

Hospitalizations for diarrhea in Quebec children from 1985 to 1998: Estimates of rotavirus-associated diarrhea

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OBJECTIVE: To characterize the incidence and duration of hospitalization due to diarrhea and to assess the proportion of hospitalizations that are attributed to rotavirus-associated diarrhea.

DESIGN: Retrospective study of hospitalization data.

SETTING: Hospitals located in Quebec.

POPULATION STUDIED: Children from one to 59 months of age who were discharged from hospital from April 1, 1985 to March 31, 1998.

MAIN RESULTS: There were 63,827 hospitalizations for diarrhea over the study period, for an average of 4910 hospitalizations/year. The epidemic curve showed a periodicity with regular alternation of high and low annual peaks. The number of hospitalizations for rotavirus-associated diarrhea was estimated according to three different methods. The estimates varied between 1353 and 1849 hospitalizations due to rotavirus-associated diarrhea/year over the 13-year period, with good agreement between

the results of the three methods for a one-month to five years of age incidence of 320 hospitalizations for rotavirus-associated diarrhea/100,000 children. The average duration of hospital stay decreased from 5.2 days in 1985 to 3.3 days in 1998.

CONCLUSIONS: The present article shows the importance of diarrhea hospitalizations among children and the alternating peak-year periodicity.

Key Words: Children; Diarrhea; Hospitalization; Quebec; Rotavirus

Hospitalisations liées aux diarrhées chez les enfants au Québec de 1985 à 1998 : estimations des diarrhées associées au rotavirus

OBJECTIF : Documenter l'incidence et la durée des hospitalisations pour diarrhée et évaluer la proportion attribuée aux infections à rotavirus dans une population d'enfants.

MODÈLE : Étude rétrospective des données hospitalières.

Résumé à la page suivante

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CONTEXTE : Hôpitaux situés dans la province de Québec.

POPULATION ÉTUDIÉE : Enfants âgés de 1 à 59 mois sortant de l'hôpital entre le 1er avril 1985 et le 31 mars 1998.

PRINCIPAUX RÉSULTATS : Il y a eu 63 827 hospitalisations pour diarrhée pendant la période visée par l'étude, c'est-à-dire en moyenne 4 910 hospitalisations par année. La courbe épidémique montrait une périodicité avec une alternance régulière de pics annuels d'effectifs élevés et d'effectifs moindres. Nous avons calculé les effectifs d'hospitalisations pour infection à rotavirus selon trois méthodes différentes : les estimations

varient entre 1 353 et 1 849 hospitalisations pour infection à rotavirus par année pour l'ensemble des treize années et il y a une bonne cohérence entre les résultats des trois méthodes pour une incidence de 320 hospitalisations pour infection à rotavirus pour 100 000 enfants âgés de 1 mois à 5 ans. La durée moyenne du séjour à l'hôpital et passée de 5,2 jours en 1985 à 3,3 jours en 1998.

CONCLUSIONS : L'enquête montre l'importance des hospitalisations pour diarrhée chez les enfants et une périodicité avec alternance de pics annuels.

Diarrhea is an important public health problem in children. Although no longer a frequent cause of death in developed countries, rotavirus remains the major cause of hospitalizations for diarrhea among children (1). Although the first commercial vaccine was withdrawn quickly from the market because of an association with intussusception (2), other vaccines are being developed and are expected soon. The benefits that are expected from these vaccines are a contentious issue in developed nations (3). Before considering the universal use of a new rotavirus vaccine, it is essential to estimate the benefit that may be expected from its introduction. Outpatient consultations and hospitalizations are the main contributors to the burden of diarrhea. The purpose of the present study was to estimate the number of hospitalizations that may be associated with rotavirus. These data are not directly available because routine microbiological testing is not performed for all children who are hospitalized for diarrhea.

In Quebec, complete computerized hospitalization data have been available since 1985. In the present study, three different methods were used to estimate the proportion of all hospitalizations with a diagnosis of diarrhea that could be attributable to rotavirus.

