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Rotavirus gastroenteritis surveillance in Azerbaijan, 2011–2016

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Abstract

Introduction: Rotavirus is a leading cause of acute gastroenteritis and mortality among children worldwide but data describing rotavirus disease in Azerbaijan are lacking. This analysis describes the rotavirus disease burden in Baku, the largest city in Azerbaijan.

Methods: We conducted active, prospective, sentinel hospital surveillance with laboratory confirmation for rotavirus among children under 5 years of age hospitalized at a large pediatric hospital in Baku during 2011–2016. Children with bloody diarrhea, or prior use of antibiotics or intravenous fluids were excluded. The guardians of enrolled children completed a questionnaire documenting clinical and demographic information. A stool specimen was collected from each enrolled child. We report the number and proportion of rotavirus positive hospitalizations during the surveillance period and a clinical description of rotavirus-positive and rotavirus-negative children.

Results: From July 2011 through June 2016, 3139 children <5 years of age were enrolled into the surveillance system. Of these, 523 (17%) were positive for rotavirus, varying from 13% to 21% by surveillance year, with a median of 16% over the surveillance period. Increase in rotavirus detections occurred during December-May. Most rotavirus infections (303/523; 58%) occurred in children aged 6–23 months.

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Conclusion: Rotavirus is responsible for approximately 16% of annual hospital admissions for acute gastroenteritis in children <5 years of age in Baku. This is lower than regional estimates. Exclusion of children with a history of antibiotic use or intravenous fluids may be accounting for this lower prevalence, and expansion of surveillance to include these groups could provide a more comprehensive picture of acute rotavirus gastroenteritis in Baku.

Keywords

Acute gastroenteritis; Pediatric; Rotavirus; Diarrhea surveillance

1. Introduction

Globally, rotavirus is a leading case of acute gastroenteritis (AGE) and mortality among children under 5 years of age [1]. In early 2000, regional mortality data estimated that among 49 countries in the European region with data available, Armenia, Azerbaijan, Georgia, Kazakhstan, Kyrgyzstan, Tajikistan, Turkey, Turkmenistan, and Uzbekistan had the highest rotavirus-related mortalities with over 10 deaths/100,000 per year among children under 5 years of age [2]. Given that no country-specific rotavirus burden estimates for Azerbaijan are available, these rates were extrapolated from neighboring countries' published rotavirus disease burden data and applied to the under 5-year-old mortality rate in Azerbaijan. Rotavirus vaccine has been shown to be effective in reducing the burden of disease in a variety of settings [3-5], and rotavirus vaccines have been projected to be cost-saving in diverse socio-economic settings worldwide, including in Europe [6-9]. Despite the burden of rotavirus disease and the availability of effective rotavirus vaccines, many countries in Europe, including Azerbaijan, have not yet introduced rotavirus vaccines into their national immunization program [10].

To date, though regional data have provided estimates of rotavirus mortality in Azerbaijan [2], no country-specific data on rotavirus burden have been published. Data such as this would help country policy makers if they consider introducing rotavirus vaccine in the future. The objective of this analysis is to describe the burden and epidemiology of rotavirus among children <5 years of age hospitalized with AGE in Baku, Azerbaijan.

2. Methods

Azerbaijan is a country in Eastern Europe with a population in 2016 of 9,705,643 and a population density of 112 people per km^2. Baku is the capital, with over 2 million inhabitants [11]. We conducted active, prospective, sentinel hospital surveillance with laboratory confirmation for rotavirus according to the World Health Organization protocol [12]. Rotavirus surveillance was conducted at Children's Infectious Disease Hospital No. 2, which is the largest hospital serving all children in Baku. Children's Infectious Disease Hospital No. 2, a 200 bed facility, 80 of which are in the enteric infection ward and 15 of which are in intensive care. Children with diarrhea are referred to this hospital for treatment. We report surveillance data from Children's Infectious Disease Hospital No. 2 from July 2011 through June 2016.

We enrolled children <5 years of age hospitalized with AGE, defined as 3 or more liquid/semi-liquid stools per day with an onset ≤7 days prior to hospitalization. Children with a history of blood in their stool, a history of antibiotic use, or receipt of intravenous fluids were excluded. For children who met the AGE case definition, their caregiver was administered a questionnaire collecting demographic and clinical information. A stool specimen was collected from the child within 48 h of hospitalization.

All stool specimens were tested for rotavirus antigen using DAKO IDEA ELISA kits.

