Rotavirus Burden among Children in the Newly Independent States of the Former Union of Soviet Socialist Republics: Literature Review and First-Year Results from the Rotavirus Surveillance Network

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Background. Data on rotavirus burden among children in the 15 newly independent states of the former Union of Soviet Socialist Republics, particularly contemporary data from poorer countries, are not widely available. These data are desired by policy makers to assess the value of rotavirus vaccination, especially since the GAVI Alliance approved financial support for the region's eligible countries. The Rotavirus Surveillance Network was established to provide these data.

Methods. We reviewed the region's literature on rotavirus burden. We established an active surveillance network for rotavirus and analyzed data from 2007 from 4 sentinel hospitals in 3 countries (Georgia, Tajikistan, and Ukraine) that were collected using standardized enrollment and stool sample testing methods.

Results. Specimens for rotavirus testing were collected before 1997 in most studies, and the majority of studies were from 1 country, the Russian Federation. Overall, the studies indicated that ~33% of hospitalizations for gastroenteritis among children were attributable to rotavirus. The Rotavirus Surveillance Network documented that 1425 (42%) of 3374 hospitalizations for acute gastroenteritis among children aged <5 years were attributable to rotavirus (site median, 40%). Seasonal peaks (autumn through spring) were observed. Genotype data on 323 samples showed that G1P[8] was the most common type (32%), followed by G9P[8] (20%), G2P[4] (18%), and G4P[8] (18%). Infections due to G10 and G12 and mixed infections were also detected.

Conclusions. The burden of rotavirus disease in the newly independent states is substantial. Vaccines should be considered for disease prevention.

Worldwide, rotavirus is the most common cause of severe acute gastroenteritis (AGE) among children aged <5 years, resulting in an estimated 527,000 deaths, 2 million hospital admissions, and 25 million outpatient visits annually [1, 2]. Despite global efforts to promote breastfeeding, oral rehydration treatment, water purification, and improved sewage handling, the diarrheal disease burden attributable to rotavirus infection has not decreased significantly over the past decade [1, 3]. Thus, widespread use of either of the 2 currently available rotavirus vaccines, the monovalent human rota-

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virus vaccine (Rotarix; GlaxoSmithKline) or the pentavalent bovine-human reassortant vaccine (RotaTeq; Merck), is considered to be the best strategy for reducing morbidity and mortality associated with rotavirus. Studies on vaccine efficacy that were conducted in the Americas and Europe have prompted the World Health Organization (WHO) to recommend rotavirus vaccination in these 2 regions [4].

These rotavirus vaccines have been licensed in >100 countries throughout the world, and some countries have introduced the vaccines in their national immunization programs (eg, countries in Latin America, the European Union, and the United States). The 15 newly independent states (Armenia, Azerbaijan, Belarus, Estonia, Georgia, Kazakhstan, Kyrgyzstan, Latvia, Lithuania, Republic of Moldova, Russian Federation, Tajikistan, Turkmenistan, Ukraine, and Uzbekistan [Estonia, Latvia, and Lithuania have become members of the European Union]) that emerged from the former Union of Soviet Socialist Republics could potentially introduce rotavirus vaccine in the near future. Over 17 million children aged <5 years reside in these countries [5]. Eight of the countries (Armenia, Azerbaijan, Georgia, Kyrgyzstan, Republic of Moldova, Tajikistan, Ukraine, and Uzbekistan) are eligible for financial support from the GAVI Alliance (formerly known as the Global Alliance for Vaccines and Immunization) to purchase new vaccines, including rotavirus vaccine. Policy makers from each of these countries will need to assess the value and cost of introducing rotavirus vaccine for children. One critical component of the decision-making process will be understanding the burden of severe rotavirus disease. Contemporary data on the burden and epidemiology of rotavirus disease in the region and the genotypes of circulating strains are limited.

To provide these data, the WHO, PATH, and the Centers for Disease Control and Prevention helped Ministries of Health establish the Rotavirus Surveillance Network (RSN) in GAVI-eligible countries in the WHO European Region. This network will compliment the activities in the rotavirus strain surveillance system established in Western Europe (EUROROTANET). Data from RSN will also raise awareness of rotavirus disease among persons who frequently care for infected children but who are not able to identify the pathogen, including clinicians, parents, and managers of public health programs. In addition, the RSN will be a valuable platform for assessing rotavirus vaccine performance after introduction and for monitoring changes in strain distribution over time.

In this article, we review studies published from 1980 through 2007 that investigated rotavirus gastroenteritis among children in the newly independent states. We also present data from the first year of surveillance for rotavirus gastroenteritis among hospitalized children that was conducted by 3 GAVI-eligible newly independent states in the RSN.

