

## ROTAVIRUS ACUTE GASTROENTERITIS AMONG FILIPINO CHILDREN IN THE YEAR 2001

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### Abstract:

This is a prospective study to determine the clinical profile of pediatric patients less than 5 years old with rotavirus diarrhea seen at the Philippine General Hospital from August 1-September 15, 2001. Ninety-one patients with acute diarrhea were included in the study. Of these 39 patients (42.9%) had rotavirus antigen in the stool as detected by the ELISA method. The mean age of the patients was 11.5 months with 61.5% of the patients belonging to the 7-12 months of age, mostly well-nourished. The stools were described as watery (74.4%), yellow in color (84.7%), with no pus, red blood cells or parasite. Average duration of diarrhea prior to consultation was  $2.5 \pm 1.8$  days with 7 episodes per day. Vomiting, fever and concomitant upper respiratory tract infection were noted in 76.9%, 64% and 23.7% of the patients respectively. A comparison of the rotavirus versus bacterial etiology of diarrhea showed fever and vomiting to be more predominant in rotavirus while dehydration was noted in bacterial isolates. Antibiotic was noted to be given to 38.5% rotavirus cases. Increased awareness of rotavirus diarrhea, regarding its high incidence and clinical profile, will help guide physicians in their rational use of antibiotics for patients with acute diarrhea.

### INTRODUCTION

#### Significance and Background

Diarrhea has been one of the top ten leading causes of childhood morbidity and mortality throughout the world and in the Philippines. In 1999, it has been the number one cause of morbidity in our country with a rate of 1215.4/100,000<sup>1</sup>. In a study by Bern and Glass, in North America the incidence of acute diarrhea was 1.3 -2.3 episodes per year<sup>2</sup>. In the Philippines, Saniel et al, noted that children under six year old have 2-3 episodes of diarrhea per year<sup>3</sup>. In 1999, the Philippine General Hospital Pediatric Emergency Room saw 14,142 patients and 2,178 of these patients had acute gastroenteritis which is about 15.4% of the cases and an average of 6 new patient per day. For the year 2000, diarrhea still has been the number one consult at the Pediatric Emergency Room of the Philippine General

Hospital and the number eight consult at the Out-Patient Department. This is an indicator of its continuing significance in our country.

Infectious causes (bacterial, viral and parasitic) account for most cases of diarrhea. With the discovery of new enteropathogens and improvements in detection techniques, the identification of etiological agents in diarrheal diseases has increased from 15-35% of cases in the early 1970's to 70-80% in the last few years<sup>4</sup>. It is also possible to detect more than one pathogen in 10-15% of cases. In general, the same pathogens are responsible for diarrhea worldwide, with only variations in the frequency of occurrence of each pathogen in different localities. In 1995, Black and Lanata reviewed 18 community studies with comprehensive microbiology data from 9 countries in which ETEC (enterotoxigenic *Escheria coli*) caused the largest proportion of diarrhea episodes with a median of 24%, followed by *Campylobacter* (7%), *Rotavirus* (5%), *Shigella* (4%), *Cryptosporidium* (2.7%) and *Entamoeba histolytica* (2%) *Giardia Lambia* showed 14%, but varies from study to study, due to various diagnostic tools used. In hospitals, rotavirus was found as the most frequent cause of diarrhea, with a median of 20%<sup>5</sup>. In a study done by Paje-Villar in 1990, *Rotavirus* was isolated in 85.7% of their samples<sup>6</sup>.

Rotavirus is the most common cause of severe diarrhea worldwide. In developing countries, rotavirus may cause 600,000 to 870,000 deaths each year, accounting for an estimated 20 to 25% of all deaths due to diarrhea and 6% of all deaths among children <5 years of age<sup>7</sup>. In the Philippine, Adkins et al, found rotavirus frequent in children less than 5 years of age<sup>8</sup>. It was noted most frequently in infants 6-11 months old in a study done by Rogacion<sup>9</sup>. It is thus the single most important cause of acute diarrhea particularly in infancy.

