SUPPLEMENT ARTICLE

The Epidemiology of Rotavirus Diarrhea in Countries in the Eastern Mediterranean Region

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Objective. Rotavirus is the leading cause of severe diarrhea among children worldwide, killing ~600,000 children annually, including 64,800 in the Eastern Mediterranean Region. Safe, effective rotavirus vaccines will be available soon, and accurate disease burden data will be needed to assess the burden of rotavirus and the value of new vaccines and monitor vaccine program impact.

Methods. To identify epidemiologic studies in which rotavirus diagnostics were applied to children with acute gastroenteritis, we performed a systematic literature review. We selected studies that met 4 criteria and extracted rotavirus data on prevalence estimates, strain identification, age distribution of patients, and seasonal trends.

Results. Of the 63 published studies with some rotavirus detection data, 29 met inclusion criteria. Among patients with diarrhea, rotavirus was detected in 40% of inpatients and 23% of outpatients. By 3 years of age, 75% of children experienced a documented rotavirus infection. Circulation of rotavirus occurred year-round, and no clear relationship between the timing of the rotavirus peak with either season or latitude was observed. Comparison of country-specific rotavirus detection rates indicated that the proportion of hospitalizations for rotavirus infection increased with income.

Conclusion. This systematic review of studies of rotavirus diarrhea among children in the countries of the Eastern Mediterranean Region documents that rotavirus is one of the most significant causes of childhood diarrhea in the region. The findings of this review will be used to establish sentinel hospital surveillance in these countries, estimate disease burden, and characterize its epidemiology using common protocols and diagnostics.

Rotavirus is the leading cause of severe diarrhea among children worldwide, killing ~600,000 children annually [1, 2]. Improved treatment using oral rehydration solution and diarrhea control measures, such as sanitation and water purification, have been effective strategies to reduce diarrhea-associated mortality over the past 2 decades. However, interventions that prevent diarrhea associated with some bacterial and parasitic agents are less effective against rotavirus diarrhea [3–5]. Consequently, the World Health Organization (WHO) and others have recommended rotavirus vaccines as the most effective strategy to prevent rotavirus-related morbidity and mortality [6, 7]. Two vaccines are currently being licensed in European and other countries, and additional vaccine candidates are in early stages of development that may become available in the future [8–11]. The promise of safe, effective rotavirus vaccines has led to intensified efforts to determine the disease burden of rotavirus in countries and regions where the vaccine should be considered for introduction.

Recent studies have estimated that ~65,000 children die each year of rotavirus infection in the 22 countries of the Eastern Mediterranean Region (EMR), as geopolitically defined by the WHO (Table 1), and from Pakistan to Morocco [1]. In this region, mortality remains high, especially in countries with the lowest per capita income, such as Pakistan, Afghanistan, Sudan,

Financial support: Centers for Disease Control and Prevention.
Potential conflicts of interest: none reported.
Supplement sponsorship: This article is part of a supplement entitled "Rotavirus Infection in Africa: Epidemiology, Burden of Disease, and Strain Diversity," which was prepared as a project of the Rotavirus Vaccine Program, a partnership among PATH, the World Health Organization, and the US Centers for Disease Control and Prevention, and was funded in full or in part by the GAVI Alliance.
The findings and conclusions in this report are those of the author and do not necessarily represent the views of the funding agency.
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The Journal of Infectious Diseases 2010;202(S1):S12–S22

0022-1899/2010/20205S1-0003$15.00
DOI: 10.1086/653579

Table 1. Annual Incidence of Death due to Rotavirus Gastroenteritis among Children <5 Years of Age in Countries of the Eastern Mediterranean Region (EMR)

Country	GNP per capita, US$	Birth cohort, ×1000	Deaths among children <5 years of age, ×1000[a]	Estimated deaths from diarrhea[b]	Estimated deaths from rotavirus infection[c]
Afghanistan	250	1136	293	61,530	12,306
Bahrain	7640	14	0	…	…
Djibouti	790	27	3	510	128
Egypt	1,400	1,911	89	15,130	3783
Iran	1760	1424	64	10,880	2720
Iraq	2170	879	103	17,510	4378
Jordan	1500	151	8	1360	340
Kuwait	19,020	50	0	…	…
Lebanon	3700	69	2	180	56
Libya	5540	128	4	360	112
Morocco	1200	707	37	6,290	1,573
Oman	4940	91	1	90	28
Pakistan	470	5506	599	125,790	25,158
Palestine	…	137	…	…	…
Qatar	12,000	10	0	…	…
Saudi Arabia	6,910	762	17	1530	474
Somalia	120	516	106	22,260	4452
Sudan	330	1100	103	21,630	4326
Syria	970	491	14	2380	595
Tunisia	2100	165	6	1020	255
United Arab Emirates	17,870	49	0	…	…
Yemen	350	901	98	20,580	4116
Total	…	…	1547	309,030	64,800

NOTE. Adapted from Parashar et al [1]. Birth cohort data are from http://unicef.org/infobycountry/index.html.