METHODS

Literature Review

We attempted to identify all articles published in the scientific and medical literature from 1 January 1980 through 30 September 2007 that described the rotavirus burden among children in the newly independent states. Articles in various languages of the region were included. PubMed and EMBASE were searched using the terms "rotavirus," "gastroenteritis," "diarrhea," "disease burden," "surveillance," and "infection," as well as country names. Bibliographies of the articles were reviewed for additional relevant publications, and country technical reports were reviewed when available. For this review, we included studies that reported rotavirus detection results for a minimum of 100 stool samples from children aged <14 years (a standard age-group classification used in publications from this region) that were tested for rotavirus with use of electron microscopy, latex agglutination, enzyme immunoassay (EIA), polyacrylamide gel electrophoresis, or reverse-transcription polymerase chain reaction (RT-PCR). For studies that reported results with use of >1 detection method, we reported the results of testing with only 1 method with use of the following hierarchy: (1) RT-PCR, (2) EIA, (3) polyacrylamide gel electrophoresis, and (4) electron microscopy or latex agglutination. When publications from the same investigators and location greatly overlapped with regard to the period of data collection, the study with the most recent data or with more information on the burden of disease was selected. Studies that reported that the duration of sample collection was <3 months were excluded.

Studies were classified on the basis of severity of disease (inpatient, outpatient, and combined) and duration of the sample collection period (≥12 months, 3–11 months, or not specified). From each publication, we extracted the proportion of cases of gastroenteritis due to rotavirus. When the value was not explicitly stated, we calculated it by dividing the number of rotavirus-positive specimens by the total number of specimens tested. The results were categorized by country, age group (<2, <5, and <14 years of age), and calendar month, as available. Median estimates of the proportion of gastroenteritis cases attributable to rotavirus were calculated for the studies overall. For studies that reported results for >1 age group, we used the result from the group closest to age <5 years for the median calculation.

RSN

Proposals for establishing an RSN site(s) were solicited by the WHO Regional Office for Europe from the Ministries of Health of the region's GAVI-eligible countries. Consultants visited the countries that expressed interest, to help determine the capability of site staff to perform rotavirus surveillance and rotavirus EIA testing, assess equipment and budget needs, and provide training. Rotavirus surveillance was established at sentinel hos-

pitals in Georgia, Tajikistan, and Ukraine in late 2006 (Figure 1). The RSN results reported here are from the 2007 calendar year. Surveillance was also established in 3 other countries (in Azerbaijan, supported by the RSN; in Kyrgyzstan and Uzbekistan, supported by the Centers for Disease Control and Prevention and Norwegian Institute of Public Health). At the time of submission, data from these countries from 2007 were not available.

Georgia. Surveillance was established at the Center of Infectious Pathology in the capital, Tbilisi. This hospital cares for children with severe gastroenteritis from all regions of Georgia, but mainly from eastern Georgia. Rotavirus testing was performed at the National Center for Diseases Control and Medical Statistics.

Tajikistan. Surveillance was established at Dushanbe City Children's Hospital for Infectious Diseases, the major children's hospital for infectious diseases in Tajikistan. Located in the country's capital, this hospital provides care to children with gastroenteritis from Dushanbe and suburban regions. Rotavirus testing was performed at the Research Institute of Preventive Medicine.

Ukraine. Surveillance was established in the 2 major cities of Ukraine, Kyiv and Odessa. In the capital Kyiv, surveillance was performed at the City Clinical Children's Hospital #1 of the National Medical Academy of Postgraduate Study, which provides care to children with gastroenteritis from 7 of 10 districts of the city. Rotavirus testing was performed at the Central Sanitary Epidemiological Station, Viral and HIV/AIDS Laboratory. In Odessa, surveillance was established at the City Children's Infectious Diseases Hospital of the National Medical University, which cares for all children with severe gastroenteritis in the region. Rotavirus testing was performed at the Central Immunology and Virology Laboratory of the Sanitary Epidemiological Station of Odessa.

Surveillance and Laboratory Methods

Surveillance methods followed those outlined in the WHO generic protocol for hospital-based surveillance of rotavirus gastroenteritis [6]. On days when surveillance was scheduled to be conducted, hospital admission logs were reviewed to identify all children aged <60 months who were admitted for AGE, defined as the occurrence of at least 3 watery or looser-than-normal stools in a 24-h period, with a duration of ⩽7 days on the day of hospital admission. Children who were hospitalized for at least 1 night were eligible for enrollment. Standard demographic and clinical data were collected on each enrolled child; in addition, site investigators could adapt data collection forms to gather additional information (eg, use of oral rehydration treatment before hospitalization) that they deemed valuable. From each child, a whole stool sample was collected in a screw-top container within 48 h of hospital admission. Stool samples were refrigerated at the hospital until delivery to the testing lab; samples were delivered in a cold box usually once weekly.