Rotavirus was first detected in 1973 by Ruth Bishop. It was seen in the electron microscope as a 70nm wheel-shaped virus-like particle in the intestinal mucosa of infants with gastroenteritis. Rotavirus is classified in the family Reoviridae. Its genome consists of 11 segments of double-stranded RNA, each coding for a viral protein. The double stranded RNA is closely associated with three structural proteins VP1, VP2, and VP3, coded by genes

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1,2 and 3 constituting the inner core of the virus. The inner core is surrounded by inner capsid made of viral protein VP6, coded by gene 6. The outer capsid comprises VP7, coded by gene 7,8 or 9 in different rotaviruses and protruding protein spikes of VP4. These outer capsid proteins, VP7 and VP4, are important in virus neutralization in vitro and in protection from natural rotavirus disease and have been a focus of interest for vaccine development. Rotaviruses are at present classified according to antigens on VP6, VP7 and VP4 and to patterns found in RNA gel electrophoresis. Six groups of rotaviruses (A-F) have been identified based on VP6 antigens and electropherotype. Group A, B and C rotaviruses have also been shown to infect humans, group A being, however by far the most important. Group A rotaviruses may be further subdivided according to antigenic differences in VP6 subgroups I and II. VP4 and VP7 stimulate production of neutralizing antibodies. As both proteins are independently responsible for virus neutralization, a dual serotype-specific classification system has been proposed. Here rotavirus can be identified by its VP7 specificity (G-types) and by its VP4 specificity (P-types). At least 14 G-serotypes have been identified in animal and human viruses. Nine of them have been characterized in humans, but G-types 1-4 are the most prominent causes of diarrhea in infants in developed countries<sup>10</sup>. Over all the virulent G-type 1 is the most prevalent rotavirus serotype worldwide, particularly in seasonal epidemic rotavirus gastroenteritis in developed countries, while G-types 1-5,8 and 9 cause diarrhea in developing countries<sup>11</sup>. In the Philippines in a study done by Bravo et al in 1997, of the 53 stool samples 15 samples belong to Group A rotavirus with a predominant subgroup II. VP7 serotyping showed only serotype 1, 2 and the rest were untypeable<sup>12</sup>.

The transmission of rotavirus takes place via the fecal-oral route and might be aided by inhalation after aerosol formation, particularly within closed areas, such as homes and hospital wards. Infection can result from as few as 10 infectious particles per ml entering the small intestine. Rotavirus survive well on contaminated hands, environmental surfaces, in tap water and in sewage. The incubation time in children is 24-48 hours. Rotavirus infections are mainly confined to the small intestine. Information on pathologic changes in the gut due to rotavirus infection is mostly based on findings in animals. Rotavirus multiplication in the gut occurs within mature epithelial cells lining the upper portions of the villi in the small intestine. This leads to cell lysis and stripping of the superficial layer of the

epithelial cells from the underlying lamina propria. Diarrhea in rotavirus enteritis is associated not directly with viral damage but with a delay in the normal differentiation of villous enterocytes, resulting in a mucosa with an inadequately developed transport system, leading to failure of nutrient absorption and osmotic diarrhea. The extent of the mucosal involvement determines the severity of clinical illness. Results of studies in humans have however, been equivocal. The physiologic basis of rotavirus diarrhea has been studied in several animal models. In miniature swine, rotaviral infection was associated with decreased intestinal lactase content, increased fecal lactose loss and increased fecal osmotic gap, which is consistent with the hypothesis that the malabsorption of carbohydrate causes osmotic diarrhea.

The typical clinical picture of rotavirus gastroenteritis includes watery diarrhea with abrupt onset vomiting and fever. Rouska and Vesikari have characterized rotavirus disease in 65 episodes with 88% of them having one or more watery stools during an episode with a mean duration of 1.0-4.6 days, 78% had vomiting and 65% had fever. Dehydration was detected in 32% of cases<sup>13</sup>.