[a] Figures for total deaths among children <5 years of age are rounded to the nearest thousand; consequently, estimates of deaths from diarrhea and deaths from rotavirus infection were not calculated for countries with <1000 child deaths.

[b] Deaths from diarrhea were derived by multiplying total deaths among children <5 years of age by the estimated proportion of deaths attributable to diarrhea, based on GNP per capita, as follows: GNP <US$ 756, 21%; GNP US$ 756–2995, 17%; GNP US$ 2995–9625, 9%; GNP >US$ 9625, 1%.

[c] Deaths from rotavirus were derived by multiplying total diarrhea deaths among children <5 years of age by the estimated proportion of diarrhea deaths from rotavirus infection, based on GNP per capita, as follows: GNP <US$ 756, 20%; GNP US$ 756–2995, 25%; GNP US$ 2995–9625, 31%; GNP >US$ 9625, 34%.

Yemen, and Somalia. Countries with a higher per capita income have fewer deaths, but the burden of severe rotavirus disease is reflected in the many hospitalizations and clinic visits among children <5 years of age that incur substantial economic costs [1]. In addition to these estimates of regional morbidity based on global models, limited information is available on the disease burden of rotavirus for individual countries of the region. Accurate projections of the benefits of a vaccine program will require reliable, current data on the disease burden for each country. These data will allow policymakers to make informed decisions about the need for rotavirus vaccines and are vital to increase knowledge and awareness of the disease among physicians and the community.

We reviewed the existing medical literature and summarized data on rotavirus diarrheal disease burden and strain distribution in the EMR as a first step toward establishing a regional surveillance network among these countries. This surveillance network will be used to define the disease burden and to identify remaining gaps in data needed to inform decisions concerning vaccine introduction.

METHODS

For our systematic review of the literature, we extracted all published articles identified in a multilingual search of the databases of PubMed and the Institute for Scientific Information Web of Science, using the names of the 22 countries in the EMR (Table 1) WHO and the key words “rotavirus,” “rotavirus infections,” “vaccines,” “incidence,” and “prevalence” [12]. We identified additional studies using the references of articles retrieved from the literature search. Our goal was to identify epidemiologic studies in which rotavirus diagnostics were applied to patients with acute gastroenteritis who were treated in clinics or hospitals.

Table 2. Rotavirus Detection among Hospitalized Children with Acute Gastroenteritis (AGE) in Countries of the Eastern Mediterranean Region

	Study characteristics				Study results	
Country, reference	Years of enrollment	Duration, months	Age, years	Method[a]	No. with AGE	Percentage with rotavirus infection
Bahrain [30]	1984–1986	25	<5	EIA	482	27
Egypt						
[53]	1992–1993	15	<1	EIA	129	44
[54]	1986	12	<2	EIA	200	40
[55]	1982–1983	12	<1.5	EIA	145	33
Iran [19]	1993–1994	12	<5	EIA	259	22
Kuwait						
[56]	1983–1984	15	<5	EIA, EM	621	44
[29]	1980–1981	12	<5	EIA, EM	343	40
Morocco [31]	1982–1983	12	<2	EIA, LA	327	20
Oman [57]	1990–1992	24	<5	EIA, EM	217	31
Saudi Arabia						
[58]	1988–1993	57	<5	EIA	1367	43
[58]	1992–1993	12	<5	EIA	359	43
[32]	1988–1989	13	<12	EIA	363	46
[59]	1985–1986	25	<2	EIA	688	44
Tunisia [33]	1995–1999	51	<5	LA	375	17
Median value (range)	…	14 (12–57)	…	…	351 (129–1367)	40 (17–46)

NOTE. EIA, enzyme immunoassay; EM, electron microscopy; LA, latex antigen.

[a] Studies for which >1 detection method is included indicates that the investigators used either technique but did not provide detailed data for each detection method separately.

From this review, we selected studies that met 4 criteria used previously to achieve reasonable quality, comparability, and representativeness of the results: (1) surveillance lasted for ⩾12 months, (2) >100 stool samples were tested for rotavirus, (3) data could be extracted for children <5 years of age, and (4) rotavirus detection was conducted using a sensitive assay, such as an enzyme immunoassay (EIA) or latex agglutination (LA) test [13–15]. Because rotavirus is detected more often among inpatients with severe disease (eg, hospitalizations) than in outpatient or community cohort studies, we separated our analysis according to the setting of patient enrollment and the assumed severity of disease (inpatient-severe, outpatient-moderate, or community cohort–mild) [16].