At the testing laboratory, stool samples were refrigerated for a maximum of 1 month until testing was performed. Stool samples that could not be tested within 1 month after collection

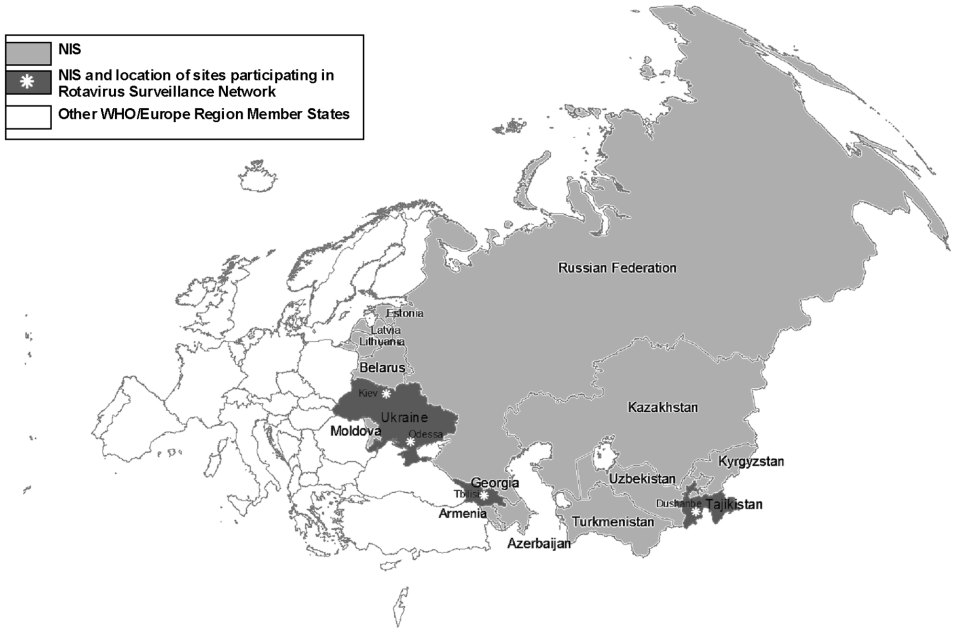

Figure 1. Location of 4 sites participating in the Rotavirus Surveillance Network. NIS, newly independent states; WHO, World Health Organization.

were aliquoted and frozen at −20°C for a maximum of 4 months until testing could be performed. Rotavirus detection was performed by specific laboratory personnel involved in the RSN by use of commercial IDEIA enzyme-linked immunosorbent assay kits (OXOID [Ely]). Testing was performed according to the manufacturer's instructions, which were translated into the Russian language. Results were determined photometrically using EIA plate readers and were reported to the hospital surveillance coordinator. Whenever possible, a second aliquot of each stool specimen was stored at the testing laboratory at −20°C to allow further testing, including rotavirus strain identification. In mid-2007, ~80 samples positive for rotavirus and 20 samples negative for rotavirus by EIA were randomly selected at each site and sent to the Enteric Virus Unit, Virus Reference Department, Centre for Infections, Health Protection Agency, in London, United Kingdom, to assess EIA performance at the originating laboratory and to characterize the circulating strains. Strain typing was performed by RT-PCR using established methods [7]. All surveillance protocols were submitted to the WHO Ethical Review Committee and were deemed to be exempted from review.

RESULTS

Literature Review

Burden of disease. We identified and reviewed 89 publications from the 15 countries. Eighty- two studies (92%) were published in Russian, 3 (4%) in a country's non-Russian native language, and 4 (4%) in English. A total of 32 publications from 8 countries met our inclusion criteria (Tables 1 and 2). Most publications (21 [66%] of 32) were from 1 country, the Russian Federation. Samples for rotavirus testing were collected within the most recent decade (1997–2007) in only 6 (19%) of the studies. Rotavirus was detected using EIA in 15 publications (47%), electron microscopy in 12 (38%), RT-PCR in 3 (9%), RNA–polyacrylamide gel electrophoresis in 1 (3%), and latex agglutination in 1 (3%).

Among the 17 studies that included only inpatients for which samples were collected over a period ⩾12 months, the median proportion of rotavirus detection was 33% (range, 16%–65%) (Table 1). For the 5 studies involving inpatients that had a sample collection period of 3–11 months, the median proportion of rotavirus detection was 37% (range, 24%–67%) (Table 2). Seven additional studies involving inpatients did not report the duration of the sample collection period (median detection, 30%; range, 17%–74%). Finally, 3 other studies included outpatients or did not specify patient type (Table 2).