METHODS

Source of data

Med-Echo is the administrative database that contains complete information on all hospitalizations in Quebec. It was created in 1982, but complete information has been available only since 1985. For each hospitalization, a principal diagnosis and up to 15 secondary diagnoses are recorded.

Study population

The study population consisted of all children from one to 59 months of age who were hospitalized for diarrhea in Quebec from April 1, 1985 to March 31, 1998. Newborn babies and those up to 28 days of age were excluded because rotavirus is rare in that population and because the International Classification of Diseases-9th revision (ICD-9) provides a specific coding for health events that occur during the neonatal period.

The following ICD-9 codes were extracted: diarrhea of determined etiology (bacterial [001–005, excluding 003.2 localized salmonella infections, and 008.0–008.5], parasitical [006–007, excluding codes 006.2–006.6 amebic abscess and localized amebiasis], viral [008.6 and 008.8]) and diar-

rhea of undetermined etiology, but presumed to be infectious (009.0–009.3) and noninfectious (558.1–558.9). A specific code for rotavirus diarrhea (008.61) was introduced in October 1992 (ICD-9, 6th edition). It was seldom used in Med-Echo; those cases of rotavirus-associated diarrhea (RAD) were included as diarrhea of viral origin. All primary and secondary diagnoses were included.

The following variables were studied: primary and secondary diagnoses, age, sex, admission date, exit date, stay duration, death and area of residence. The encrypted health insurance number was used to eliminate double registration.

Two consecutive hospitalization episodes were considered as only one hospitalization when there were 15 or fewer days between them. This happened in 1.7% of the episodes. For calculation of the length of stay, only the first episode was considered. The global results were increased by an insignificant factor when the length of the repeat episode was added to the length of the first episode.

Rotavirus estimate

Three methods were used to estimate the number of hospitalizations for rotavirus-associated diseases.

The first method was described by Ho et al (4) and by Jin et al (5). The difference in the number of winter hospitalizations for diarrhea, minus the number of summer hospitalizations for diarrhea, was considered to be the number of hospitalizations caused by rotavirus. This approach was based on the seasonality of rotavirus that was observed in 88 health centres in Canada, Mexico and the United States, which revealed that there were few rotavirus cases during summer months (6).

The second method of estimation used the proportion of laboratory-confirmed rotavirus infection among diarrhea-related hospitalizations that was measured by Waters et al (7) in the Toronto, Ontario area in 1998. In that study, RAD cases represented approximately 37% of those patients tested by enzyme immunoassay and approximately 36% of those tested by electron microscopy. This etiological fraction was calculated for the period between November 1 and June 30, 1998. In the present study, this proportion was applied to all diarrhea cases registered in Med-Echo for these same months of each year.

The third method calculated RAD hospitalizations by using either monthly weighted estimates or age weighted estimates that were observed between 1974 and 1982 in a Washington, DC hospital (8).

TABLE 1
Diarrhea-related hospitalizations (all diagnoses) among children younger than five years of age in Quebec, April 1, 1985 to March 31, 1998

Year	Winter (Dec to May)	Summer (June to Nov)	Total
April 1985 to Nov 1985	1306*	2362	3668*
Dec 1985 to Nov 1986	3240	1860	5100
Dec 1986 to Nov 1987	2764	1704	4468
Dec 1987 to Nov 1988	3107	1731	4838
Dec 1988 to Nov 1989	2328	1785	4113
Dec 1989 to Nov 1990	4460	1557	6017
Dec 1990 to Nov 1991	2164	2231	4395
Dec 1991 to Nov 1992	4204	1515	5719
Dec 1992 to Nov 1993	2592	1847	4439
Dec 1993 to Nov 1994	3711	1315	5026
Dec 1994 to Nov 1995	2957	1498	4455
Dec 1995 to Nov 1996	3941	1176	5117
Dec 1996 to Nov 1997	2867	1544	4411
Dec 1997 to March 1998	2061†	N/A	2061†
Total	41,702	22,125	68,827

*Partial Year—April to May 1985; †Partial year—December 1997 to March 1998; Dec December; Nov November

Rotavirus infection indicators

Several indicators were suggested by Lebaron et al in 1990 (6) to measure trends in rotavirus epidemiology: the peak season (two consecutive months with the highest number of detections), the onset of rotavirus season (the month in which detections first exceeded the monthly mean), the duration of rotavirus season (the number of months during which detection exceeded the mean) and the epidemic intensity (defined as the ratio of the number of detections for the peak month to the number of detections for the mean observed during the season).