Detection rates and associated 95% confidence intervals (CIs) were computed using the number of rotavirus detections and the study denominator. For consistency, the detection rate was abstracted from tables or text reporting the number of diarrheic samples positive for each pathogen detected. In some studies, >1 pathogen was identified; therefore, we reported detection rate as the number of cases cause by a particular agent inclusive of cases caused by multiple pathogens. For the purpose of summary of rotavirus detection rate in inpatient- and outpatient-based studies, point estimates and standard errors from individual studies were combined using a random-effects model with methodology developed by DerSimonian and Laird [17] and reporting point estimates with 99% CIs. This method is considered to be more conservative than a fixed-effects model and weights studies by both sample size and between-study variance. The use of 99% CIs also assures a more robust estimate of any given detection rate. Furthermore, because of known variations in study design, methodologies, population characteristics, and other factors, heterogeneity of detection rates across studies was assessed graphically with Forest plots and statistically with nonparametric methods and heterogeneity statistics [17].

Additional data extracted from each study, when available, included incidence of rotavirus infection (in cohort designs), age distribution of rotavirus-positive children (for predefined age groups: 0–5, 6–11, 12–23, 24–35, 36–47, and 48–59 months), and geographic and seasonal trends. If studies were described in enough detail, we plotted seasonal data by calendar month and peaks were defined as periods during which the rate of rotavirus detection exceeded the annual median for at least 3 consecutive months. Finally, we plotted per capita Gross Domestic Product (GDP) by rotavirus detection rate to evaluate the hypothesis that wealthier countries have a higher proportion of cases of rotavirus diarrhea because of the reduced fraction of bacterial and parasitic diarrhea in these settings.

Table 3. Rotavirus Detection among Children Treated in Outpatient Settings for Acute Gastroenteritis (AGE) in Countries of the Eastern Mediterranean Region

	Study characteristics				Study results	
Country, reference	Years of enrollment	Duration, months	Age, years	Method[a]	No. with AGE	Percentage with rotavirus infection
Bahrain [30]	1984–1986	25	<5	EIA	216	6
Iran						
[19]	1993–1994	12	<5	EIA	445	12
[18]	1986–1987	15	<5	RPHA	915	25
Jordan						
[20]	1999–2001	25	<10	EIA	220	41
[21]	1992–1993	16	<5	EIA	220	35
Pakistan						
[60]	1990–1997	96	<5	EIA	818	14
[61]	1985–1987	24	<3	EIA, EM	758	14
[62]	1981–1982	12	<3	EIA	>200	21
Saudi Arabia [22]	1987–1988	24	<2	EIA	240	38
Somalia [63]	1983–1984	24	<14	EIA	911	25
Median value (range)	…	24 (12–96)	…	…	343 (216–915)	23 (6–41)

NOTE. EIA, enzyme immunoassay; LA, latex agglutination; RPHA, reverse passive hemagglutination.
[a] Studies for which >1 detection method is included indicates that the investigators used either technique but did not provide detailed data for each detection method separately.

RESULTS

Of the 63 published studies identified that contained some data on rotavirus detection, 29 met the inclusion criteria for this review. We excluded studies that were shorter than 12 months ($n = 22$) or enrolled too few patients from whom stool samples were collected ($n = 11$). Of the 29 studies included, 14 (48%) were conducted among hospitalized children, 10 (34%) included children treated as outpatients, and 5 (17%) summarized longitudinal studies of 3 cohorts of children followed up for diarrhea in the community. The studies that met inclusion criteria represented 11 (50%) of the 22 EMR countries. Furthermore, only 5 (17%) of these 29 studies presented data collected during the past 10 years.

Inpatient. A total of 14 studies from 8 countries reported data on children hospitalized for acute diarrhea who were screened for rotavirus (Table 2). Most studies ($n = 9$) were conducted in the 1980s, and only one enrolled patients >5 years of age. Detection rates for rotavirus ranged from 17% to 46%, with a median of 40%. When pooling these studies, we identified significant variation of prevalence estimates in inpatient studies (heterogeneity χ^2, 291.7; degrees of freedom [df], 13; $P < .001$), and the summary estimate for the prevalence of rotavirus infection in inpatient settings was 35% (99% CI, 28%–43%), lower than the median (40%) calculated using nonparametric statistics. We failed to identify any factors that could explain the heterogeneity, including age of patients, country of study, study size, or the historical year of surveillance. However, studies with markedly lower detection rates had ⩾1 limitations, including use of questionable exclusion criteria, less sensitive collection method (ie, use of rectal swabs), or less sensitive detection assay (ie, LA).

