

Resource utilization and costs of treating severe rotavirus diarrhea in young Mexican children from the health care provider perspective

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ABSTRACT

Background. Rotavirus is the most common cause of severe diarrhea in infants. The economic costs of treating severe rotavirus can be quite significant and are important to include in any evaluation of prevention programs. The aim of this study was to determine utilization of health care resources and costs incurred due to severe diarrhea associated with rotavirus infection in Mexican children < 5 years of age. **Material and methods.** The costs of rotavirus infection evaluated in this observational study consisted of hospital, emergency room care and out-patient visit expenses at three hospitals of the Mexican Institute of Social Security throughout 1999-2000. Service costs were estimated from costs of care for rotavirus versus non-rotavirus diarrhea obtained through a follow-up study data of 383 children and administrative records. **Results.** Diarrhea cases due to rotavirus infection comprised 36% of the sample. Participants with rotavirus diarrhea spent an average of 3.2 days in the hospital, 5.9 hours in the emergency room, and had 1.3 visits to an out-patient physician's office. Some differences in the consumption of health care were found between rotavirus and non-rotavirus diarrhea cases, although the mean costs of rotavirus and non-rotavirus cases were not significantly different. The mean cost per case of severe rotavirus diarrhea was estimated to be US\$936. The total cost of treating severe rotavirus diarrhea, including 5,955 rotavirus hospitalizations for 2004, was estimated at US \$5.5 million. **Conclusion.** Health care costs due to treatment for severe rotavirus diarrhea are a significant economic burden to the Mexican Social Security system.

Utilización de recursos y costos del tratamiento de la diarrea grave por rotavirus en niños mexicanos desde la perspectiva del prestador de servicios de salud

RESUMEN

Antecedentes. Rotavirus es el agente causante de diarrea severa en niños más común en el mundo. Los costos económicos asociados son cuantiosos y es sumamente relevante incluirlos en las evaluaciones de cualquier programa preventivo. El objetivo de este estudio es estimar la utilización de recursos y los costos de la diarrea severa causada por rotavirus en niños Mexicanos menores de cinco años desde la perspectiva del prestador de servicios. **Material y métodos.** Los costos de la infección por rotavirus evaluados en este estudio observacional incluyeron hospitalizaciones, visitas a urgencias y consultas externas en tres hospitales pertenecientes al Instituto Mexicano del Seguro Social durante 1999-2000. Los costos de los servicios fueron estimados a partir del estudio de seguimiento de 383 casos causados por rotavirus y de los causados por otros enteropatógenos, así como de bases de datos administrativos. **Resultados.** Los casos positivos a rotavirus fueron 36% de la muestra en ellos y se encontró un promedio de consumo de servicios de 3.2 días de hospitalización, 5.9 horas en sala de urgencias y 1.3 visitas al médico. Algunas diferencias en el consumo de servicios de salud se encontraron entre casos de diarrea positivos y no positivos a rotavirus. Sin embargo, los costos promedio de casos de rotavirus y no rotavirus no fueron diferentes estadísticamente. El costo promedio por evento de diarrea severa por rotavirus fueron 936 dólares americanos. Los costos causados por diarrea grave por rotavirus, para el Instituto consideraron 5,955 hospitalizaciones y fueron estimados en 5.5 millones de dólares. **Conclusiones.** Los costos de tratamiento de diarrea grave causada

Key words. Diarrhea. Rotavirus. Resource utilization. Costs. Mexico.

Palabras clave. Diarrea. Rotavirus. Utilización de recursos. Costos. México.

INTRODUCTION

Diarrheal diseases are a major cause of mortality and morbidity in children < 5 years of age living in low and middle-income countries (LMIC); they were among the five most common in Mexico in 2004.¹ Severe diarrhea is a life-threatening component of diarrheal diseases that may lead to hospitalization or death, thereby incurring large costs to the health care sector. There are two primary reasons for a strong interest in health care costs due to rotavirus disease: rotavirus is the enteropathogen responsible for the majority of severe diarrhea in young children,^{2,3} and the limited success of other preventive measures in controlling this disease calls for vaccine development.^{4,5} Treatment costs due to this virus are an important consideration in deciding preventive strategies because they may modify the cost-effectiveness and cost-saving capacity of the program.⁶

In high-income countries (HIC), one reason for implementing a rotavirus vaccination program is the reduction of large health care costs. In LMIC, costs averted by vaccination are expected to be lower due to less infrastructure and access to health care facilities.⁷ Further economic evaluations of preventive programs need to assess what amount of treatment costs could be averted through vaccination.