Seasonality. Three studies provided rotavirus detection rates by calendar month (Figure 2); higher detection was observed from December through March (Belarus) [8], October through March (northwestern Russian Federation) [17], and January through April (western Russian Federation) [23]. Other studies did not provide detailed results but described that higher rotavirus detection occurred during particular seasons or months: autumn (Tajikistan) [39], autumn and winter (Georgia [11, 12] and western Russian Federation [16]), autumn through spring (Moldova) [14], winter (northwestern Russian Federation) [26, 28, 31, 33], or winter and spring (western and southwestern Russian Federation [19, 20], Moldova [15], and Belarus [9, 40]).

Rotavirus serotypes/genotypes. The results of 4 studies that characterized rotavirus strains with use of G serotyping or G and P genotyping assays are summarized in table 3. G1 was the most common strain identified in 3 studies [10, 21, 22]. In a study from Birobidzhan in eastern Russian Federation [38], almost all isolates were G3P[8]. One additional study [41] described the changes in strain types in Nizhniy Novgorod (western Russian Federation) over a 19-year period: G1P[8] predominated in the mid-1980s, 3 different genotypes (G1P[8], G3P[8], and G4P[8]) were frequently detected during the first half of the 1990s, and G1P[8] again predominated during the late 1990s and early 2000s.

RSN

Burden of disease. In 2007, 3374 (67%) of the 5008 children eligible for enrollment were recruited at the 4 sentinel hospitals in the 3 countries combined (Table 4). The mean monthly proportion of children eligible for enrollment who were enrolled in the surveillance system ranged from 45% to 92%, depending on the site. Overall, rotavirus was detected in 1425 (42%) of 3374 samples from the enrolled children (those aged <5 years and hospitalized for AGE). Rotavirus was detected in 38% of enrolled children in Tajikistan, 40% in Georgia, and 41% and 49% in Odessa and Kyiv (Ukraine), respectively (mean site detection rate, 42%; median, 40%). Age (in years) was available from Ukraine and Georgia sites. Of the hospitalized children with rotavirus aged <5 years, 740 (64%) of 1158 were aged <2 years.

Seasonality. Hospitalizations for rotavirus gastroenteritis were detected year-round at each site, with variability by season (Figure 2). In Tajikistan, peak detection (58%–65%) occurred from October through December. Detection was highest during the winter and spring months at the other 3 sites (Georgia: 52%–64% during December–April; Kyiv, Ukraine: 70% in December and 54%–76% during February–May; Odessa, Ukraine: 61%-63% in November and December and 41%–46% during March–May). Rotavirus accounted for ⩾14% of cases of AGE among enrolled children during each month at each site, except in Georgia during June, when it accounted for only 6%. In Odessa, rotavirus was detected in ⩾23% of samples from children each month.

Rotavirus genotypes. Strains were able to be typed in 323 samples. The most common rotavirus strain was G1P[8] (102

Table 1. Rotavirus Detection Results from 17 Studies Involving Only Inpatients, with a Sample Collection Period ⩾1 Year

		Study characteristic			Patient characteristic		
Study	Location	Period of sample collection	Duration of sample collection, years	Rotavirus detection method	Age group	No. of samples tested	Percentage of samples positive for rotavirus
Gudkov et al. [8]	Belarus	1993–1995	3	EIA	<14 years	15,207	20
Pron'ko et al. [9]	Belarus	2006	1	EIA	<14 years	578[a]	37
Ginevskaya et al. [10]	Estonia	1989–1992	3	EIA	<3 years[b]	1442	26
Sakvarelidze et al. [11]	Georgia	1984–1985	>1[a]	EM	1–2 years <5 years	564	55 29[c]
Ginevskaya et al. [12]	Georgia	1984–1986	1.5	EIA	<3.5 years	845	28
Tamendarova et al. [13]	Kazakhstan	1985–1986	1	EM	<14 years	322	41
Spynu et al. [14]	Moldova	1989	1	EIA	<3 years	126	24[d]
Spânu et al. [15]	Moldova	1993–1996	4	LA	<6 months 7–12 months 1–3 years <14 years	1342 543 299 2289	11 27 20 16[c]
Antsupova et al. [16]	Russian Federation (Nizhniy Novgorod)	1981–1985	4	EM	6–24 months	920	33[d]
Vasil'ev et al. [17]	Russian Federation (St. Petersburg)	1984–1985	1	EIA	<5 years	491	40
Novikova et al. [18]	Russian Federation (Nizhniy Novgorod Oblast')	1984–1991	7	EM	<6 years	6635	27[d]
Novikova et al. [19]	Russian Federation (Nizhniy Novgorod)	1984–1996	12	EM	<14 years	6293	27[d]
Simovan'ian et al. [20]	Russian Federation (Rostov-on-Don)	1989[e]	1	EM	<1 year	400	65
Novikova et al. [21]	Russian Federation (Nizhniy Novgorod and Dzerjinsk)	1997–2005	8	RNA-PAGE	<14 years	6545	39[d]
Novikova et al. [22]	Russian Federation (Nizhniy Novgorod Oblast')	2004–2005	1	RT-PCR	<14 years	1337	33
Podkolzin et al. [23]	Russian Federation (Moscow, St. Petersburg, Nizhniy Novgorod, Tyumen, Chelyabinsk, Makhachkala, and Khabarovsk)	2001–2006	5	RT-PCR	<1 year <10 years	1768 4267	31 33[c]
Isakbaeva et al. [24]	Uzbekistan	2003–2004	1	EIA	<5 years	716	27