Until the 1970's, physician and pediatrician believed that diarrheal diseases in developing countries, were mostly caused by bacteria which needed to be treated with antibiotics. Several studies have shown that rotavirus was the prevalent enteropathogen worldwide, in children under 5 years of age, especially at the age of 6-24 months. Vesikari and Ruuska noted rotavirus in 26% of the 336 children with ages between 7-12 months<sup>13</sup>. In Indonesia, Soenarto noted rotavirus were most common in children aged 7-24 months<sup>14</sup>. Local studies done by Rogacion<sup>9</sup> and Villa<sup>15</sup> also noted, rotavirus occurring at the age of 6-11 months. Thus, antibiotics should not be prescribed to these children within this age group with diarrhea of viral etiology. Health scientist and health programmers were rapidly informed about these findings through their annual meetings, conferences and other scientific activities, which made the suggested management strategies on rational use of antimicrobial drugs more acceptable. However, parents would rather still ask for antibiotics from physicians or self-medicate their children because of the frequency of the diarrhea. Such conditions however cannot be dismissed as just viral. Thus, it is important to familiarize ourselves with its clinical features in our local setting and compare this findings with the study done by Rogacion et al 13 years ago<sup>9</sup>.

## OBJECTIVES

The primary objective of this study is to determine the clinical profile of patients with rotavirus acute gastroenteritis with respect to the following clinical and laboratory parameters. Age in months, sex, duration of diarrhea prior to admission, occurrence of fever prior to admission and temperature during admission, occurrence of vomiting prior to admission, presence of abdominal pain prior to admission for children more than 2 years old, manner of feeding, nutritional status – based on the National Center for Health Statistics data as standard, degree of dehydration – based on the World Health Organization Classification, character of stools and total stool output prior to admission, associated signs and symptoms present with diarrhea, stool exam.

This study also aims to determine the clinical profile of patients with pure bacterial isolates, without history of antibiotic intake, based on the above parameters and compare it with the clinical profile of patients with pure rotavirus isolate.

Lastly, this study also aims to determine the frequency of antibiotic use in the treatment of diarrhea.

## MATERIAL AND METHODS

### A. Study Design

This was a prospective descriptive study of pediatric patients seen at the Pediatric Emergency Room and Out-Patient Department of the Philippine General Hospital.

### B. Subjects

All patients aged 0-60 months seen at the Pediatric Emergency Room and Out-Patient Department of the Philippine General Hospital from August 1, 2001 to September 15, 2001 with gastroenteritis of less than 7 days were included in the study.

### C. Definition of Terms

Gastroenteritis was defined as the occurrence of vomiting and or diarrhea. Diarrhea was defined as passage of two or more liquid or semi-solid stools or single watery stools per day by a child prior to admission with a duration of not more than 7 days. Presence of surgical conditions, intoxication and persistent diarrhea were excluded from the study.

### D. Data Collection

A complete history was taken by the principal investigator on consult with emphasis on the duration

and frequency of diarrhea and vomiting, presence of fever and character of stools, presence of abdominal pain, manner of feeding, intake of antibiotic and its duration and associated signs and symptoms. The physical examination emphasized the vital signs, degree of dehydration and nutritional status. All the data were recorded in the data collection form.

### E. Laboratory

Three stool samples were collected upon admission or consult. The first stool sample was sent for routine stool examination for the presence of parasite and ova and for the presence of red blood cells and pus cells at the Clinical Microscopy Section of the Philippine General Hospital. The second stool sample was sent for bacteriologic culture at the Microbiology Section of the Philippine General Hospital. Using standard methods, stools were cultured for the following pathogens: *Salmonella*, *Aeromonas*, *Camphylobacter*, *V. Cholerae* and *Shigella*. Stool cultures were further tested for the presence of enteropathogenic *Escherichia coli* strains using test sera anti-coli. The third stool sample was tested for the presence of Rotavirus antigen by the use of an Enzyme Linked Immunoabsorbent Assay (ELISA) kit (IDEIA Rotavirus, Dako, Denmark House, United Kingdom). All the stools samples were tested at the same time after being stored at - 20°C refrigerator. The test utilizes a polyclonal antibody detect group specific protein (VP6), present in rotavirus A. Microwell plates are coated with a rotavirus specific rabbit polyclonal antibody. Sample is added to the microwell simultaneously with a rotavirus specific antibody conjugated to a horseradish peroxidase enzyme. Rotavirus antigen present in the sample is captured between antibody on the solid phase and enzyme conjugated antibody. The presence of specifically bound enzyme labeled antibody in the wells results in a color change, which is topped by the addition of acid. Color intensity significantly above background levels is indicative of the presence of rotavirus antigen in the specimen or control. Results are read photometrically by a plate reader.