Several cost analyses of rotavirus diarrhea treatment in complete or partial economic evaluations have been conducted since the 1990s; most were conducted in HIC before 2002. Compared to studies conducted in LMIC, those in HIC included more detailed treatment costs and integrated societal perspectives.⁷⁻¹⁹ The four studies in LMIC that were published between 2005 and 2007 only contained aggregated cost information. In these studies, costs were primarily estimated from a health services perspective using an international approach for one country or a group of countries.^{7,16-19}

Vaccination programs targeting infants to prevent rotavirus infection were under review in several LMIC, including Mexico, by 2004. Evaluating the cost of treating rotavirus disease in one of the largest health care organizations operating within a representative middle income country can inform decision makers regarding the potential cost, which could be

prevented by a vaccination program. Furthermore, there is a demonstrated need for detailed information around the number of youth affected and associated treatment costs to assist with further economic analyses. Accordingly, the aim of this study is to determine the resource utilization and costs of severe rotavirus-associated diarrhea in children insured by the Instituto Mexicano del Seguro Social (IMSS). IMSS is the largest health care provider in the country, covering approximately 40% of the 104.5 million Mexicans. As decisions regarding the introduction of vaccine-preventable disease interventions are made by public health care providers, the health care provider perspective employed in this study is particularly important.

MATERIAL AND METHODS

A prospective observational study was conducted from September 1999 to August 2000 to capture information about a sample of children hospitalized due to severe diarrhea in three urban IMSS-hospitals located in northern, central, and southern areas of Mexico City. There are thirteen similar IMSS-hospitals admitting children in this city and those selected were strategically identified to represent the pediatric services in second level hospitals. A surveillance team of nurses visited the hospitals to obtain information from medical records of diarrheal episodes including clinical data, etiology, hospital resources provided, received treatments and health care services consumed per patient. The children included in the sample were selected on the basis of the following inclusion criteria: hospitalized with diagnosis of acute diarrhea; younger than five years old; Mexico City resident for the last six months; and parents acceptance to participate in the study.²⁰ An episode of severe diarrhea was defined as the passage of three or more loose or watery stools in 24 hours period that required hospitalization. The study was approved by the Institutional Review Board of the IMSS.

A 20-point scale was used to grade the severity of diarrheal episodes. This measure, known as the Vesikary scale, was the sum of values (1, 2 or 3 points) given to the severity of seven symptoms: dura-

tion of diarrhea in days, greatest number of diarrheal stools over a 24 hour period, duration of vomiting in days, greatest number of vomiting episodes over a 24 hour period, fever, dehydration and intensity of treatment needed (with 0, 1 and 2 values).²¹ The value of the scale totaling 11 or more was considered a moderate to severe diarrheal episode as in a recent randomized study including Mexican children.²² Stool samples of children were collected during the first 24-48 hours after arriving to the hospital. Cases meeting the criteria for moderate to severe episode were tested for viral, bacterial and parasitic enteropathogens during hospitalization and according to the sequence of health care provided. Specific agents tested for comprised rotavirus, adenovirus, astrovirus, *shigella SP*, *Salmonella sp*, *Vibrio cholerae*, *Escherichia coli*, *campylobacter sp*, *G Lamblia*, *E histolytica*, *Cryptosporidium*, *Cyclospora*, *Microspora* and *Isospora sp*. Methods used were of similar sensitivity and specificity in order to reduce bias; the method details and results were reported elsewhere.²⁰

Costs were estimated from the perspective of the health care provider. Direct medical costs of severe diarrhea assessed included hospitalization, emergency room visits, and visits to the physician's office. We designed a questionnaire to collect detailed information concerning resource consumption before, during, and after a severe diarrhea episode-associated hospitalization based on clinical guidelines for the recommended treatment of diarrheal diseases in Mexico.²³ Data about the length of stay in the hospital, the number of emergency room visits, and the number of visits to the physician's office before or after the episode for each episode were collected.