Outpatient. In the 10 outpatient studies that met criteria for inclusion, the median detection rate was 23% (range, 6%–41%), and 6 of the studies were conducted in the 1980s (Table 3). As with the inpatient analysis, we identified significant heterogeneity among prevalence estimates from outpatient studies (heterogeneity χ^2, 256.4; df, 9; $P < .001$), with a summary estimate of 23% (99% CI, 15%–30%), identical to the median detection rate calculated using nonparametric statistics.

We failed to identify the source of heterogeneity of detection rates for variables including age of patients, the size of the study, or the historical year of surveillance. Most studies (80%) used EIA for detection; thus, we could not compare detection rates among all studies by assay (ie, EIA vs LA or electron microscopy). Detection rates reported in multiple studies in the same country were somewhat consistent, with the exception of 2 studies from Iran. Both were performed at outpatient clinics in Teheran, but the study with the higher detection rate (25%) included 6 clinics, whereas the study with 3 clinics had a lower detection rate [18, 19] . The highest detection rates were reported in 2 studies from Jordan—one in a rural area (41%) and the other in a refugee camp (35%)—and an additional study from Saudi Arabia (38%) [20–22].

Community cohort studies. Annual incidence data from

Table 4. Rotavirus Detection among Children from Community Studies of Children with Acute Gastroenteritis (AGE) in Countries of the Eastern Mediterranean Region

	Study characteristics			Study results	
Country, reference	Years of enrollment	Age, years	Duration, months	No. with AGE	Incidence rate[a]
Egypt					
[23]	1995–1998	<3	36	397	0.19
[24]	1995–1996	<3	12	274	0.24
[25]	1981–1983	<2	24	363	0.27
[26]	1981–1983	<15	24	3243	0.27[b]
Pakistan [27]	1987–1993	<1	64	618	0.55
Median value (range)	…	…	25 (12–64)	397 (274–3243)	0.27 (0.19–0.55)

[a] Incidence rate measured in incidence per person-year of potential exposure. All specimens detected using enzyme immunoassay.
[b] Rate available only for children <12 months of age.

the 5 longitudinal cohort studies (4 from Egypt and 1 from Pakistan) that met our criteria for this review indicate that by the age of 3 years, 75% of children had a documented rotavirus infection (Table 4). Of note, the 4 studies reported from Egypt summarized incidence rates in 2 patient populations [23–26]. Although these 5 studies were conducted in populations <3 years of age, the Pakistani study only included children <1 year of age and reported a remarkably higher incidence [27]. Because few studies adequately measured incidence of rotavirus infection, no attempts were made to summarize estimates or measure heterogeneity.

Age distribution of patients with rotavirus disease. Eleven studies involving hospitalized patients, 2 that enrolled outpatients, 1 that enrolled both, and 2 cohort studies provided detailed data on the age distribution of the patients (Figure 1). Eight of the 11 studies provided sufficient data to plot age distribution curves of all patients <2 years of age with rotavirus diarrhea, and a younger age distribution was observed in studies from Kuwait, Morocco, and Bahrain. By 12 months of age, 88%, 84%, and 83% of cases of rotavirus infection among children from Kuwait, Bahrain, and Morocco, respectively, had occurred, and the incidence in the remaining countries ranged from 66% (Egypt) to 44% (Pakistan) [26, 28–31]. Most of the rotavirus infections (>90%) were observed by 3 years of age in all studies except 1 from Saudi Arabia, which reported that 85% of cases had occurred by age 2 years (data not shown) [32]. In all but one study, more than half of the children with rotavirus infection had experienced illness by 12 months of age, and more than half ($n = 5$) of the studies indicated that >70% of cases occurred during the first year of life.

After stratifying the data, no clear correlation was observed between geographic location (ie, latitude) of the study, income