These indicators of rotavirus infection were extended to all diarrhea hospitalizations.

For crude incidence rates, the total number of Quebec children from one month to five years of age in this same 13-year period was used as the denominator.

Statistical analysis

For data analysis, SAS Institute Inc (USA) software was used and one hospitalization stay was the statistical unit. Frequency distributions were studied and crude rates were calculated with a 95% CI to compare variables of interest.

For comparison, Pearson χ^2 tests were performed for qualitative variables.

RESULTS

Diarrhea-related hospitalizations

There were 63,827 diarrhea-related hospitalizations among one-month to five-year-old children in Quebec from April 1, 1985 to March 31, 1998, for a cumulative denominator of

TABLE 2
Diarrhea-related hospitalizations (all diagnoses) among children younger than five years of age in Quebec, April 1, 1985 to March 31, 1998 by civil year

Civil year	Season			Epidemic intensity
	Month of onset	Duration (months)	Peak season	
1986	January	5	March-April	1.891
1987	January	6	March-April	1.553
1988	January	5	Feb-March	1.578
1989	March	5	Nov-Dec	1.752
1990	January	5	Feb-March	2.061
1991	April	5	April-May	1.287
1992	January	5	Feb-March	1.826
1993	February	6	April-May	1.425
1994	January	5	Feb-March	1.808
1995	January	6	April-May	1.529
1996	January	5	March-April	2.157
1997	February	5	April-May	1.758

Onset of rotavirus season – month in which detections first exceeded the monthly mean; Duration of rotavirus season – number of months during which detection exceeded the mean. Peak season – two consecutive months with the highest number of detections; Epidemic intensity – defined ratio of the number of detections for the peak month to the number of detections for the mean. Dec December; Feb February; Nov November

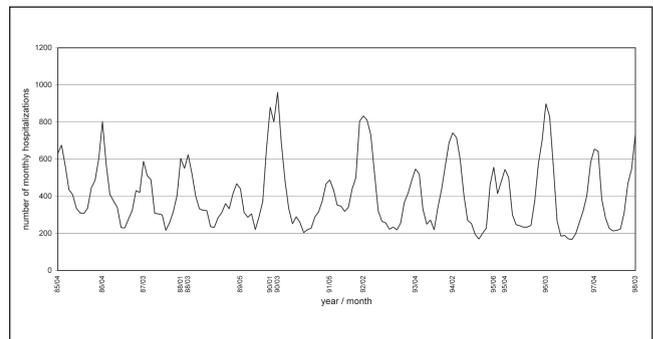


Figure 1 The number of monthly diarrhea-related hospitalizations (all diagnoses) among children younger than five years of age, Quebec, April 1, 1985 to March 31, 1998

5.8 million person-years. The annual number of cases varied between 4113 and 6017 hospitalizations (Table 1). Quebec had an average birth cohort of 90,000 children during those years.

Although the onset of rotavirus season was generally in January (Table 2), the winter period was defined as December to May, and the summer period as June to November. The duration of the diarrhea season varied from five to six months, which confirmed that the six-month period was appropriate. Peak season in diarrhea-related hospitalizations was shared equally between February to March, March to April and April to May (Table 2). The epidemic curve for diarrhea hospitalizations (Figure 1) showed a periodicity in which high annual peaks were noted in even-numbered years, followed by low peaks in odd-numbered

TABLE 3
Numbers and crude incidence rates, by age group, of diarrhea-related hospitalizations (all diagnoses) among children younger than five years of age in Quebec, April 1, 1985 to March 31, 1998

