Prospective Hospital-Based Surveillance to Estimate Rotavirus Disease Burden in the Gauteng and North West Province of South Africa during 2003–2005

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Background. Rotavirus is considered to be the most common cause of serious acute dehydrating diarrhea worldwide. However, there is a scarcity of information on rotavirus disease burden in sub-Saharan Africa.

Methods. We conducted prospective, hospital-based surveillance for rotavirus diarrhea among children <5 years of age at the tertiary care Dr. George Mukhari Hospital (DGM) and at the Brits district Hospital (BH) in the Gauteng and North West Provinces in South Africa; we estimated that up to 80% of children <5 years of age in their catchment areas who are hospitalized for diarrhea are admitted to one of these hospitals.

Results. At DGM, 2553 children <5 years of age were admitted for diarrhea from January 2003 through December 2005, and 852 children <5 years of age were treated for diarrhea at BH during 2004–2005. We examined stool specimens from 450 children (53%) at BH and from 1870 children (73%) admitted to DGM. An estimated 22.8% (95% confidence interval [CI], 21.2%–24.5%) of the children hospitalized with diarrhea at DGM were rotavirus positive, and the corresponding figure at BH was 18.2% (95% CI, 14.9%–22.1%). Among children <5 years of age admitted to DGM for any reason, an estimated 5.5% (95% CI, 5.1%–6.0%) had rotavirus diarrhea. Our incidence estimates suggest that 1 in 43–62 children in the area is likely to be hospitalized with rotavirus diarrhea by 2 years of age.

Conclusions. Prevention of serious rotavirus illness by vaccination will substantially reduce not only the disease burden among young children but also the case load in South African health care facilities.

Diarrheal diseases are a major public health problem, with high associated morbidity, mortality, and economic loss for families and communities. Poor children in low- and middle-income countries have the greatest burden of diarrhea [1, 2]. Rotavirus is the most common cause of hospitalization with dehydrating diarrhea in children. Children in the poorest countries account for more than three-quarters of rotavirus-related deaths globally [3]. Rotavirus diarrhea is not preventable by improved sanitation or water supply, and decreasing its public health impact is, thus, dependent on case management with rehydration therapy and on primary prevention by vaccination [4]. If ongoing trials of rotavirus vaccines already licensed in industrialized countries and future trials of rotavirus vaccines currently under development show that they are efficacious and safe in children in low- and middle-income countries, countries with proven high rotavirus disease burden may

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consider including rotavirus vaccines in their national immunization programs [5–7]. It is accordingly important to measure the proportion of children hospitalized with acute diarrhea who have rotavirus disease and the incidence of such severe illness in the community.

Although the African Rotavirus Network surveillance has provided extensive information on the serotype distribution of rotavirus strains infecting African children [8] (I Peenze, personal communication), data on rotavirus disease burden in sub-Saharan Africa are scarce and are mostly from studies undertaken years ago [9–11]. However, many studies in Africa, including South Africa, Ghana, Malawi, Tunisia, Côte d'Ivoire, Cameroon, Guinea-Bissau, Kenya, and Nigeria, indicate that rotavirus contributes substantially to childhood diarrhea on the continent [12–21].

Previous studies have determined the proportion of South African children <5 years of age who are admitted to tertiary care hospitals with diarrhea that have rotavirus disease [13]. However, the studies have been too small to precisely estimate these proportions in smaller age categories, and no attempts have thus far been made to estimate the incidence of such severe disease in the communities served by these hospitals and by district hospitals.

To advise decision-making for future vaccination, we intended to, with adequate precision, determine the proportion of children <5 years of age who are hospitalized with diarrhea and who have rotavirus disease. We also stratified the estimates by age and, referring to previous findings [11–13, 22], studied the seasonality of rotavirus diarrhea. Moreover, we attempted to determine these proportions in both a tertiary and a district hospital and estimate the incidence of severe rotavirus diarrhea in the communities served by these hospitals.

