

The Burden and Cost of Ambulatory Cases of Rotavirus Gastroenteritis in Central Israel

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ABSTRACT: **Background:** While the burden of rotavirus infection with regard to hospitalizations has been extensively investigated, there are sparse data on the cost and impact of this infection on the ambulatory part of the health system in Israel.

Objectives: To investigate the burden of rotavirus infection on the ambulatory system in Israel.

Methods: Infants younger than 3 years examined for acute gastrointestinal symptoms in four pediatric clinics had their stool tested for rotavirus. The parents were contacted 7–10 days later and questioned about the symptoms of illness, medications given, use of diapers, consumption of formula, and any loss of parents' workdays.

Results: Rotavirus was detected in 71 of the 145 stool samples tested (49%). A total of 54 parents responded to the telephonic survey. Patients' mean age was 15.4 months. Three patients were hospitalized due to the illness. The mean duration of fever was 1.7 days. Infants with rotavirus gastroenteritis had on average 2.25 days of vomiting and 7.5 days of diarrhea. The average number of workdays lost was 2.65 days per RVGE case. The cost of the average case of RVGE in Israel is 257 euros; 69.64% of this cost (179 euros) is due to parental work loss.

Conclusions: Our results indicate that the economic impact of the ambulatory cases in Israel is quite significant.

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KEY WORDS: rotavirus, gastroenteritis, cost, ambulatory patients, burden

Rotavirus is the leading cause of diarrhea hospitalization among children worldwide [1]. It was calculated that rotavirus causes 440,000 annual deaths in children under the age of 5 years worldwide. Recent studies suggest that as global deaths from childhood diarrhea decreased during the past two decades, the proportion of diarrhea hospitalizations attributable to rotavirus may have increased. Studies published between 1986 and 1999 indicated that

rotavirus causes approximately 22% of childhood diarrhea hospitalizations (range 17–28%). From 2000 to 2004, this proportion increased to 39% (29–45%). A prospective, sentinel hospital-based surveillance of rotavirus disease in nine Asian countries demonstrated a median rotavirus detection of 45% among children hospitalized with diarrhea [2]. This phenomenon likely reflects a relatively slower rate of decrease in hospitalizations for rotavirus compared with other causes of severe childhood diarrhea. This finding could be attributed to several factors. First, interventions to improve hygiene and sanitation are less likely to have a substantial impact on diarrhea rotavirus, which is often spread from person to person. Second, oral hydration therapy is less applicable for patients with severe rotavirus gastroenteritis due to the severe vomiting associated with this illness. Third, unlike other microorganisms responsible for childhood diarrhea, no specific treatment for rotavirus infection is available [3].

The burden of this infection with regard to hospitalizations has been extensively investigated and recent data suggest that about 4000 infants are hospitalized annually in Israel for RVGE [4]. However, there are no data regarding the impact of this infection on the ambulatory system in Israel. It is important to estimate this burden for two reasons. First, two new vaccines have recently been approved for use in Israel and in several other countries, and estimation of the ambulatory portion is necessary for the medical insurer to assess whether the vaccines are cost-effective. Second, it is important to quantify the indirect burden experienced by parents and families. In several childhood illnesses such as chickenpox, the indirect cost is considerably higher than the direct medical costs [5] since many parents have to take time off work or other activities to care for their ill child. The aim of this study was to assess the impact of the ambulatory portion of RVGE on the households, the health care system and society, according to data on resource use, expenditure and lost income.

PATIENTS AND METHODS

This prospective study was performed in four primary pediatric clinics in three urban centers in central Israel (two clin-

RVGE = rotavirus gastroenteritis

ics in the city of Rishon Lezion, one in the city of Holon, and one in the city of Modi'in).

Infants younger than 36 months who presented with acute gastrointestinal symptoms during the winter months (October 2007 to January 2008) had their stool tested for RV at the clinic or at the central laboratory of Maccabi Health Services, using a rapid test (RotaStick One-Step, medNet GmbH, Germany). To avoid selection bias and since stool studies are not performed routinely, the clinicians participating in the study obtained stool specimens from all children who presented with acute gastroenteritis during the study. Acute gastroenteritis was defined as the onset of diarrhea within 5 days prior to the clinic visit with or without vomiting. The sensitivity of the test according to the manufacturer's information is 95% on average and the specificity 99%. The parents were contacted by telephone 7–10 days later. The interview was conducted by a research coordinator specifically trained to administer the survey, using a standard questionnaire designed to collect clinical and resource utilization data. Responders were asked to provide the following details relating to the RVGE episode: symptoms of illness (duration of fever, diarrhea and vomiting), number of physician contacts (including office visits and emergency room visits), medications administered, diaper usage, diet change, additional cases of gastroenteritis in the household, complications incurred, and hospitalizations. Finally, responders were queried regarding the number of days that the caregivers missed work.