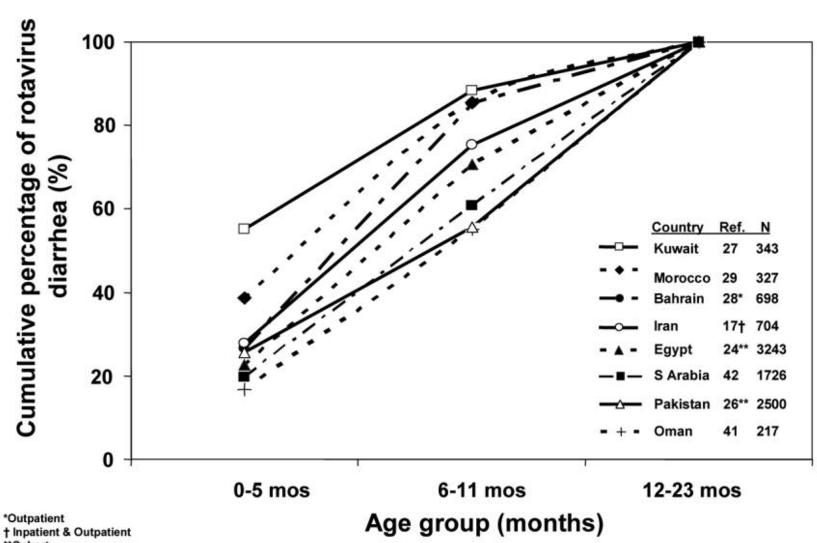

Figure. 1. Cumulative percentage of children with rotavirus diarrhea, by age

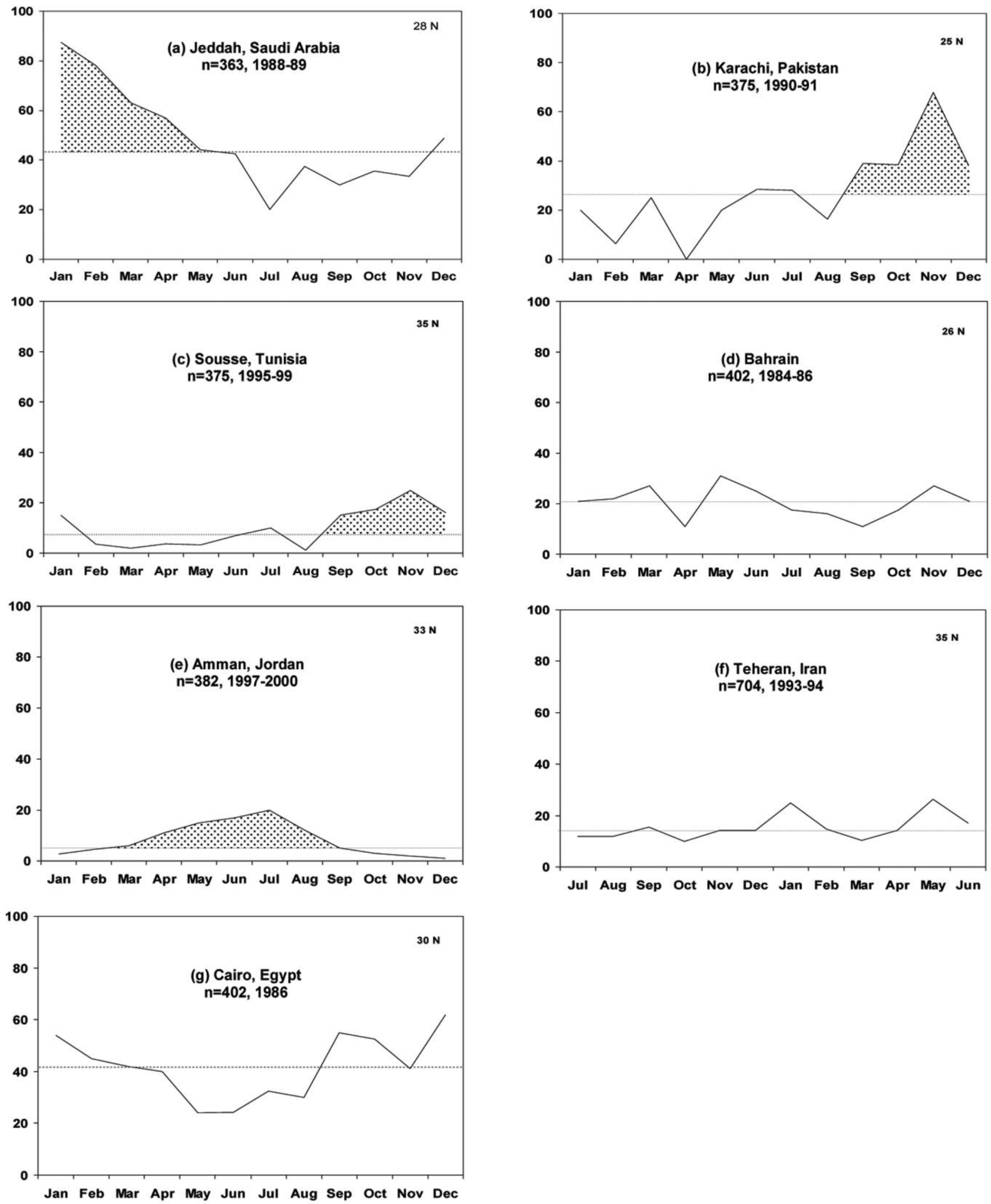

Figure. 2. Percentage monthly rate of cases of diarrhea with excretion of rotavirus in the Middle East and North Africa. The yearly median is marked, and shaded areas indicate peaks >3 months. Data in *a* are from [32], in *b* are from [27], in *c* are from [33], in *d* are from [30], in *e* are from [65], in *f* are from [20], and in *g* are from [54].