MATERIALS AND METHODS

Study population, hospitals, and catchment areas. Gauteng and the North West Province of South Africa have a temperate climate with 4 seasons characterized by summer rainfall (mid-October to mid-February) and moderately cold and dry winters from May through July. On 1 January 2003, we initiated a study to examine stool samples for rotavirus from children with diarrhea who were admitted to the tertiary care, 1600-bed Dr. George Mukhari Hospital (DGM) located in Ga-Rankuwa District in Gauteng Province. On 2 July 2003, we initiated a similar surveillance at the 60-bed Brits district Hospital in the neighboring Madibeng district of the North West Province. Ga-Rankuwa, Soshanguve, and Mabopane districts (Gauteng Province) and parts of the Madibeng district in the North West Province constitute the catchment areas of DGM, and the Madibeng district is also served by Brits Hospital. This report is based on data collected at the 2 hospitals through the end of December 2005.

In these areas, which include urban, rural, and informal communities with moderate to low socioeconomic status, there were 84,484 children <5 years of age [23]. The government caters for basic services, such as water and sewage, to ~90% of the population in DGM catchment areas and to ~60% in Madibeng district. The unemployment in the area is >40%, and ~20% of adults in the DGM catchment areas had not completed primary school; the corresponding figure in Madibeng district was ~35% [24].

We conducted the surveillance according to part I of the World Health Organization (WHO) "Generic Protocol for Hospital-Based Surveillance to Estimate the Burden of Rotavirus Gastroenteritis in Children" [25]. Ethical approval was obtained from the Research Ethics and Publication Committee of the Medical University of Southern Africa (now University of Limpopo [Medunsa Campus]). We obtained verbal informed consent from parents or other caregivers accompanying children <5 years of age who were admitted to the 8-bed Brits pediatric ward or were treated in its casualty unit or admitted to the DGM pediatric ward for diarrhea. The reason for not distinguishing between the outpatients and those admitted to the small pediatric ward at Brits hospital is that, at Brits, in contrast to DGM, most children with dehydrating diarrhea, even those in need of intravenous rehydration, are rehydrated in the casualty unit and not in the ward.

The caregiver completed questionnaires designed to capture vital and sociodemographic information, illness history, and any treatment provided by alternative health care providers before inclusion in the study. The hospital log book was used to count the total number of children <5 years of age who were admitted during the study period.

On the basis of their knowledge of existing health care utilization patterns, senior health care officials in the area (community pediatrician Dr N Mogale and district family physician for the North West Province Dr John Tumbo) were asked to estimate the proportion of children <5 years of age in the DGM and Brits catchment areas who required treatment for acute diarrhea in a health care facility who were likely to be referred to or seek treatment at one of these hospitals. Their educated guess was 65%. Moreover, preliminary analysis of a health utilization survey in Madibeng that we undertook from March through November 2004, according to part II of the aforementioned WHO generic protocol [25], suggested that 76% (95% confidence interval [CI], 72%–80%) of children with diarrhea who required hospital treatment sought care at the DGM or Brits Hospital (authors' unpublished data).

We obtained information from the Statistics South Africa 2001 census on child populations in the 4 catchment regions [23]. Although acknowledging that, because of higher mortality, we would slightly underestimate the number of children in the younger age categories, we assumed an equal distribution of

children across the first 5 years of life. We also assumed that our population experienced a 2% population growth [23]. These figures were used to derive the denominators to calculate overall and age-specific incidences of severe rotavirus diarrhea.

Stool sample collection and testing for rotavirus. A case report form was completed, and stool specimens were collected from the children <5 years of age within 48 h after admission to exclude nosocomial infections. A pea-sized fecal specimen was suspended in 9 mL of distilled water, then vortexed for ~2 min and stored at 4°C until further analysis using a commercially available enzyme immunoassay (IDEIA Rotavirus test; Dako) according to the manufacturer's instructions [13, 18].