NOTE. The median overall number of samples tested was 920 (range, 126–15,207), and the median overall percentage of samples that tested positive for rotavirus was 33% (range, 16%–65%). EIA, enzyme immunoassay; EM, electron microscopy; LA, latex agglutination; PAGE, polyacrylamide gel electrophoresis; RT-PCR, reverse-transcription polymerase chain reaction.

[a] Personal communication with author.
[b] The upper age limit was not clearly described, but the majority of children tested were aged less than the stated age.
[c] Value used for calculation of the median estimate for children aged <5 years when results for >1 age group were available.
[d] Percentage of samples positive for rotavirus among children with acute gastroenteritis of unknown etiology.
[e] Year of publication for studies that did not report year of sample collection.

Table 2. Rotavirus Detection Results from 15 Additional Studies Involving Only Inpatients, with a Sample Collection Period of 3–11 Months or Not Reported, and Studies Involving Outpatients

			Study characteristic			Patient characteristic		
Study	Location	Patient type	Period of sample collection	Duration of sample collection	Rotavirus detection method	Age group, years	No. of samples tested	Percentage of samples positive for rotavirus
Abenova et al. [25]	Kazakhstan	NR	1988–1990	2 years	EIA	<2[a]	2629[b]	25
Khaustov et al. [26]	Russian Federation	Inpatient	1980–1982	4 months for each of 3 years	EM	1–9	176	30
Makarova et al. [27]	Russian Federation (Leningrad [now St. Petersburg] and Moscow)	Inpatient	1983–1984	11 months	EIA	<14	1487	24[c]
Antsupova et al. [28]	Russian Federation (Nizhniy Novgorod)	Inpatient	1984[d]	NR	EM	<3	194	30[c]
Vorotyntseva et al. [29]	Russian Federation (Moscow)	Inpatient	1984[d]	NR	EM	<3 <12	92 153	40 35
Vashukova et al. [30]	Russian Federation (Leningrad [now St. Petersburg])	Inpatient and outpatient	1984–1987	3 years	EIA	<2 3–6 <14	3293 832 4715	30[c] 21[c] 26[c]
Gorbachev et al. [31]	Russian Federation (Moscow)	Inpatient	1986[d]	NR	EIA	<14	1062	22[c]
Bukrinskaia et al. [32]	Russian Federation (Moscow)	Inpatient	1986–1987	5 months	EIA	<2 <10	143 201	38 34
Khaustov et al. [33]	Russian Federation (Kemerovo and Oshskaya Oblast')	Inpatient	1986–1987	NR	EM	⩽1.5	363	17
Bukrinskaia et al. [34]	Russian Federation (Leningrad [now St. Petersburg] and Moscow)	Inpatient	1987–1988	4 months	EIA	<10	651	37
Bukrinskaia et al. [35]	Russian Federation (Moscow)	Inpatient	1988[d]	NR	EIA	1–2 <12	289	27 22
Vorotyntseva et al. [36]	Russian Federation (Moscow)	Inpatient	1988[d]	NR	EM	<3 <12	92 153	40 36
Zarubinskii et al. [37]	Russian Federation (Rostov–on–Don)	Inpatient	1989[d]	NR	EM	<2	866	74
Phan et al. [38]	Russian Federation (Birobidzhan)	Inpatient	2003–2004	5 months	RT-PCR	<4	100	67
Rafiev et al. [39]	Tajikistan (Khujand [former Leninabad] and 5 regions)	Inpatient and outpatient	1999[d]	3 years	EIA	<2 3–6 <14	3278 817 4675	30 21 26

NOTE. EIA, enzyme immunoassay; EM, electron microscopy; LA, latex agglutination; NR, not reported; RT-PCR, reverse-transcription polymerase chain reaction.

[a] The upper age limit was not clearly described, but the majority of children tested were aged less than the stated age.

[b] Six hundred rotavirus-positive stool samples (24.8%) were reported.

[c] Percentage of samples positive for rotavirus among children with acute gastroenteritis of unknown etiology.

[d] Year of publication for studies that did not report year of sample collection.