Table 5. Summary of Rotavirus G and P Types Identified in Countries of the Eastern Mediterranean Region

Country, reference	Years	No. tested	Typing method	G type, %				P type, %			Mixed types, %	Nontypeable, %
				G1	G2	G3	G4	P4	P6	P8		
Egypt												
[24]	1995–1996	46	RT-PCR	13[a]	**70**	0	0	**74**	…	11	7	9
[53]	1992–1993	62	EIA	**18**	3	6	**18**	…	…		16[b]	39
Pakistan [60]	1990–1997	112	EIA and RT-PCR	**27**	8	0	**26**	…	…	…	2[c]	38
Saudi Arabia [64]	1988–1992	245	EIA	**53**	11	7	16	…	…	…	2[d]	13
Tunisia [33]	1995–1999	65	EIA and RT-PCR	**57**	3	0	14	19	16	**39**	5[e]	22

NOTE. Boldface indicates predominant strains. EIA, enzyme immunoassay; RT-PCR, reverse-transcription polymerase chain reaction.

[a] One G8 strain detected; mixed types: G1/G2 strains; nontypeable P types: 13%; P[14], 2%.

[b] G1/G4 strains.

[c] G2/G4 strains.

[d] G1/G4–1, G3/G4–2, G2/G3–1.

[e] G1/G2–2, G1/G4–1, P4/P6: 3%, nontypeable P types: 23%.

categories, and the age distribution of patients with rotavirus infection. Moreover, the age distribution did not differ by treatment setting.

Seasonality of rotavirus disease. All the studies demonstrated circulation of rotavirus year-round, and no clear relationship between the timing of the peak in rotavirus activity with either season (cooler vs warmer months) or latitude was observed between countries (Figure 2). In Saudi Arabia, Pakistan, and Tunisia, clear peaks in rotavirus detection occurred during the cooler months; in Jordan, peaks occurred in the warmer season; and in Egypt and Iran, seasonal fluctuation was less marked. However, duplicate studies conducted in the same country or even the same city showed little consistency (data not shown) [18, 19].

Serotype prevalence. Only 5 studies from 4 countries provided data on rotavirus VP7 (G) serotypes, and 2 studies reported VP4 (P) types (Table 5). G1 and G4 strains predominated throughout the 1990s. Two studies reported P types. In Egypt, P[4] was the most common strain, but a very rare serotype, P[14], was also reported, and in Tunisia, P[8] strains predominated [24, 33]. The high number of mixed infections in Egypt is remarkable (as a prerequisite for reassortment). Most studies report a high percentage of nontypeable strains (Table 5). The current technology is likely to reduce the number of nontypeable strains significantly.

Rotavirus prevalence by GDP. Previous studies indicated that the proportion of diarrhea-related hospitalizations attributable to rotavirus increases with increasing national income, presumably because of improvements in hygiene and sanitation that decrease exposure to bacterial and parasitic pathogens that also cause diarrhea [1, 2]. To test this hypothesis, we plotted the median rotavirus detection rate for each country by per capita GDP and noted an association (R^2, 0.38) (Figure 3*A*).

Because of the limited number of studies that met criteria for this review, we also calculated median rotavirus detection rates after classifying the countries into the following World Bank income groups: low, low-middle, high-middle, and high (Figure 3*B*). The proportion of rotavirus-related hospitalizations increased consistently with increasing income (R^2, 0.92). The median for low income countries (<$US 760) was 8%, for low-middle–income countries ($US 760–3029) was 21%, for high-middle–income countries ($US 3030–9360) was 31%, and for high-income countries (⩾$US 9361) was 42%.

DISCUSSION

This systematic review of studies of rotavirus diarrhea among children in the countries of the EMR documents the heavy burden of disease seen in all countries where it is the most significant cause of severe diarrhea among patients seen in hospitals and clinics. According to current estimates, rotavirus is responsible for ~65,000 deaths annually among children in the EMR; these deaths could be averted with a safe and effective vaccine [1]. Children hospitalized for diarrhea were more likely to have rotavirus detected (40%) than those treated as outpatients (23%), confirming that rotavirus infection has a higher prevalence among children with more-severe diarrhea. Although most rotavirus-associated deaths occur in developing countries, the disease is not limited to low-income settings. In fact, the proportion of diarrhea-associated hospitalizations attributable to rotavirus is higher in developed countries because environmental interventions, such as sanitation and water purification, greatly reduce infection with bacterial and parasitic agents but are ineffective against rotavirus. Finally, the community cohort studies indicated that by 3 years of age, 75% of children have experienced at least 1 episode of rotavirus diarrhea.