Hospitalization costs contained eight inputs: pharmaceuticals, diagnostics, infant formula, medical staff, food and clothing, curative material, utilities, and capital costs. The cost of one emergency room visit was considered to be equivalent to one day of hospitalization. This assumption has been used previously to assign a value to the costs of ambulatory services.^{16 17} The cost of one physician's office visit was taken from a previous cost study of outpatient consultation in primary care IMSS facilities.²⁴ The variable and fixed costs of hospitalization were computed following particular procedures. Pharmaceuticals (oral rehydration and intravenous solutions, antibiotics, and others), diagnostics (laboratory and x-ray tests), and infant formula were measured by direct inventory of the quantities used per patient. Daily quantities were added together to determine total consumption per child during each diarrheal episode.

Costs per patient-day of physicians and nurses were estimated based on their annual salaries divided by the annual number of patient-days in the pediatric wards. The resulting cost per day was multiplied by the number of days that each child spent in the ward. Costs of food and clothing, curative material, utilities (telephone, security, administration, electricity, and water), and capital costs (building and equipment) were considered fixed costs. The fixed cost per day in wards was determined by dividing total expenditures by total number of patient days in the pediatric wards. The cost per patient was calculated by multiplying the fixed cost per day by the number of days each child spent in the pediatric wards.

Valuations of costs consisted of assigning prices (or unitary costs) to quantities of resources used. Pharmaceutical and diagnostic tests were priced at market value. The price of infant formula was taken from our own estimates. The mean salaries of physicians and nurses were taken from the IMSS medical-staff database.²⁵ Capital costs and costs of utilities corresponding to the pediatric wards were allocated to final service departments by using the step-down method. This method consists of first allocating the costs into basic, intermediate, and final cost centers of the hospital based on the number of personnel. Costs apportioned to basic centers are then reallocated to intermediate and final centers. Finally, costs concentrated on intermediate service centers are allocated to final service centers (hospitalization and consultation) in the same manner.^{26 27}

Information on food, clothing, and curative material as well as expenditure on utilities (telephone, security, administration, electricity, laundry, and water) was provided by the administrative departments of each hospital. Capital costs were determined by the annual-equivalent cost of health care facilities, using a discount rate of 5% over 20 years for equipment and furniture, and 30 years for buildings. Costs per square meter of building were valued at Mex \$11,700. Costs were reported in 2004 Mexican pesos (Mex \$) and US dollars (US\$). The National Consumer Price Index (INPC) was used to convert prices from 1999-2000 to the year 2004. The 2004 exchange rate for converting currency was Mex \$11.4 per US \$1 based on data reported by the National Bank of Mexico.

Data analysis of resources used and costs for severe rotavirus and non-rotavirus diarrhea cases before, during, and after episodes of severe diarrhea hospitalization was conducted using Stata 8.0 and 9.0 software and Microsoft Excel 2003. The rotavirus group consisted of all cases detected as ELISA

positive-for-rotavirus in stool samples. The rotavirus group included cases with rotavirus as a unique identified agent, as well as rotavirus infections mixed with other enteropathogens. The Student's t test was used to compare mean values of hospitalization days, mean number of hours in the emergency room, and mean costs per child. The Chi-square test was used to compare proportions. In addition, a pie-graph described the relative participation of inputs in the mean cost.