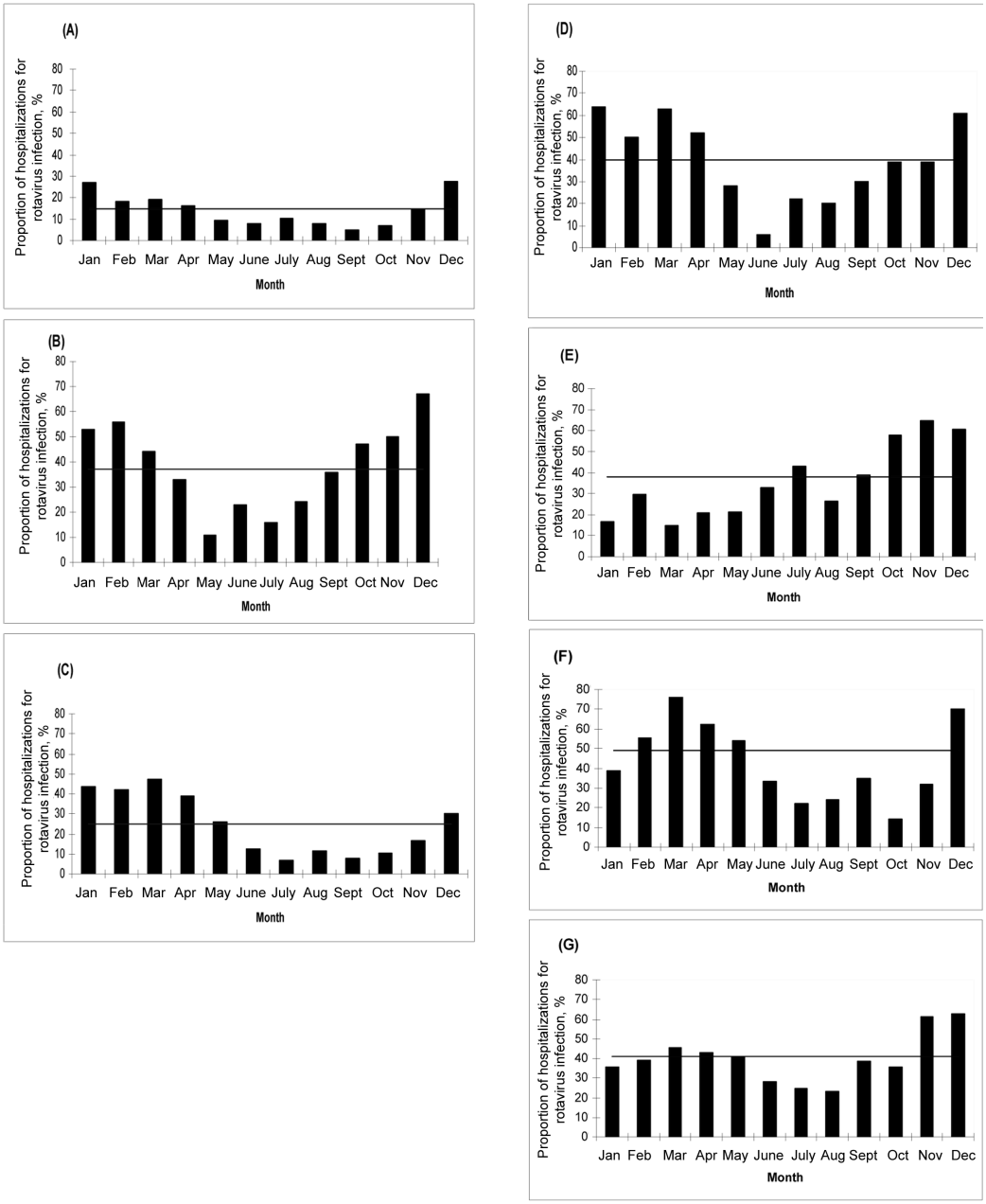

Figure 2. Proportion of hospitalizations for gastroenteritis due to rotavirus, by month. Data are from a literature review *(A, B,* and *C)* and from the Rotavirus Surveillance Network (RSN; *D, E, F,* and *G*). Horizontal lines indicate overall annual proportion. *A,* Belarus (1993–1995) [8]. *B,* Russian Federation (1984–1985) [17]. *C,* Russian Federation (2001–2006) [23]. *D,* Georgia (2007; data from RSN). *E,* Tajikistan (2007; data from RSN). *F,* Kyiv, Ukraine (2007; data from RSN). *G,* Odessa, Ukraine (2007; data from RSN).

[32%]), followed by G9P[8] (63 [20%]), G2P[4] (59 [18%]), and G4P[8] (59 [18%]) (Table 3). More than 1 G type was detected in 13 samples (4%). G12 was the sole G type in 7 samples (2%) and was combined with another type in 4 additional samples. G10 was the sole G type in 1 sample (0.3%) and was combined with G12 in another sample.