Analysis. Data were entered and analyzed using Microsoft Excel, Microsoft Access, and R [26]. We calculated the proportions of children with diarrhea at DGM and Brits Hospital that had rotavirus in their stool samples and their corresponding 95% CIs with use of the Wilson method [27]. We used generalized linear models from a binomial family with a logarithmic link function to compare the proportions of children with rotavirus infection at the 2 hospitals and to describe the relationship between this proportion and age. This analysis was done separately for infants (ie, children <1 year of age) and for older children, because there were statistically significant differences in these relationships between the 2 age groups.

To derive the numerators for the annual age-specific incidence of severe rotavirus illness, we counted the number of children treated for diarrhea at Brits Hospital from 1 January 2004 through 31 December 2005 who had rotavirus-positive stool specimens. In each age category, we estimated the number of rotavirus diarrhea cases treated at Brits Hospital in 2003 to equal that of the mean number during the subsequent 2 years. Assuming that the proportion of children with rotavirus infection was the same among children from whom we did and could not examine a stool specimen, we estimated the total number of rotavirus infections treated at Brits Hospital in each age category. The 95% CIs of these estimates were calculated on the basis of the observed rather than estimated number of rotavirus infections; thereby, the precision of our estimates was not increased beyond what our observations could justify. We added the number of children admitted for diarrhea to DGM (from 1 January 2003 through 31 December 2005) who we, with the same assumption, estimated to be rotavirus positive to the sum of these estimates and the corresponding estimates of the number of cases during 2004 and 2005. The standard error of each proportion and the corresponding 95% CIs were estimated on the basis of a weighted mean of independent binomial variances for the 2 hospitals. To estimate the 2 outer bounds of the actual number of children in the catchment areas of the 2 hospitals who were treated at a health care facility for rotavirus diarrhea, these numerators were adjusted by dividing them by 0.65, representing the aforementioned educated guess of 65% hospitalizations that was anticipated to be captured by our hospitals, and 0.8, which represents the upper 95% confidence limit of the same estimate derived from our health utilization survey. As the denominator, we used the number of children in each age category estimated to be living in the 3 DGM catchment areas and in Madibeng during 2003, 2004, and 2005.

RESULTS

Seasonality of rotavirus diarrhea. There were hospitalizations for rotavirus diarrhea throughout our study, with seasonal peaks during the cool and dry months (April through September of 2003, 2004, and 2005) at DGM (Figure 1). At Brits Hospital, we observed the same pattern but saw no children <5 years of age with rotavirus infection during some of the warmest summer months. In contrast, the number of hospitalizations not associated with rotavirus infection peaked during the summer months (October through March).

Proportion of cases of rotavirus diarrhea. Among the 11,721 patients admitted to the DGM pediatric ward, 9886 (84%) were <5 years of age. Of these, 2553 (26%) were admitted for diarrhea. We examined stool specimens for rotavirus for 1870 (73%) of these patients and from 450 (53%) of the 852 children <5 years of age who visited Brits Hospital for diarrhea during 2004 and 2005.

Among children admitted with diarrhea to DGM and from whom we obtained a stool specimen, the median maximal number of bowel movements during any 24-h period and the number of days with vomiting before admission, according to the caretakers, were 4 and 1, respectively, identical to the corresponding values for those from whom we did not obtain a specimen. On the other hand, the median age of those with a stool specimen was 8 months, compared with 11 months in those from whom we did not collect a specimen. When estimating the number of all children admitted to DGM who had rotavirus diarrhea, we accordingly applied the age stratum–specific proportions of stool specimens positive for rotavirus among children had a stool specimen obtained also to those who did not, thereby adjusting for the different age distribution between the 2 groups of children.