Months of age	Number of hospitalizations due to diarrhea	Proportions by age group		Quebec cumulated population (13 years)	Crude incidence rate by age group and 95% CI*
		Percentage	95% CI		
1-11	22,455	35.1	34.8% to 35.5%	1,062,569	2113.2 (2085.9 to 2140.6)
12-23	18,493	28.9	28.6% to 29.3%	1,169,859	1580.7 (1558.1 to 1603.3)
24-35	10,998	17.2	16.9% to 17.5%	1,175,353	935.7 (918.3 to 953.1)
36-47	6978	10.9	10.6% to 11.1%	1,180,402	591.1 (577.3 to 604.9)
48-59	4903	7.6	7.4% to 7.8%	1,191,539	411.4 (399.9 to 422.9)
Total (1-59 months)	68,827	100.0		5,779,772	1104.3 (1095.8 to 1112.8)

*Crude incidence rate by age group and 95% CI per 100,000 children of the same age groups

TABLE 4
Hospital stay duration, by age group, for diarrhea-related hospitalizations (all diagnoses) among children younger than five years of age in Quebec, April 1, 1985 to March 31, 1998

Months of age	Hospital stay duration (days)		
	Number	Mean±SD	Median
1-11	22,455	6.0±36.2	3
12-23	18,493	3.8±15.1	3
24-35	10,998	3.3±13.7	2
36-47	6978	3.5±24.6	2
48-59	4903	2.8± 4.2	2

years. In low incidence years, the peak numbers reached 400 to 600 monthly hospitalizations compared with 600 to 1000 monthly hospitalizations in high incidence years. Epidemic intensity varied from 1.287 in 1991 to 2.061 in 1990. For example, in 1991, the month with the highest number of hospitalizations had 28.7% more hospitalizations than the monthly mean. In 1990, the peak month had more than twice as many hospitalizations as the yearly average.

The crude incidence rates decreased with increasing age (Table 3), from 2113.2/100,000 one- to 11-month-old children (95% CI 2085.9 to 2140.6) to 411.4/100,000 48- to 59-month-old children (95% CI 399.9 to 422.9). Boys were hospitalized more frequently for a diarrheal episode than were girls (54.8% and 45.1%, $P < 0.001$).

For diarrheal episodes, mean hospital stay duration varied from 6.0 days in one- to 11-month-old children to 2.8 days in 48- to 59-month-old children (Table 4). The overall annual mean duration decreased from 5.2 days (in 1985) to 3.3 days (from 1996 to 1998). It also varied from 2.9 days to 5.8 days within various regions throughout the province.

A viral etiology was confirmed in 24.9% of all diarrhea-related hospitalizations; bacterial and parasitic infections were confirmed in 5.4% and 0.2% of all diarrhea-related hospitalizations, respectively. Presumed infectious etiologies and presumed noninfectious etiologies represented 8.2% and 62% of total hospitalizations for diarrhea, respectively.

RAD

The three methods gave relatively close estimates of the incidence of RAD: The estimated annual mean was 1505.9 hospitalizations for RAD with the Ho et al (4) and Jin et al (5) method, 1424.0 hospitalizations for RAD with coefficient 0.37, provided by Ford-Jones et al (7), and 1352.8 and 1849.0 RAD with Brandt's (8) monthly and age-specific coefficients, respectively (Table 5).

DISCUSSION

In routine inpatient hospital practice, laboratory tests are not used consistently to microbiologically confirm rotavirus infection. Therefore, direct data are lacking to determine the proportion of diarrheal episodes due to rotavirus, and other methods must be used to estimate the burden of hospitalizations that may be prevented by a new vaccine.

Because 92% of rotavirus infections are observed among children under five years of age (9), the present study was limited to this age group. The present case definition was similar to what has been used by other investigators (10).

One remarkable feature of the epidemic curve is the annual alternation of low and high monthly peaks. The reason for this periodicity is not known. One hypothesis is that it takes two years to accumulate a sufficient number of susceptible children to produce a full-blown epidemic. Brandt et al (8) reported this, specifically for rotavirus-proven infection, which implied that studies of RAD incidence should be conducted over at least two years.