The cost for workdays missed was calculated according to the average gross daily earning in Israel (360 shekels/day, equivalent of 67.4 euros; source: The Israeli Annual Statistic Report). Hospitalization cost was calculated according to the length of hospitalization, since in the Israeli health system the cost of hospitalization to the health management organization is based on a fixed price for each hospitalization day (1800 NIS/day of hospitalization, source: The Israeli Annual Statistic Report). The cost in dollars and euros was calculated according to the following exchange rate: 1 euro = 5.34 NIS.

Data regarding hospitalization rate and length of hospitalization of RVGE in Israel were taken from a recent study done in Israel [4].

The data were recorded on an EXCEL spreadsheet. Comparisons between the distribution of dichotomous and continuous variables were done by the chi-square test and Student's *t*-test respectively. The study was approved by the ethics (Helsinki) committee of Wolfson Medical Center and Maccabi Health Services.

RESULTS

During the study period 145 children aged 4–29 months (mean age 15 months) had their stool examined for RV; 71

stool samples (49%) tested positive for RV. Of these 71 families of RV-positive infants 54 were contacted by telephone and cooperated with the telephonic interview.

The patients' mean age was 15.5 ± 6 months (range 4–29). Age distribution was as follows: 5 infants were 0–6 months of age, 13 were 7–12 months old, 33 were 13–24 months old, and 3 children were 2–3 years old.

The mean duration of fever was 1.7 days (range 0–7 days). Infants were examined 1.9 times on average (range 1–6) by their pediatrician during an RVGE episode and had on average 2.25 days of vomiting (range 0–7) and 7.5 days of diarrhea (range 3–21). Eighteen children (35.3%) were treated with probiotics, 4 (7.8%) with oral rehydration solutions, 2 (3.9%) with anti-vomiting agents and one infant was treated with antibiotics. Nine children were examined in the emergency department and three were hospitalized for RVGE.

A rice-enriched formula was used in 18 cases (35.3%) and 8 infants (15.7%) had their formula changed to a lactose-free diet. The average case of RVGE required 230% increased usage of diapers as compared to baseline consumption. The average workday loss was 2.65 days (range 0–11) per RVGE case. RVGE cases resulted in an additional 0.73 cases in the household (range 0–5 additional cases).

The clinical characteristics of children with RVGE and those with gastroenteritis who tested negative to rotavirus are presented in Table 1. There were no significant differences with regard to clinical features and resource utilization between RVGE and non-RVGE episodes except for vomiting, which was significantly more prolonged in children with RVGE (2.25 vs. 1.3 days on average respectively, *P* = 0.03).

The cost of each for the parameters included in this analysis (unit costs) is presented in Table 2. The calculated cost of an average case of RVGE seen at the pediatrician's office is 257.39 euros. The major part of this cost (179 euros, 69.64%) was due

Table 1. Clinical characteristics of children with rotavirus GE and those with GE who tested negative to rotavirus

	RV(+) *	RV(-) **	P value
	N=54	N=27	
Age (yrs)	1.29 ± 0.50	1.29 ± 0.50	NS
Fever (days)	1.75 ± 1.76	1.5 ± 2.11	NS
Diarrhea (days)	7.5 ± 3.6	6.7 ± 4.3	NS
Vomiting (days)	2.25 ± 2.13	1.3 ± 2.28	0.03
Ambulatory visits	1.88 ± 1.11	1.7 ± 0.75	NS
Hospitalization (days)	0.11 ± 0.5	0.27 ± 1.48	NS
No. of work days lost	2.65 ± 3.03	2.4 ± 3.65	NS
ER visits	0.23 ± 0.5	0.13 ± 0.35	NS

Data are presented as mean ± SD

* Patients with rotavirus gastroenteritis RV(+)

** Patients with gastroenteritis who tested negative to rotavirus RV(-)

NIS = new Israeli shekels

Table 2. The costs for the parameters of health care and indirect cost included in the analysis (unit costs)

	Cost in NIS	Cost in Euros
Office visit	38	7.12
ER visit	600	112.36
Hospitalizations*	1800	337
Medications		
Antibiotics	15	2.81
Antiemetics	6	1.12
Probiotics	70	13.1
Glucose electrolyte solution	21	3.94
Peptobismol	14	2.62
Extra diapers	1	0.19
New formula	40	7.49
Work days lost#	360	67.4