Costs of severe rotavirus diarrhea from the health care provider perspective were extrapolated nationally by multiplying the mean cost of a rotavirus-diarrhea episode by the number of hospitalization episodes considered to be rotavirus diarrhea-associated in children < 5 years of age insured by the IMSS according to the prevalence of rotavirus diarrhea cases identified in this study. The overall number of diarrhea-related hospitalizations was taken from the database of all IMSS hospital discharges according to the health statistics information office of IMSS for the year 2000 of 10th International Classification of Diseases (ICD-10) with diagnosis of gastroenteritis (A01–A03; A04; A05; A06.0–A06.3; A06.9; A07.0–A07.2; A07.9; and A08–A09).²⁸

In order to deal with the uncertainty that the assumptions and information represents, a sensitivity analysis was conducted estimating the total costs of treatment when variables were modified up to 30% of the base case values. Variables expected to have the largest influence on total costs were labor, other fixed costs and number of rotavirus cases.

RESULTS

Three hundred and eighty-three children were considered for the analysis since they had complete information for the 12-month period of the study. The mean age was 18.4 months (95% CI: 17.0; 19.7), and females accounted for 42% of the sample. The mean severity score of diarrhea episodes was 13.5 points (95% CI: 13.1; 13.7). The mean hospital stay per child was 3.3 days (95% CI: 3.1; 3.5). Most children (93%) were hospitalized for 5 or fewer days. Nearly all participants (96%) reported utilizing emergency room services prior to hospitalization, at an average of 6.4 hours (95% CI: 5.6; 7.1 hours) per visit. In addition, 83% attended at least one appointment at the physician's office before or after hospitalization with an average of 1.4 visits. The mean cost of severe

Table 1. Average quantities and costs of treatment of severe diarrhea among children under age five in three Mexican IMSS hospitals (In 2004 US dollars).

Service	Mean	Cost per unit (US dollars)	Costs per event (US dollars)
Hospitalization	3.3 days	212	702
Emergency-room visit	6.4 hours	212	212
Physician's office visit	1.4 visits	49	67

Table 2. Differences in resource consumption during treatment of severe diarrhea between rotavirus and non-rotavirus diarrhea cases in three IMSS hospitals in Mexico City.

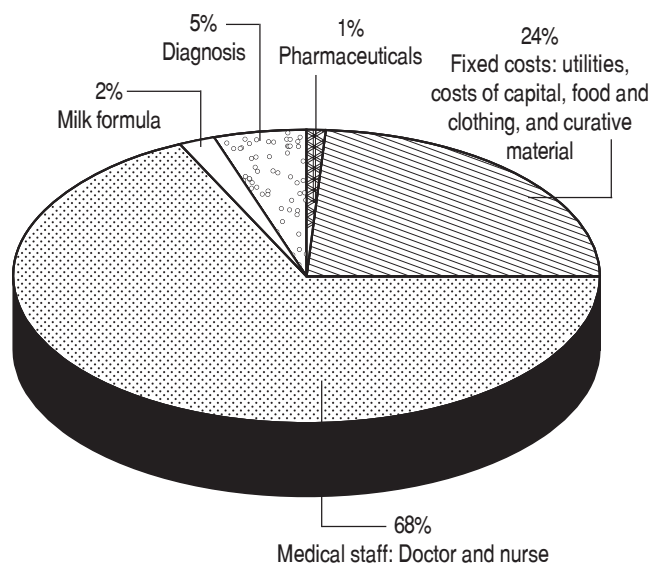
	RV cases* n = 136	Non-RV cases * n = 247	P value**
Age (mean months)	13.9 (8.68)	20.9 (15.6)	0.000
Severity (mean score)	14.5 (2.5)	12.9 (2.8)	0.000
Hospitalization (mean days)	3.2 (1.4)	3.4 (2.1)	0.303
Emergency room (% of use)	96.3	96.0	0.300
Emergency room (mean hours)	5.9 (5.8)	6.6 (7.6)	0.290
Out-patient visits (% of use)	88.2	86.2	0.045
Out-patient visits (mean visits)	1.3 (0.7)	1.4 (0.9)	0.398
Antibiotics (% of use)	17.6	40.4	0.000
Oral rehydration therapy in pediatric ward (% of use)	23.3	20.3	0.53
Intravenous rehydration in pediatric ward (% of use)	78.3	62.1	0.004
Diagnostic tests (% of use)	75.7	84.9	0.026

* Standard deviations in parentheses. ** Significance of difference of means test (t-test) or difference between proportions (chi-square) test.

diarrhea episode per child, assuming the cost per visit to the emergency room was equivalent to one day of hospitalization, was Mex \$11,178 (95% CI: 10,409; 11,946) or US \$980 (95% CI: 912; 1,049) (Table 1).