We also noted several important features of rotavirus epidemiology that should be used to help guide vaccine program implementation. Some countries exhibited peaks of rotavirus

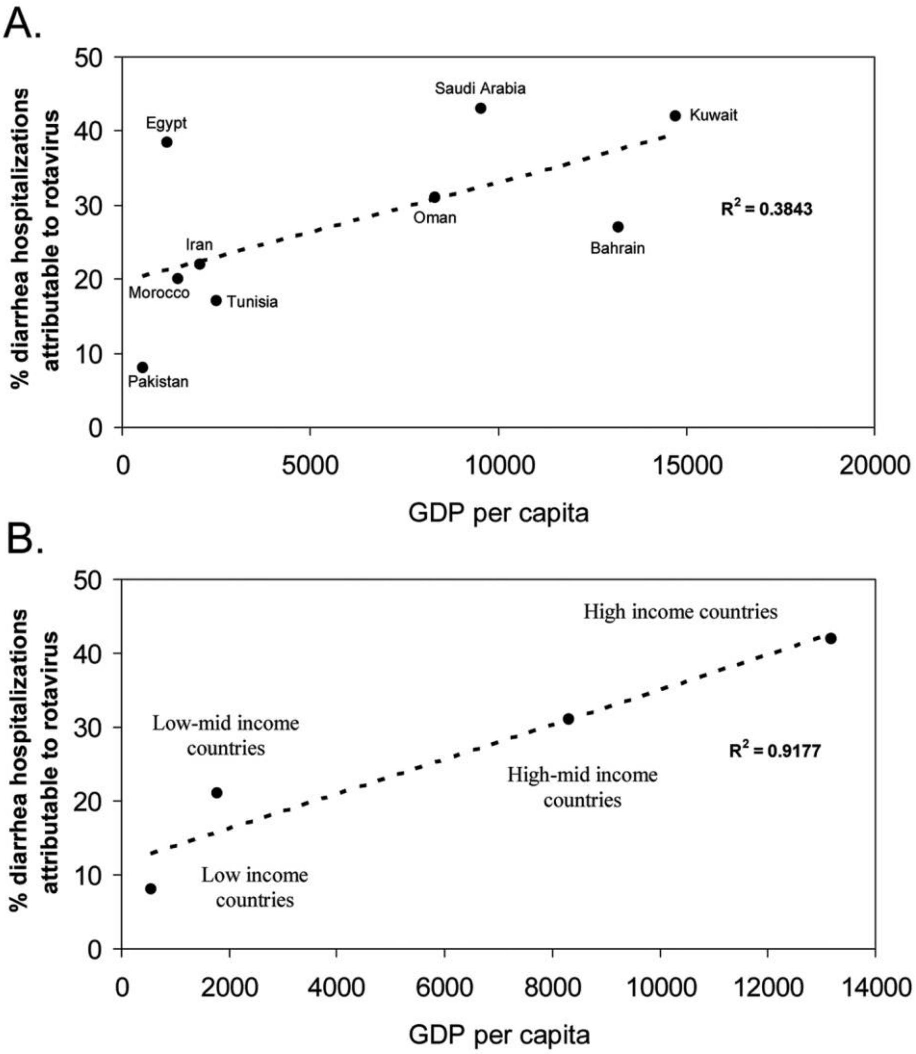

Figure. 3. *A,* Median rotavirus-positive diarrhea hospitalizations by Gross Domestic Product (GDP) per capita. *B,* Median rotavirus-positive diarrhea hospitalizations by median World Bank per capita GDP classification.

activity during the cooler months, but duplicate studies in the same country often did not confirm these findings, and no clear geographic trend could be established. Strain data indicated that, overall, G1 was the most common circulating strain; however, in 2 countries, it appeared to be codominant with G4. G2 was dominant in 1 study, and limited VP4 data indicated that P[4] and P[8] were most common. Among studies with detailed data on age distribution, nearly all hospitalizations (median, 90%; range, 84%–100%) occurred among children <2 years of age, and most (median, 60%; range, 44%-84%) detections affected infants (children <12 months of age). The fact that asymptomatic carriage in nurseries was documented and may be significant for nosocomial outbreaks further underscores the importance of early vaccination [34–36]. Therefore, a vaccine must be administered to young infants, because most disease occurs during the first few months of life.