The proportions of children with rotavirus infection at Brits Hospital for whom we examined a stool specimen were 44 (18.7%; 95% CI, 14%–24%) of 235 in 2004 and 38 (17.7%; 95% CI, 13%–23%) of 215 in 2005; the total for these 2 years was 82 (18.2%; 95% CI, 14.9%–22.1%) of 450 (Table 1). The corresponding proportions among children admitted to DGM were 126 (19.3%; 95% CI, 16%–22%) of 652 in 2003, 115 (24.5%; 95% CI, 21%–29%) of 470 in 2004, and 195 (26.1%; 95% CI, 23%–29%) of 747 in 2005; the total was 436 (23.3%; 95% CI, 21.5%–25.3%) of 1870. Table 1 also displays the age-specific proportions of children <5 years of age who were

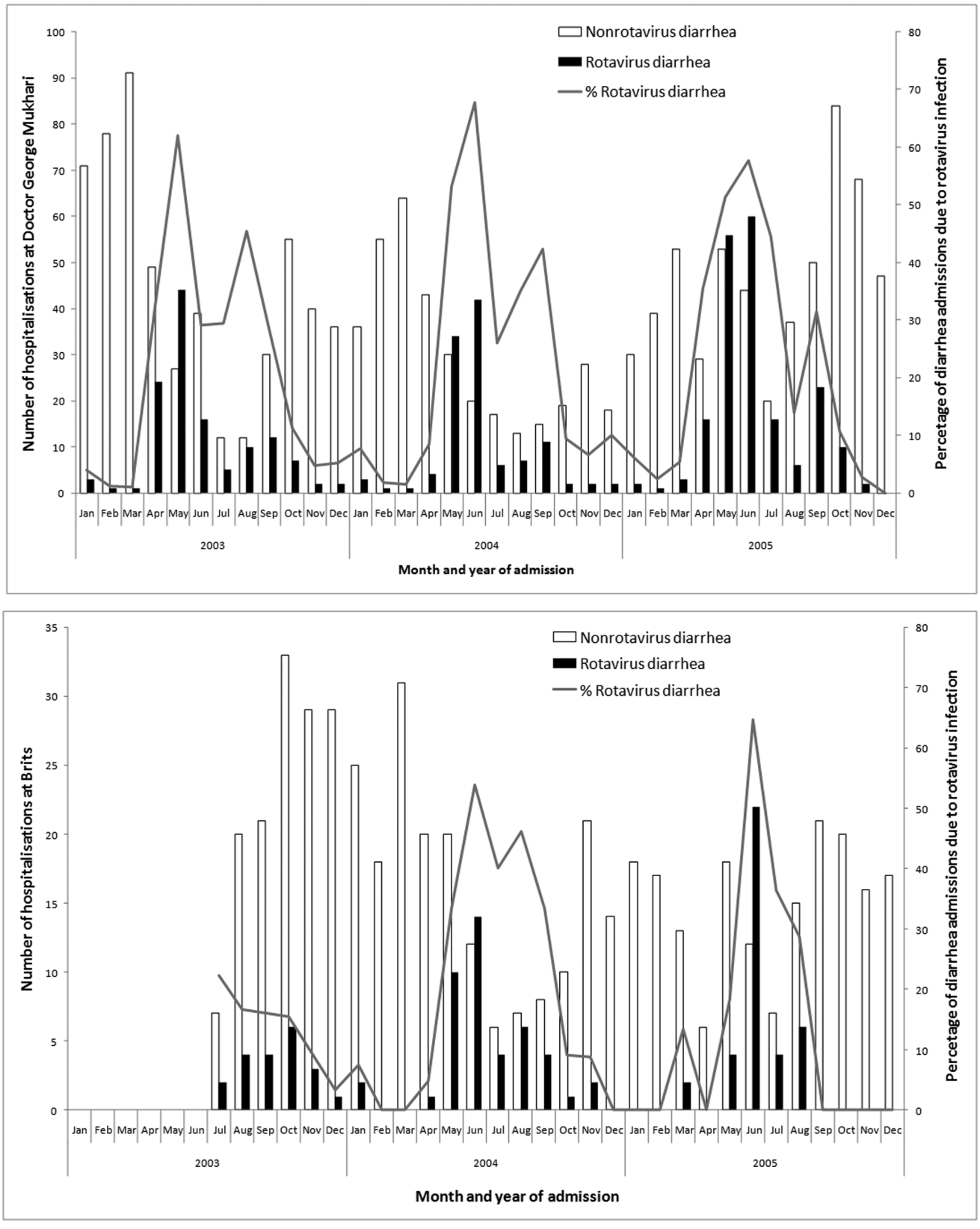

Figure 1. Proportion of rotavirus diarrhea among children <5 years of age admitted to Dr. George Mukhari Hospital (From January 2003 through December 2005) in the Gauteng and treated for diarrhea at Brits Hospital (from July 2003 through December 2005) in the North West Provinces of South Africa. The number of hospitalizations is shown as bars, distinguishing between cases from which we isolated rotavirus *(black)* and the other cases *(white).* The curve indicates the percentage of diarrhea cases from which we isolated rotavirus.

Table 1. Children Hospitalized at Dr George Mukhari Hospital and Treated at Brits Hospital in the Gauteng and North West Provinces of South Africa for Diarrhea with Rotavirus-Positive Stool Specimens during 2003–2005

	Dr George Mukhari Hospital (1 January 2003–31 December 2005)			Brits Hospital (1 January 2004–31 December 2005)		
Age, months	Children with rotavirus diarrhea/tested children (%) [95% CI]	No. of children admitted with diarrhea	Estimated no. of children with rotavirus diarrhea (95% CI)	Children with rotavirus diarrhea/tested children[a] (%) [95% CI]	Estimated no. of children admitted with diarrhea[b]	Estimated no. of children with rotavirus diarrhea[b] (95% CI)
0–2	29/218 (13.3) [9.4–18.5]	270	36 (25–50)	4/75 (5.3) [2.1–12.9]	213	11 (4–28)