Rotavirus-associated diarrhea cases accounted for 36% of all diarrhea episodes. The mean values of age and severity of diarrhea in rotavirus infected children were significantly different from the rest of children (Table 2). Children with rotavirus positive diarrhea were younger and suffered more severe episodes than the non-rotavirus cases ($p = 0.000$) but the costs of treatment were not different. This difference in severity of episode between the groups was associated with differences in the consumption (measured as the percentage of use) of inputs including visits to the physician's office (0.045), antibiotics ($p = 0.000$), intravenous rehydration ($p = 0.004$) and diagnostic tests ($p = 0.0026$) (Table 2). While the use of expensive laboratory tests for pathogen detection in the non-rotavirus group contributed to higher treatment costs, significant differences in mean costs of treatment were not found (Table 3).

Hospitalization accounted for 72% of the mean costs of a severe rotavirus diarrhea episode, while emergency room visits and outpatient visits to the physician accounted for 23% and 5%, respectively; similar figures were found for non-rotavirus diarr-



Mean costs of rotavirus diarrhea episode (us\$ 936) are integrated by:

- Hospitalization (US \$665).
- Emergency room visits (US \$208).
- Ambulatory visits to physician (US \$63).

Figure 1. Distribution of hospitalization cost per children with severe rotavirus.

Table 3. Costs of treatment of severe rotavirus and non-rotavirus diarrhea among children under age five in three Mexican IMSS hospitals (In 2004 US dollars).

Category/input	RV (n = 136) mean (SD)	Non-RV (n = 247) mean (SD)	P value [†]
Costs of severe diarrhea	936 (512)	1004 (720)	0.330
Hospitalization	665 (275)	723 (428)	0.154
Emergency room	208 (204)	213 (244)	0.842
Visit to the physician's office	63 (33)	68 (48)	0.315
Antibiotics* (hospitalization)	2.2 (3.9)	3.9 (7.7)	0.456
Rehydration* [‡] (hospitalization)	6.8 (5.4)	5.6 (6.3)	0.102
Diagnostic tests* (hospitalization)	27.2 (26.7)	35.3 (32.9)	0.013

*Average costs include only those cases consuming this service. [†] T test of averages and proportions differences assuming uniform variance. [‡] Includes costs of oral and intravenous rehydration therapies.

Table 4. Treatment costs of severe rotavirus diarrhea in children for the IMSS sensitivity analysis (In 2004 US dollars).

Variable changed	Low estimate (-30%)	Base case	High estimate (+30%)
Doctor and nurse	4.7	5.5	6.3
Other fixed costs	5.2	5.5	5.8
Total fixed costs	4.4	5.5	6.6
Rotavirus prevalence	3.8	5.5	7.1
All variables	3.1	5.5	8.6

hea episodes (Table 3). Regarding hospitalization costs due to severe rotavirus diarrhea, the largest component was medical staff costs (68%) and fixed costs (24%), with a smaller contribution from pharmaceuticals, infant formulas, and diagnostics (Figure 1). The costs of treating severe rotavirus diarrhea were estimated to be approximately Mex \$62.59 million or equivalent to US \$5.49 million. Results were based on 5,955 inpatient events which correspond to 36% of the total IMSS hospitalizations for 2004. In addition we estimated that 5,737 emergency-room visits and 6,919 physician visits were due to rotavirus. Costs of hospitalization included 3.2 days of hospitalization (US \$665), one visit to the emergency room (US \$208) in 96.3 % of the cases, and one outpatient physician's office visit (US \$49) in 88.2% of children.