Because the average annual incidence rate of diarrhea-related hospitalizations was 11/1000 children younger than five years of age (Table 3), the cumulative incidence rate over five years would then be 55/1000 children. In other words, a child's risk for hospitalization for diarrhea in the first five years of life would be 1/18. This is approximately twice the risk that was observed in Toronto in 1998 (11). The Toronto data were collected over one year only. The lower estimate in that study may have been due to a different pattern of hospitalization in the Toronto area, a 'small year' in terms of diarrhea or the differences in the methodology used by the two studies. The authors of the Toronto study mentioned that they likely underestimated the hospi-

TABLE 5
Methods of comparing rotavirus-associated diarrhea hospitalizations among children younger than five years of age, Quebec, April 1, 1985 to March 31, 1998

Year	Ho et al and Jin et al (references 4 and 5)	Ford-Jones (reference 7)	Brandt et al (reference 8)	
			Monthly weights	Age weights
April 1985 to November 1985	N/A	(806.2)	(304.6)	(1356.4)
December 1985 to November 1986	1380	1453.3	1293.5	1907.7
December 1986 to November 1987	1060	1253.9	1156.5	1654.1
December 1987 to November 1988	1376	1377.5	1377.4	1813.2
December 1988 to November 1989	543	1114.8	964.9	1517.8
December 1989 to November 1990	2903	1854.8	1986.0	2291.5
December 1990 to November 1991	-67	1123.6	879.7	1664.3
December 1991 to November 1992	2689	1754.5	1852.4	2224.0
December 1992 to November 1993	745	1243.2	1073.5	1672.0
December 1993 to November 1994	2396	1557.3	1649.8	1911.5
December 1994 to November 1995	1459	1295.0	1231.8	1634.1
December 1995 to November 1996	2765	1630.2	1649.9	1945.9
December 1996 to November 1997	1323	1285.0	1095.5	1659.6
December 1997 to March 1998	N/A	(762.5)	(1071.3)	(789.0)
Total	19,577	18,512.2	17,587.4	24,041.5

Coefficient of 0.37 applied for all columns for eight months; Parentheses indicate partial year; NA Not applicable

talization rate. The results of the present study seem to confirm this statement.

It is interesting to note that the three methods that were used in the present study provided relatively similar estimates of the number of RAD-related hospitalizations. Each method has its weaknesses. The first one, used by Ho et al (4) and Jin et al (5), was based on the hypothesis that all excess diarrhea-related hospitalizations observed in winter were due to rotavirus infections, which is an oversimplification of reality. The second method used a coefficient that was measured prospectively in Toronto hospitals in 1998. Unfortunately, the present study showed that the incidence of rotavirus diarrhea varies from year to year, while this observation was made over a one-year period only. The third method may be the most satisfactory because Brandt et al (8) collected prospectively the proportion of RAD over all hospitalizations for diarrhea over a seven-year period and provided age- and month-specific proportions. The age-specific estimate was the only one that diverged slightly from the others. Put together, the three methods provide a robust estimate of the mean annual number of hospitalizations due to RAD (Table 5) – approximately 320 hospitalized RAD cases/100,000 children or 1500 RAD-related hospitalizations/year for the whole province of Quebec.

The mean duration of hospitalizations for all diarrheas decreased over the years of the study despite significant differences between regions. In the past few years, it stabilized at 3.3 days. This figure may be slightly inflated by the presence of a few noninfectious chronic diarrhea cases and by the secondary diarrhea cases, which were likely to have been primarily nosocomial. The 15,155 diarrhea cases that were registered as secondary diagnoses represent 23.7%

(95% CI 23.4 to 24.0) of all diarrhea-related hospitalizations. The large number of noninfectious diarrheas is an artefact of the coding practice that puts all diarrheas without specific laboratory evidence of infection in this category.

CONCLUSIONS

The present retrospective study showed the importance of diarrhea-related hospitalizations among children up to five years of age, and highlighted the potential impact that might result from the introduction of a rotavirus vaccine.

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