3–5	111/366 (30.3) [25.8–35.2]	466	141 (120–164)	27/118 (22.9) [16.2–31.2]	335	77 (54–105)
6–8	119/372 (32.0) [27.5–36.9]	485	155 (133–179)	13/68 (19.1) [11.5–30.0]	193	37 (22–58)
9–11	76/259 (29.3) [24.1–35.2]	349	102 (84–123)	18/64 (28.1) [18.6–40.1]	182	51 (34–73)
0–11	335/1215 (27.6) [25.1–30.2]	1570	434 (395–473)	62/325 (19.1) [15.2–23.7]	923	176 (140–219)
12–17	65/318 (20.4) [16.4–25.2]	438	90 (72–110)	10/57 (17.5) [9.8–29.4]	162	28 (16–48)
18–23	16/125 (12.8) [8.0–19.8]	198	25 (16–39)	7/39 (17.9) [9.0–32.7]	111	20 (10–36)
12–23	81/443 (18.3) [15.0–22.2]	636	115 (95–141)	17/96 (17.7) [11.4–26.5]	273	48 (31–72)
0–23	416/1658 (25.1) [23.1–27.2]	2206	549 (509–601)	79/421 (18.8) [15.3–22.8]	1196	224 (183–272)
24–59	20/212 (9.4) [6.2–14.1]	347	33 (21–49)	3/29 (10.3) [3.6–26.4]	82	9 (3–22)
Total	436/1870 (23.3) [21.5–25.3]	2553	582 (548–646)	82/450 (18.2) [14.9–22.1]	1278	233 (191–282)

NOTE. CI, confidence interval.

[a] During 2004–2005.

[b] During 2003–2005, assuming that the age distribution of the children who did not provide a stool specimen was the same as for those who did, that the proportion of children with rotavirus diarrhea were the same irrespective of whether they had provided a stool specimen, and that the number of diarrhea cases in 2003 were the same as the mean number of cases in 2004 and 2005.

treated at Brits Hospital and admitted to the DGM pediatric ward and who were identified as having rotavirus diarrhea, as well as the number of children admitted with diarrhea to DGM and treated at Brits Hospital who we estimated to have rotavirus diarrhea, assuming the same age-specific isolation proportions in all diarrheal cases and that, at Brits Hospital, the number of cases in 2003 was the same as the mean number of cases in 2004 and 2005. The annual age-adjusted proportion of children admitted to DGM who had rotavirus diarrhea was 582 (22.8%; 95% CI, 21.2%–24.5%) of 2553.