The sensitivity analysis suggested that the prevalence of rotavirus diarrhea had the most significant effect on the costs of treatment followed by costs of doctors, nurses and other fixed costs (Table 4). Costs of treatment at the national level varied from US \$3.84 to \$7.14 million when the baseline prevalence of 36% was varied from 25.2% to 46.8%. National treatment costs varied from US \$4.68 to \$6.3 million when salaries were varied $\pm 30\%$. National costs varied from US \$3.08 to \$8.56 million when all variables were included in the sensitivity analysis (Table 4).

DISCUSSION

This study provides evidence on the costs of treating severe rotavirus diarrhea using data collected from rotavirus positive diarrhea cases in IMSS hospitals. A detailed cost analysis was undertaken over a period of one year including one fall-winter and one spring-summer season to account for seasonal effects. The pattern of health care resource use in rotavirus versus non-rotavirus cases was compared. Although we expected that the higher severity of rotavirus-associated diarrhea episodes would be more costly, only treatment costs for rehydration therapy, antibiotics, and diagnostic tests were significantly different for rotavirus cases. Because fixed costs comprised the largest proportion of the total cost, variable costs had no significant effect on the total costs for the two groups. This study confirmed the hypothesis that the costs of treatment for rotavirus-associated diarrhea are significant for the largest health-care provider in Mexico, which reported nearly 6,000 hospitalizations in 2004.

The pattern of resource consumption presented for this population could be considered as represen-

tative of social security recipients. If health care costs were compared between health care providers, IMSS costs are expected to be higher than those of public facilities for uninsured populations and lower than the costs of private providers (29). Additional research is necessary to identify the differences in costs which may be caused due to the varying quality of health care provided by each organization (30).

While the findings are of note, certain limitations must be considered. We were unable to verify whether unit prices for emergency room visits had different price structures compared to hospital stays. Our estimates were also made under the assumption that the cost of one day of hospitalization was equivalent to the cost of one visit to the emergency room. A detailed analysis of resource use in emergency room services is necessary to overcome this limitation. In addition, unit cost of doctor's office visits was not investigated first hand. The procedures used by the study we adopted price structures from may render the costs of ambulatory care incomparable. If costs of ambulatory care are significant when considering different degrees of severity of diarrhea, the unit costs of health care must be estimated using a methodology similar to the one followed for hospital costs.

Regarding the non-medical costs associated with rotavirus diarrhea, there are two perspectives which can be adopted. First, if children are insured by IMSS, the health care costs of severe diarrhea are expected to be covered mostly by IMSS at the time of receiving health care. However a more complete analysis of the costs of severe diarrhea would include the other direct costs paid by families. Families may pay additional health care expenses for private sector resource use and may be subject to additional costs due to time off from work or other related issues. This information would provide a better assessment of the global costs of rotavirus infection.

The fixed costs of personnel and infrastructure are a significant part of the health care costs of severe diarrhea, and biases in their measurement contribute to uncertainty. We were unable to test whether measurement bias was present due to differing hospital scales. However, we conducted a sensitivity analysis to determine the extent to that fixed costs affected the costs of each health care provider. We found that variations in personnel costs (i.e., doctor and nurse salaries) were more substantial modifiers of the overall health care cost than other fixed costs. Further studies should take this into consideration.

In summary, this study provided a valuable description of the economic impact of rotavirus diarrhea in Mexican infants. This analysis was based on direct measurement of prevalence and resource use in rotavirus and non-rotavirus cases of hospitalized children cared for by the largest health care provider in Mexico. The cost of treating severe rotavirus diarrhea for this organization was estimated to be almost US \$5.49 million, but ranged from US \$3.0 to \$8.5 million when the prevalence and fixed costs were varied simultaneously in the analysis. Despite some differences in the resource use pattern among the two groups (rehydration, antibiotics and diagnosis), we found that mean costs were not different by rotavirus infection status. Another relevant finding was that the most important contributor to overall severe rotavirus diarrhea costs was medical staff, followed by fixed costs (capital, utilities, and food, clothing and curative material). However, the prevalence of rotavirus diarrhea in hospitalized children was the factor responsible for the most variation in national costs for the IMSS. This study assists health care decision makers in estimating the economic impact of preventive strategies to prevent severe rotavirus diarrhea for children in Mexico.

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