investigation of rotavirus epidemiology following vaccine introduction in other countries allayed fears concerning vaccine performance. The rotavirus vaccine was introduced into the national immunization programme in the United States (US) in 2006. Since vaccine introduction, the number of rotavirus-positive tests declined by 74%-90% compared to pre-vaccine baseline data. A trend that emerged during the monitoring of five post-vaccine seasons in the US (2007 -2012) was a pattern of biennial increases in rotavirus activity. These increases were, however, substantially below pre-vaccine rotavirus levels. The average rotavirus detection rate in the US varied between 10% in "high" years and 4% in "low" years. Some areas of the US have reported differences in rotavirus prevalence between high and low years of up to 12%.[4] Similarly, the 2013 rotavirus season in South Africa may represent a

biennial "high" season. The South African "high" season may also be greater than the "high" seasons recorded in the US because the vaccine effectiveness in South Africa is only 57% after two doses.[2] This is substantially lower than the 91-92% vaccine effectiveness reported in the US.[4]

The recent case-control study described by Groome et al.[2] demonstrated vaccine effectiveness of 71% against G12P[8] strains, 62% against strains with the G or P in the vaccine formulation and 52% against strains without a G or P in the vaccine formulation. The circulation of the G2P[4] strains in 2013 may have resulted in slightly lower vaccine effectiveness compared to the 2012 season. This case-control study also found little difference in vaccine effectiveness between cases where only rotavirus was detected versus cases where rotavirus and an additional enteric virus was found.[2] These results suggest that concomitant infections were not erroneously attributed to rotavirus and that reduced vaccine effectiveness is due to other factors. However, the study did not evaluate the effect of bacterial and parasitic enteric pathogens on vaccine effectiveness calculations and this line of investigation should be pursued in future.

Conclusion

It is likely that the South African 2013 rotavirus season signified the biennial "high" season, similar to trends seen in the US after rotavirus vaccine introduction. However, due to lower vaccine efficacy and effectiveness, the excess in the number of rotavirus cases and prevalence may be greater than the levels in the US. Continued monitoring of the rotavirus seasons between 2014 and 2017 will allow calculation of excess rotavirus cases that can be expected during "high" seasons in the South African population. Health facilities in South Africa are advised to be prepared for the 2015 rotavirus season, predicted to reach a peak in June 2015.

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