At both hospitals, the proportion of children <5 years and >2 years of age who had rotavirus diarrhea was approximately 10%, and the proportion of children aged 1 year who had rotavirus diarrhea was 18%. Among all children aged 12–59 months, the regression model showed that this proportion decreased by 4% (95% CI, 2%–6%) for every 1-month increase in age. In contrast, among infants, the proportion with rotavirus diarrhea was much higher at DGM (27.6%; 95% CI, 25.1%–30.2%) than at Brits Hospital (19.1%; 95% CI, 15.2%–23.7%). After adjusting for age, the proportion of infants with rotavirus infection was 40% (95% CI, 11%–81%) higher at DGM than at Brits Hospital, and after adjusting for hospital, it increased by 6% (95% CI, 3%–8%) for every 1-month increase in age. Table 1 shows that three-quarters of the children who were hospitalized at DGM or treated at Brits Hospital for rotavirus diarrhea were infants; 9 of 10 were <1.5 years of age, and 95% were <2 years of age.

Overall and age-specific incidence of severe rotavirus diarrhea. According to StatsSA, there were 84,484 children <5 years of age in the 4 catchment regions for the 2 study hospitals: 6218 in Ga-Rankuwa, 19,318 in Mabopane, 28,882 in Soshanguve, and 30,066 in Madibeng. On the basis of the aforementioned assumption that, in each age category, the proportions of children with rotavirus infection were the same irrespective of whether they had provided a stool specimen that had undergone analysis, we estimated that 582 patients with of severe rotavirus diarrhea were admitted to DGM during this period. Similarly, assuming that, at Brits Hospital, in each age category, the number of patients with diarrhea in 2003 was the mean of that in the subsequent 2 years and that the proportion of children with rotavirus infection was the same irrespective of whether they had provided a stool specimen, we estimated that 233 children were treated for rotavirus diarrhea at Brits Hospital during the entire 3-year period. Thus, overall, 815 cases of rotavirus diarrhea were included in our numerator of the incidence calculations; the age breakdown is given in Table 2. Dividing these numerators by the 80%–65% estimated coverage of hospitalization anticipated to be captured by our hospitals and by the number of children (overall and in each age category) estimated to be living in the 3 DGM catchment areas and in Madibeng during 2003, 2004, and 2005, we obtained a mean annual incidence rate of rotavirus infection ranging from 379 cases (95% CI, 348–410 cases) to 466 cases (95% CI, 428–504 cases) per 100,000 children <5 years of age; the corresponding incidence rate among children aged <2 years ranged from 874 cases (95% CI, 802–947 cases) to 1076 cases (95% CI, 987–1165 cases) per 100,000 children (Table 2).

The incidence was relatively low during the first 3 months of life, highest during the last 9 months of infancy, and decreased sharply thereafter (Table 2). Our estimates indicate that

Table 2. Estimated Annual Incidence of Rotavirus Diarrhea Requiring Hospital Attention in North West and Gauteng Provinces of South Africa, 2003–2005