Each year, a randomly selected subset of rotavirus positive and negative specimens was sent to the Rotavirus Regional Reference Laboratory in Minsk, Belarus, for external quality assurance testing and genotyping of the subset of rotavirus positive specimens.

Descriptive data are reported for enrollment, rotavirus testing, and genotype results per year during the surveillance period. Surveillance years were defined as July of one year through June of the following year. Children were classified as either rotavirus-positive or rotavirus-negative based on the ELISA test results and these groups were compared with respect to demographic and clinical characteristics. Chi-square testing was used to compare proportions, with p-values < 0.05 considered statistically significant.

3. Results

From July 2011 through June 2016, 3251 children <5 years of age hospitalized for the treatment of AGE were eligible for inclusion (Table 1). Of these, 3139 (97%) were enrolled and provided a stool specimen which was tested for the presence of rotavirus. Of these tested children, 523 (17%) were positive for rotavirus. The proportion of hospitalizations for AGE attributable to rotavirus varied from 13% to 21% by surveillance year, with a median of 16% over the surveillance period. An increase in the number and proportion of AGE cases due to rotavirus was observed during December – May (Fig. 1).

Sixteen percent of children aged 0–5, 6–11 and 12–23 months tested positive for rotavirus, while 18% of those aged 24–59 months were rotavirus positive. Most rotavirus infections (303 of 523; 58%) occurred in children aged 6–23 months and one-third of rotavirus infections (171 of 523; 33%) occurred in children <1 year of age (Table 2). A similar proportion of rotavirus-positive (308 of 523; 59%) and rotavirus-negative (1620 of 2616; 62%) children were male. Most patients, regardless of rotavirus status, had diarrhea for 1–4 days before hospital admission and were hospitalized for 7 days or more. Most children also experienced vomiting, irrespective of rotavirus status. A higher percentage of rotavirus positive children experienced fever (83% vs 77%; $p < 0.01$) compared to their rotavirus negative counterparts. Rotavirus positive children experienced more occasions where the frequency of diarrhea episodes was 4–5 in a 24 h period as compared to their rotavirus negative counterparts (79% vs 68%, respectively; $p < 0.01$). Genotype predominance varied by surveillance year; however, during the entire surveillance period, G4P[8] was the overall predominant genotype accounting for 124 of 308 (40%) of the rotavirus positive cases (Table 3).

4. Discussion

Rotavirus was responsible for 16% of all AGE hospitalizations annually among children <5 years of age at our sentinel site in Baku during the surveillance period. The majority of rotavirus infections occurred during the cooler winter months. This seasonal trend is consistent with what has been demonstrated elsewhere in Europe [13-15], prior to rotavirus vaccine introduction. The annual burden observed in Azerbaijan is similar to estimates extrapolated from regional analyses, which report that 21% [2] of AGE admissions are attributable to rotavirus among lower-middle income countries in Europe, which include Azerbaijan. However, recent data from observational studies in neighboring countries such as Armenia and the Republic of Moldova, show that pre-rotavirus vaccine introduction, the burden of rotavirus infection in this same age group was found to be 38% [15] and 45% [14], respectively.

This lower percentage of rotavirus infections among AGE hospitalizations in children <5 years is likely multifactorial. First, we excluded enrollment of children with a history of antibiotic use or receipt of intravenous fluids, thus potentially missing severe cases of diarrhea, which are frequently a result of rotavirus infection. Second, the cumulative age distribution of children enrolled through our surveillance program tended to be older compared to other studies. Only 33% of rotavirus positive children were <12 months of age, whereas data from regions with varying levels of socioeconomic development show that this proportion is between 40 and 88% [16,17]. Over half (57%) of the rotavirus-positive cases occurred among children in the 6–23 month age group, which is at the lower limit of what has been reported in other European studies, where 58–77% of rotavirus infections were found in this age group [18]. With fewer children enrolled in the age group most heavily affected by rotavirus infection, the observed rotavirus prevalence may be lower than the true prevalence. Additionally, although our sentinel surveillance site is the largest children's hospital serving enteric illness in Baku, another hospital serves the majority of the infant population in the city. If children <1 year were more likely to be taken to these other hospitals, we would have under-enrolled the age group that is typically most affected by rotavirus infection, which would also cause the observed rotavirus prevalence to be lower than the true prevalence. Finally, surveillance staff reported logistical difficulty in obtaining stool specimens from children in diapers (personnel communication); this may also have led to inclusion of fewer children under 2 years of age.