*Cost of 1 day of hospitalization in a pediatric ward

#Gross daily earning in Israel

ER = emergency room

Table 3. Cost of an average case of RVGE seen in the pediatric clinic*

	Cost in NIS	Cost in euros
HMO costs		
Office visits	19	3.55
ER visit	100	18.7
Hospitalizations#	190	35.6
Medications	30	5.6
Total HMO cost	339	63.45
Cost to the household (Out-of-pocket)		
Medications (co-payment)	30	5.6
Extra diapers	25	4.67
New formula	25	4.67
Out-of-pocket cost	80	14.94
Indirect cost to society		
Work days lost	954	179
Total	1373	257.39

* Cost was calculated for one event of RVGE.

Hospitalization cost was calculated according to the data in ref.3

NIS = new Israeli shekels, HMO = health management organization

to work loss. The cost incurred by the health service was 63.4 euros (24.6% of the total cost), and out-of-pocket expenditure incurred by the parents was estimated at 14.94 euros (5.8% of the total cost). The breakdown of costs is presented in Table 3.

DISCUSSION

The availability of two new rotavirus vaccines [6,7] promoted increased interest in the costs incurred due to rotavirus

gastroenteritis. Assessment of these costs is essential for determination of the cost-effectiveness of the new vaccines. Several analyses of the burden and cost of RVGE have been published. Ansaldi et al. [8] examined the 1 year cumulative incidence of gastroenteritis in a cohort of Italian children aged 0–5 years in order to define the clinical burden of RVGE. They found that one-third of gastroenteritis cases requiring an office visit or telephone consultation were due to rotavirus infection. Roberts and co-workers [9] examined the costs of cases of intestinal infections in general (including RVGE) for patients treated by general practitioners in England. According to their estimation, the average cost of a RVGE case was 183.6 euros. Giaquinto et al. [10] calculated the costs of community-acquired RVGE in seven European countries. They reported that the total societal cost per episode of RVGE ranged from 166 to 473 euros in the primary care setting, 334–770 euros in the emergency room and 1525–2101 euros in the hospital setting. The mean number of workdays lost ranged from 2.3 to 7.5 days.

Lorgelly and colleagues [11] investigated the prevalence and the burden of RVGE in the community. Forty-eight percent of their sample was found to have RVGE, and the average total cost of a child presenting with RVGE was £141 (162 euros). The average direct medical cost was £58.8 (67.5 euros) and the average indirect cost was £82.3 (94.5 euros) per episode.

Rotavirus is the reason for almost 4000 hospitalizations in Israel annually (2.7% of the annual birth cohort in Israel), and the average duration of hospitalization is 3.9 days [4]. In this study we looked at the burden and the cost of a typical RVGE episode presenting at the pediatrician's office in order to obtain the missing data necessary for determining the impact of RV infection in Israel, which is the burden of ambulatory RVGE cases. The intention of this study was not to examine in detail the clinical characteristics of RVGE; however, there were no significant differences with regard to clinical features and resource utilization between RVGE and non-RVGE episodes except for vomiting, which was significantly more prolonged in children with RVGE (2.25 vs. 1.3 days on average respectively, $P = 0.03$).

According to our results, the cost of the average case of RVGE in Israel is 257 euros. The major part of this cost (69.64%, 179 euros) is due to the indirect cost to society incurred by the parental work loss associated with the child's illness. The other causes of this cost are hospitalizations (13.8%), emergency room visits (7.26%), medications and office visits (5.73%), and extra costs for purchasing new formula and diapers (3.62% of the total cost of an RVGE episode).

Our results reflect several characteristics of RVGE in Israel: In the peak winter season rotavirus causes about 50% of diarrhea episodes in infants younger than 3 years old that

necessitate office visits. Also, the average RVGE presenting to the pediatrician required almost two office visits. This relatively high rate of office visits may be partially due to the Israeli health system where a primary pediatrician visit is almost free of charge since it is completely covered by the medical insurance.

The limitations of this investigation include the number of patients included in the final analysis and potential bias of patient selection since only 76% of the 71 families of RV-positive infants were contacted for the interview. In addition, the cost of laboratory investigations was not added to this estimated burden; however, according to the clinical guidelines, stool analysis is not a routine procedure in the typical case of acute gastroenteritis in Israel.

Our results indicate that the economic impact of the ambulatory cases is quite significant. These results may be helpful for cost-effectiveness analysis of rotavirus routine vaccination in Israel.

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