Age (months)	Estimated no. of children with rotavirus diarrhea/no. of tested children[a]	Percentage of rotavirus-positive children ± SE[b] (95% CI)	Estimated 95% CI of the children with rotavirus diarrhea	Estimated population		Annual incidence of rotavirus diarrhea with 80% referral,[c] cases per 100,000 children per year (95% CI)	Annual incidence of rotavirus diarrhea with 65% referral,[c] cases per 100,000 children per year (95% CI)
				2001	2003- 2005		
0–2	47/483	9.7 ± 1.7 (6.4–13.1)	31–63	4614	14,690	400 (261–539)	492 (322–663)
3–5	218/801	27.2 ± 2.1 (23.0–31.4)	184–252	4614	14,690	1855 (1569–2141)	2283 (1931–2635)
6–8	192/678	28.3 ± 2.2 (24.0–32.6)	163–221	4614	14,690	1634 (1385–1882)	2011 (1705–2317)
9–11	153/531	28.8 ± 2.7 (23.6–34.1)	125–181	4614	14,690	1302 (1065–1539)	1602 (1311–1894)
0–11	610/2493	24.5 ± 1.1 (22.2–26.7)	554–666	18,456	58,760	1298 (1179–1416)	1597 (1451–1743)
12–17	118/600	19.7 ± 2.1 (15.5–23.9)	93–143	8132	25,893	570 (448–691)	701 (552–851)
18–23	45/309	14.6 ± 2.9 (8.8–20.3)	27–63	8132	25,893	217 (132–303)	267 (162–372)
12–23	163/909	17.9 ± 1.7 (14.5–21.3)	132–194	16,264	51,786	393 (319–468)	484 (392–576)
0–23	773/3402	22.7 ± 1.0 (20.8–24.6)	709–837	34,720	110,546	874 (802–947)	1076 (987–1165)
24–59	42/429	9.8 ± 2.0 (6.0–13.6)	26–58	49,765	158,454	33 (20–46)	41 (25–57)
Total	815/3831	21.3 ± 0.9 (19.5–23.0)	748–882	84,485	269,000	379 (348–410)	466 (428–504)

NOTE. CI, confidence interval; SE, standard error.

[a] Based on the sum of the estimated number of children given in Table 1 (ie, for Dr George Mukhari Hospital and Brits Hospital).

[b] Estimated SE of proportion, based on a weighted mean of independent binomial variances for the 2 hospitals.

[c] Corrected for 80% or 65% coverage of all hospitalizations anticipated at the 2 hospitals.

1 in 40 (504 × 5/100,000) to 1 in 57 (348 × 5/100,000) children <5 years of age in this population is hospitalized with rotavirus diarrhea by 5 years of age. Likewise, we estimate that 1 in 43 (1165 × 2/100,000) to 1 in 62 (802 × 2/100,000) children is hospitalized with rotavirus diarrhea by 2 years of age.

DISCUSSION

To our knowledge, this is the first estimation of population-based incidence of hospitalization for rotavirus diarrhea in Africa. The high incidence of severe rotavirus diarrhea reflects the substantial public health impact of this potentially preventable disease. The recent South African Health Review 2006 indicates that diarrheal diseases accounted for 10.2% of deaths in South African children <5 years of age in 2000 [28]. This and the fact that less than half of the mothers in South Africa may be using oral rehydration therapy appropriately when their children have diarrhea [29] emphasize the need for implementing effective preventive measures against rotavirus disease.

Of interest, our incidence estimates are close to those of a North Indian study [22]. In both studies, the rotavirus disease burden was highest among children 2–11 months of age, decreasing substantially thereafter. Rotavirus seems to have considerably lower pathogenicity in children >2 years of age [30]. Our analysis indicates that, in South Africa, rotavirus infection causes 1 in 43 to 1 in 62 children to be hospitalized during their first 2 years of life. Our incidence rate estimates among children <2 years of age ranged from 802 to 1165 per 100,000. Assuming that our study area is representative of all of South Africa, where the total population of children <2 years of age is estimated to be 2.2 million [23, 31], we suggest that from 17,644 (802 × 2,200,000/100,000) to 25,630 (1165 × 2,200,000/100,000) children are admitted yearly for treatment of rotavirus diarrhea at hospital facilities in the country. The WHO has recently estimated that 271 (95% CI, 224–318) South African children die of rotavirus diarrhea annually [32]. If our death estimates for the country is valid, this corresponds to a case-fatality risk among children hospitalized with rotavirus diarrhea ranging from 0.9% (224 deaths per 25,630 children) to 1.8% (318 deaths per 17,644 children), figures that to us seem reasonable. Using 2 different approaches to estimate death toll, the estimates of the WHO and our estimates are, in other words, reassuringly similar. Thus, rotavirus diarrhea contributes importantly to the disease burden in young children, and this report emphasizes the need for vaccination at an early age when rotavirus vaccines are incorporated into child health promotion programs.