We demonstrated that approximately 16% of severe AGE hospitalizations per year at this tertiary care facility were due to rotavirus infection, which could be reduced through routine use of rotavirus vaccine. Rotavirus vaccine introduction was shown to decrease AGE hospitalizations due to rotavirus by two-thirds in the Republic of Moldova [14], where there was even a suggestion of indirect protective effects among unvaccinated children. Similar findings were seen in Armenia, where there was a 75% reduction in rotavirus hospitalizations due to rotavirus AGE after vaccine introduction among infants, as well as 30% reduction in children too old to have received vaccine [15]. These findings have been reported from other geographical settings [19-21], where impact on diarrhea mortality and economic burden [22] was also observed after rotavirus vaccine introduction.

This analysis is limited by several factors. First, this surveillance system which was based in one hospital may not necessarily be representative of Baku, nor Azerbaijan, since there are several infectious disease hospitals in Baku, and younger and/or more ill children may have presented elsewhere for care. A previous sentinel site for rotavirus surveillance had been operational but due to a hospital construction and subsequent surveillance interruptions, this site was not included in this analysis. Second, children enrolled in this sentinel site were older than the peak age of rotavirus positivity seen elsewhere, and those with prior receipt of antibiotics or intravenous fluids were not enrolled. These may have represented missed opportunities to enroll children with AGE, resulting in the lower percent positive rotavirus infections noted in our population. Despite these limitations, we demonstrated rotavirus burden in this large pediatric hospital in Baku.

5. Conclusion

Rotavirus was detected in approximately 16% of annual hospital admissions for AGE in children <5 years of age in Baku, the largest city in Azerbaijan. Strengthening surveillance to ensure capture of infants and children previously treated with antibiotics or intravenous fluids and expanding surveillance to include the hospital in Baku that serves children <1 year of age may reduce the number of missed RV AGE cases and present a more accurate depiction of RV AGE burden.

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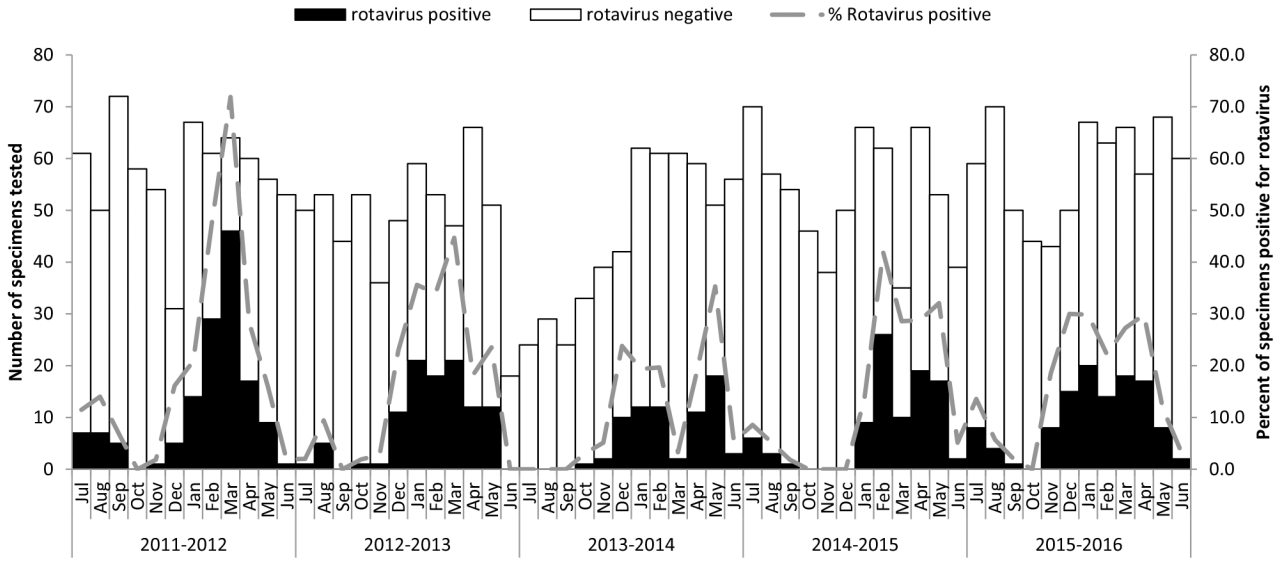

Fig. 1.

Seasonality of Rotavirus Diarrhea Among Hospitalized Children <5 Years of Age, Azerbaijan 2011–2016.