Relative to other regions in the world, the median rotavirus detection rate (40%) among hospitalized children with diarrhea in the EMR falls in the intermediate range between the higher level (45%) reported in Asia and lower rates found in Latin America (38%) and Africa (24%) [13, 14, 37]. The findings of this study were also consistent with global reviews of rotavirus illness and deaths reported by Parashar et al [1, 2]. During manuscript preparation, a few other studies on rotavirus in EMR pediatric populations were reported and are worth further description. In a hospital-based study in Tehran, Iran, Farahtaj et al [38] reported a 25% detection rate, consistent with an earlier study (22%) [19], with G1P[8] and G9P[8] accounting for 59% and 16% of isolates, respectively. Two studies from Tunisia included mixed patient populations (outpatient and hospitalized) and overlapping periods of surveillance [39, 40]. These studies found a 25%–40% detection rate among hospitalized children and a 16%–18% detection rate in outpatient settings. A winter peak for rotavirus (but not astrovirus or adenovirus) was noted in one study during 2003 and 2005 [39]. G1 and G4 accounted for 69% of isolates over a 10-year period of study, although unconventional G8 and G9 types were noted to occur [40]. The first genetic characterization of isolates among 172 children from Kuwait with severe diarrhea (44% rotavirus detection rate) was notable, because although G1 was most common (63.8%), G9 was second in frequency (10.2%) [41]. In a network of clinics in Upper Egypt, rotavirus was found as the single most common infectious agent detected among children either hospitalized or brought to outpatient care (36%–46%) for acute gastroenteritis [42]. Finally, one additional study conducted from March through May 2005 that involved 260 children hospitalized for acute diarrheal illness in Iraqi Kurdistan reported a detection rate of 37%, with G1P[8] and G2P[4] accounting for more than half of the strains isolated [43]. Although these data do not change the general findings of the systematic review of included studies, they underscore the significance of rotavirus as an etiologic agent of severe childhood diarrhea in the EMR, compared with other regions, and provide additional disease burden and genotyping data that can be used to evaluate the cost-effectiveness of current rotavirus diarrhea prevention measures. In addition, although not included in the EMR (and therefore not meeting eligibility criteria), several studies have reported rotavirus detection rates among countries in the surrounding region, including Algeria, Turkey, or Israel [44–52]. These studies could be considered as additional information to inform EMR on rotavirus burden in the region, and findings of this systematic review should be considered as generalizable and serve purpose to these countries of close proximity.

The primary limitation of this study is the lack of recently published, appropriately conducted surveillance studies conducted in the EMR, and this likely led to an underestimation of the true magnitude of rotavirus disease burden. In fact, 5 of the 6 studies with detection rates of ⩽20% had ⩾1 limitation, including less sensitive collection (rectal swabs) or detection methods (eg, LA or electrom microscopy). Of the 30 studies, 19 were conducted in the 1980s, and only 1 study included data from 2001; there were no data available from after 2001 from studies that met our inclusion criteria. This lack of data also limited our ability to definitively identify seasonal peaks and associated geographic patterns of rotavirus disease, which is known to exhibit highly characteristic seasonal and geographic trends. Furthermore, the findings from existing studies may not be generalized, because many are concentrated in select hospitals or cities in the few countries that have the financial or logistical resources necessary to perform rotavirus surveillance. Although this review cannot provide an up-to-date, comprehensive report of rotavirus disease in the EMR, it is the first step necessary to establish future surveillance in the region, and our findings demonstrate the primacy of rotavirus among childhood diarrheal agents in these countries.

This review provides insights to establish the Eastern Mediterranean Rotavirus Surveillance Network, a network of sentinel hospitals that will be used to conduct surveillance for rotavirus in the region. These studies will use a uniform protocol, with a common stool collection procedure, a single diagnostic tool, reference methods to characterize strains, a uniform period of observation, and enrollment of children <5 years of age. Proper surveillance must include data from more countries in the region, represent the diverse patient populations, and capture information regarding the effect of comorbid illnesses (eg, malnutrition and immunodeficiency) on vaccine effectiveness and dosing schedule. Specimen collection should be limited to stool specimens (and not rectal swabs) and should use EIA as the primary detection assay. Strain characterization will be necessary to detect novel serotypes and reassortant strains and to determine whether they are prevented with the new vaccines. Data must be collected year-round to characterize seasonal fluctuations of rotavirus and look for patterns in the region. Studies should enroll all children <5 years of age with acute gastroenteritis to identify the age distribution of disease burden and to determine the correct age and time of year to ensure that vaccination has its greatest impact. Use of a uniform rotavirus surveillance protocol in all countries would enable public health officials to compare detection rates among countries and to monitor vaccine program impact over time in countries where a rotavirus vaccine is added to the vaccination schedule. Finally, an accurate picture of rotavirus disease burden may enhance community and physician awareness, which would greatly increase the impact of any future vaccine programs.

Acknowledgments

We thank Mr Manoj Gera for his invaluable editorial assistance preparing this manuscript for publication.

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