Of 9886 children <5 years of age who were treated at DGM, 2553 (26%) were admitted for diarrhea. Among these, we estimated that 582 (22.8%; 95% CI, 21.2%–24.5%) had rotavirus diarrhea. This is in line with hospital-based studies from many other countries [12] but somewhat lower than that in other studies reported recently [33]. Differences in percentage of rotavirus isolation among studies can be ascribed to a multitude of factors, including differences in age distributions of admitted children; different referral patterns, including delays of reaching hospitals; and varying degrees to which home- and clinic-based rehydration therapy are used.

We found that, among children treated for diarrhea at our

2 study hospitals, the proportion with rotavirus infection increased during the first year of life and decreased thereafter. This is in line with previous observations of rotavirus pathogenicity in a West African community setting [30] and may be explained by waning protection from breast milk and transplacentally transferred maternal antibodies from birth until 1 year of age, followed by a gradual acquisition of immunity thereafter. Assuming that rotavirus was the cause of diarrhea only in children <2 years of age [30], 549 (582 minus 33; ie, 5.5% [95% CI, 5.1%–6.0%]) of all admissions of children <5 years of age to DGM were because of rotavirus infection. This shows that deploying an effective rotavirus vaccine with high coverage could substantially reduce not only the disease burden in the community but also the load on the pediatric ward of hospitals and, thereby, health facility costs. A separate economic analysis included in this issue [34] examines the high financial burden of rotavirus diarrhea at DGM, highlighting the benefits that rotavirus immunization could have on the health system in South Africa.

Confirming earlier reports, we observed rotavirus diarrhea throughout the year but with distinct winter peaks during yearly epidemics lasting from March and April to September and October. During the winter peaks, the proportion of cases of rotavirus diarrhea could exceed 50%, and during the summer months, it was <5%; these findings may have implications for immunization and case-management strategies.

This study has some limitations. First, we cannot be certain that the proportion of rotavirus infection among children from whom we failed to obtain a stool specimen was the same as that among those from whom we did. However, their similar stool frequency and days with vomiting and the fact that we adjusted for the age imbalance between these 2 groups at DGM makes this an unlikely source of serious bias. Second, the corrective factor of 65% (public health experts' estimate) to 80% (upper 95% CI of the proportion obtained in our health utilization survey) may be inaccurate. On the other hand, this large, prospective survey in which most children of a relatively well-described population visited a district hospital and a tertiary care hospital over up to a 3-year period and in whom rotavirus was identified using standardized protocols is likely to generate data adequate for disease burden estimations in this and in similar African populations. Finally, our extrapolations of the incidence of rotavirus diarrhea from our area to all of South Africa are based on uncertain assumptions. On the other hand, our figures are in line with those of the WHO, lending credibility to both estimates. These estimates will hopefully be adjusted during evaluation of the impact of the national rotavirus vaccination program.

In conclusion, our findings indicate that the deployment of a safe and effective rotavirus vaccine, the only known preventive measure against rotavirus diarrhea, should be a public health priority in South Africa. The data presented here can contribute to pave the way for cost-effectiveness studies of rotavirus vaccination programs when they are now rolled out in the country. The decrease of oral rehydration therapy use in many regions of the world [35], the importance of rotavirus-associated gastroenteritis in sub-Saharan Africa as reported in this issue and elsewhere [33], and the recent promising interim analysis of a phase III efficacy study of rotavirus vaccination in South Africa [36] suggest that rotavirus immunization will have a large impact on the health of young African children.

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