DISCUSSION

As in every region studied, rotavirus exacts a heavy toll among young children living in the newly independent states. Data from previously published reports were primarily from 1 country (the Russian Federation) and suggested that rotavirus was

Table 3. Rotavirus Strain Types from Literature Review and the Rotavirus Surveillance Network (RSN)

Study	Location	Years	Typing method	No. of samples tested	G type, %									P type, %				
					G1	G2	G3	G4	G9	G10	G12	Mixed	NT	P4	P6	P8	P9	Mixed
Ginevskaya et al. [10]	Estonia	1989–1992	EIA	314	36	5	4	6	…	…	…	…	50	…	…	…	…	…
Novikova et al. [21]	Russian Federation (Nizhniy Novgorod and Dzerjinsk)	1997–2005	RT-PCR	2454	80	9	7	3	…	…	…	…	1	9	4	85	1	…
Novikova et al. [22]	Russian Federation (Nizhniy Novgorod Oblast')	2004–2005	RT-PCR	1337	38	28	20	11	…	…	…	…	2	28	…	67	3	…
Phan et al. [38]	Russian Federation (Birobidzhan)	2003–2004	RT-PCR	100	…	…	87	…	…	…	…	13	…	…	…	…	…	…
RSN	…	2007	RT-PCR	323	33[a]	18	4	19[b]	20	<1[c]	2[d]	4[e]	…	20	2[f]	76	…	2[g]

NOTE. EIA, enzyme immunoassay; NT, nontypeable; RT-PCR, reverse-transcription polymerase chain reaction.

[a] G1P[4], 3 isolates.
[b] G4P[4], 1 isolate.
[c] G10P[6], 1 isolate.
[d] G12P[6], 3 isolates; G12P[8], 2 isolates; G12P[6]/P[9], 1 isolate; G12P[8]/P[9], 1 isolate.
[e] G1/G2P[4]/P[8], 3 isolates; G1/G9P[8], 3 isloates; G2/G4P[4]/P[8], 1 isolate; G3/G9P[8], 1 isolate; G4/G9P[8], 1 isolate; G4/G12P[8], 2 isolates; G4/G12P[6], 1 isolate; G10/G12P[6], 1 isolate.
[f] G10P[6], 1 isolate; G12P[6], 3 isolates; G4/G12P[6], 1 isolate; G10/G12P[6], 1 isolate.
[g] G1P[8]/P[9], 1 isolate; G1/G2P[4]/P[8], 3 isolates; G2/G4P[4]/P[8], 1 isolate; G12 P[8]/P[9], 1 isolate; G12 P[6]/P[9], 1 isolate.

Table 4. Enrollment and Rotavirus Detection Rates among Children Aged <5 Years Who Had Acute Gastroenteritis at 4 Sites in the Rotavirus Surveillance Network, 2007

Site	Total no. of enrolled children	No. (%) of enrolled children with a rotavirus-positive stool specimen	Range of monthly percentage of rotavirus-positive stool specimens among enrolled children	Mean monthly enrollment rate among eligible children, %
Georgia	703	281 (40)	6–64	73
Tajikistan	702	267 (38)	15–65	45
Kyiv, Ukraine	947	463 (49)	14–76	92
Odessa, Ukraine	1022	414 (41)	23–63	71
All	3374	1425 (42)	6–76	67

responsible for ~33% of hospitalizations for gastroenteritis among children in various age groups. Using a standardized WHO surveillance protocol, 4 sites in the region's new RSN documented that 42% of hospitalizations for acute gastroenteritis among children aged <5 years were attributable to rotavirus.

As our literature review indicates, several investigators in the region have worked to improve detection and understanding of the pathogen and its epidemiology. Although many previous studies provide useful information, only a limited number were described as prospectively evaluating all children with AGE or a systematically selected sample within the age group at high risk of disease over at least a 1-year period. Many of the results presented here were derived from studies in which the primary objective was to compare the performance of rotavirus detection assays; such studies began at the level of the laboratory rather than the level of the patient. Many studies were performed during the 1980s, when electron microscopy was used, which is less sensitive than currently available standardized EIAs. The few recent reports that were found were primarily from the Russian Federation. Furthermore, many studies provided results only for the group of children aged <14 years, limiting applicability toward understanding the burden among young children at greatest risk of severe rotavirus disease, and some presented results only for children with AGE of unknown etiology.