Table 1

Enrollment of children <5 years of age with diarrhea and results of rotavirus testing: Azerbaijan, Jul 2011-Jun 2016.

Rotavirus surveillance year	Number of children eligible	Number (%) of children enrolled and tested	Number (%) of children with rotavirus positive stool
Jul 2011-Jun 2012	739	687 (93)	141 (21)
Jul 2012-Jun 2013	634	578 (91)	103 (18)
Jul 2013-Jun 2014	544	541 (99)	71 (13)[a]
Jul 2014-Jun 2015	636	636 (100)	93 (15)[a]
Jul 2015-Jun 2016	698	697 (100)	115 (16)[a]
Median all years	636	636 (99)	103 (16)
Total	3251	3139 (97)	523 (17)

[a]Indicates $p < 0.05$ for comparison of proportion rotavirus positive in that year compared to reference year of 2011–2012.

Table 2

Characteristics, clinical symptoms, treatment and outcome of children <5 years of age hospitalized with rotavirus and non-rotavirus diarrhea: Azerbaijan, Jul 2011-Jun 2016.

Characteristics[a]	Rotavirus positive cases n (%)	Rotavirus negative cases n (%)	p-value
Sex			0.19
Male	308 (59)	1620 (62)	
Female	215 (41)	996 (38)	
Age group			0.84
0–5 months	47 (9)	241 (9)	
6–11 months	124 (24)	650 (25)	
12–23 months	179 (34)	911 (35)	
24–59 months	173 (33)	814 (31)	
Clinical symptoms before admission			
Duration of diarrhea in days			0.87
1–4	366 (70)	1841 (70)	
5	115 (22)	582 (22)	
6–7	42 (8)	193 (7)	<0.01
Maximum number of diarrhea episodes in 24-h period			
3	104 (20)	790 (30)	
4–5	414 (79)	1789 (68)	
6 or more	5 (1)	37 (1)	
Experienced vomiting[b] (% yes)	371 (71)	1924 (74)	0.21
Experienced fever (% yes)	432 (83)	2005 (77)	<0.02
Length of hospital stay[c]			0.96
0	14 (3)	61 (2)	
1–2	68 (13)	336 (13)	
3–4	76 (15)	357 (14)	
5–6	86 (16)	432 (17)	
7 or more	278 (53)	1427 (55)	
Outcome at discharge[d]			1.00
Died	0 (0)	1 (<1)	

[a] Percentages calculated based on cases with available information; those with missing or unknown data are excluded.

[b] Excludes 2 Rotavirus negative cases with experienced vomiting missing.

[c] Excludes 1 Rotavirus positive and 3 Rotavirus negative cases with information on length of stay in hospital missing.

[d] Excludes 1 Rotavirus positive case with information on outcome at discharge missing.

Table 3

Distribution of G- and P-typed strains by rotavirus surveillance year – Azerbaijan, Jul 2011-Jun 2016.

Rotavirus strains	Rotavirus surveillance year					
	Jul 2011-Jun 2012 n = 56 (%)	Jul 2012-Jun 2013 n = 60 (%)	Jul 2013-Jun 2014 n = 47 (%)	Jul 2014-Jun 2015 n = 60 (%)	Jul 2015-Jun 2016 n = 85 (%)	Total Strains n = 308 (%)
G4 P[8]	19 (34)	13 (22)	9 (19)	28 (47)	55 (65)	124 (40)
G1 P[8]	8 (14)	14 (23)	14 (30)	9 (15)	5 (6)	50 (16)
G3 P[8]	1 (2)	14 (23)	8 (17)	11 (18)	6 (7)	40 (13)
G9 P[8]	17 (30)	8 (13)	8 (17)	4 (7)		37 (12)
G2 P[4]	3 (5)	2 (3)	7 (15)		8 (9)	20 (6)
G12 P[6]	3 (5)	4 (7)		3 (5)	2 (2)	12 (4)
G2 P[8]	2 (4)	1 (2)			3 (4)	6 (2)
G9 P[6]					3 (4)	3 (1)
G4 P[6]	1 (2)	2 (3)				3 (1)
G12 P[8]				1 (2)		1 (<1)
GM[a] P[8]	2 (4)	1 (2)		3 (5)	1 (1)	7 (2)
GM P[6]		1(2)				1 (<1)
G2 P[M]			1 (2)	1 (2)	1 (1)	3 (1)
G3 NT[b]					1 (1)	1 (<1)

[a]Mixed genotype.

[b]Non-typeable.