The RSN provides a platform for collecting epidemiological and clinical data and stool samples in a standardized way and for detecting rotavirus in stool samples with a standardized, sensitive assay to accurately determine the current burden of rotavirus disease. Such standardization allows comparisons of results among countries and regions, as well as changes over time. The data from the RSN indicate that ~2 of 5 children aged <5 years who are hospitalized with AGE in Georgia, Tajikistan, and Odessa, Ukraine, and ~1 of 2 in Kyiv, Ukraine, are hospitalized because of rotavirus infection. These results are somewhat higher than the median found in the review of the region's literature, at least in part because of the reasons described above. However, these results are similar to the higher results of 44% obtained during the first year (2001–2002) of surveillance through the Asian Rotavirus Surveillance Network, which also used the WHO rotavirus surveillance protocol [42]. A recent publication from collaborators in the AGE observational study in 7 European countries (REVEAL) demonstrated that rotavirus caused at least 53% of hospitalizations in each of the countries among children aged <5 years who were hospitalized for AGE during 2004–2005, with a maximum value of 69% detected in Italy [43]. The proportional estimate of severe rotavirus disease among all causes of severe gastroenteritis depends, in part, on the frequency of infection due to other enteric pathogens among children in the country, as well as on hospitalization practices for children who present with AGE. Determining population-based rates of severe rotavirus disease, as was done in REVEAL, would be a valuable next step for RSN sites that can accurately enumerate their population under surveillance.

Data from the RSN on the seasonality of rotavirus disease augment the data in the published literature from the region. As in other temperate zones, seasonality was demonstrated in the newly independent states region, but unlike the clear winter peak observed in some western European countries and the Americas [44], rotavirus detection did not peak only in the winter months in all newly independent states. The rotavirus season appears to peak earlier in the region's southeastern area (eg, October–December in Tajikistan) and continues later in locations further north and west (eg, through May in Ukraine). Hospitalizations for rotavirus disease occurred every month of the year at each of the RSN sites.

The most common rotavirus genotype identified in the RSN in 2007 was G1P[8] (32%). Two earlier studies from the region reported a G1 prevalence similar to this result, and another reported a higher prevalence. With exclusion of isolates with >1 genotype, G1–G4 and G9 types combined made up 97% of the RSN isolates, similar to the proportion in Europe (≥96%) [45, 46] and globally (>90%) [47]. The relatively high prevalence (20%) of the "emerged" strain G9P[8] found in the RSN

has been reported from several other areas [45, 47]. Some unusual genotypes (G1P[4], G4P[4], G10P[6], G12P[6], and G12P[8]) were also detected in the RSN. These may represent zoonotic introduction or reassortants that naturally occur among human rotavirus genotypes [47–49]. Mixed infections with >1 rotavirus genotype were detected in 4% of the RSN samples, in the range of the overall mixed infections estimates of 2%–5% detected in Europe, Australia, and North America and lower than the 10%–15% estimated from Africa, Asia, and South America [47]. In the recent European REVEAL study, however, no mixed rotavirus infections were identified among the 1031 samples positive for rotavirus by EIA that were genotyped, but this finding may be associated with the methodology used for virus characterization [45]. Three samples from the RSN contained the unusual genotype P[9] in combination with another P type, representing an opportunity for reassortment between human and animal rotavirus strains. It is possible that the greater diversity of cocirculating genotypes detected in the RSN samples may be attributable, in part, to improved, more-sensitive methods that include use of primers for detecting genotypes that were not available in the earlier studies. The dynamics of genotype persistence versus change, by area and by time, are not well understood [47, 50]. Genotyping results from a larger number of samples collected over a longer period in the RSN countries will be a valuable contribution to the region's literature.

As policy makers wrestle with important decisions regarding timeline and financing for the introduction of new vaccines, cost-benefit data become increasingly essential. Data on the burden of rotavirus disease from each country or from similar countries will be a critical component of these analyses. A cost-effectiveness analysis has already been conducted in Uzbekistan, where a rotavirus vaccine program was estimated to avert US$369,000 in direct and indirect costs for rotavirus hospitalizations alone in 1 birth cohort and was projected to be cost-effective with vaccine prices in the range of US$2–25 per child [24].

In conclusion, in view of the heavy burden of rotavirus disease in the newly independent states that was revealed by this epidemiological surveillance and the high clinical efficacy of the 2 available rotavirus vaccines [51–53], introducing rotavirus vaccine and achieving coverage at levels similar to those achieved with other routine infant vaccines could prevent a substantial component of the total diarrhea-associated morbidity and mortality in this region. In addition, costs of hospitalization, lost productivity, and resource expenditure by families that are associated with severe gastroenteritis could be reduced significantly by the introduction of these vaccines. Rotavirus vaccine would be a valuable public health asset in the newly independent states, especially in the 8 GAVI-eligible countries, where it is now available at heavily subsidized prices. Other countries in the European region need to conduct cost-benefit analyses for their own populations to assess the potential impact of the vaccine. Finally, postmarketing surveillance built on the foundation of the RSN will permit countries to document the impact of vaccine introduction on severe rotavirus disease.

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