## RESULTS

Ninety one patients were included in the study 43 (74.7%) of the patients were between 7-12 months old and 19 (27.5%) were between 2-6 months old with a mean of  $14.0 \pm 14.6$  months 54 (59.3%) were male and the rest female. The majority of the subjects came from within the vicinity of the Philippine General Hospital. 33% came from

Manila, 11% from Parañaque and the rest from other parts of Metro Manila but 9 subjects or 10% came from the nearby provinces of Cavite and Laguna. The following tables show the isolated pathogens, demographic profile degree of hydration and symptoms of patients.

**Table I. Isolated Enteropathogens**

Type of Isolate	Number	Percent	Number	Percent
Single Isolates			55	60.4%
Rotavirus	39	42.9%		
<i>E. coli</i>	10	11%		
Poly I				
Poly II				
Poly III				
<i>Vibrio cholera ogawa</i>	5	5.5%		
<i>Shigella</i>	1	1%		
Multiple Isolates				
Bacteria + Rotavirus			8	8.8%
<i>E. coli</i> Poly I + Rotavirus	2	2.2%		
<i>E. coli</i> Poly II + Rotavirus	2	2.2%		
<i>E. coli</i> Poly III + Rotavirus	2	2.2%		
<i>Vibrio cholera ogawa</i>	2	2.2%		
No Isolates			28	30.8%

**Table II. Age and Sex of the Patient**

Clinical Parameters	No. of Cases	%
Age	39	
0-1 month	0	0
2-6 months	8	20.5%
7-12 months	24	61.5%
13-24 months	4	10.3%
25-36 months	2	5.1%
37-48 months	0	0
49-60 months	1	2.6%
Sex		
Male	28	71.8%
Female	11	28.2%

**Table III. Patients Characteristics Prior to Consultation**

	No. of Cases	%	Mean	Standard Deviation	Range
Duration of diarrhea (hours)			2.5 days	1.8	4 hours - 7 days
Frequency of Stool Motions			7 times	4.2	1-20 times
Duration of vomiting	30	76.9%	1.9 days	1.7	5 hours- 7 days
Duration of fever	25	64%	2.3 days	1.6	8 hours -7 days
Manner of Feeding					
Breastfed	0	0			
Breastfed & Formula Fed	5	12.8%			
Formula Fed	34	87%			
Intake of Antibiotic	15	38.5%			
Duration of Antibiotic Intake			2.0 days		1-5 days
Other Infection					
URTI	9	23.7%			
Pneumonia	2	5.3%			

**Table IV. Nutritional Status of the Patients Upon Consultation**

Clinical Parameters	No. of Cases	%
No Stunting, No Wasting	9	23.1%
No Stunting, Mild Wasting	7	17.9%
No Stunting, Moderate Wasting	6	15.4%
No Stunting, Severe Wasting	0	0.0%
Mild Stunting, No Wasting	3	7.7%
Mild Stunting, Mild Wasting	6	15.4%
Mild Stunting, Moderate Wasting	0	0.0%
Mild Stunting, Severe Wasting	1	2.6%
Moderate Stunting, No Wasting	1	2.6%
Moderate Stunting, Mild Wasting	2	5.1%
Moderate Stunting, Moderate Wasting	2	5.1%
Moderate Stunting, Severe Wasting	1	2.6%
Severe Stunting, No Wasting	1	2.6%
Severe Stunting, Mild Wasting	0	0.0%
Severe Stunting, Moderate Wasting	0	0.0%
Severe Stunting, Severe Wasting	0	0.0%

**Table V. Patient Degree of Dehydration Upon Consultation**

Degree of Dehydration	No. of Cases	%
No	12	30.8%
Some	24	61.5%
Severe	3	7.7%

**Table VI. Pure Bacterial Isolates without History of Antibiotic Intake**

ORGANISM	NUMBER	PERCENT
<i>E. coli</i>	7	58.3%
<i>E. coli</i> Poly I	2	16.7%
<i>E. coli</i> Poly II	3	25%
<i>E. coli</i> Poly III	2	16.7%
<i>Shigella</i>	1	8.3%
<i>Vibrio cholera</i> <i>ogawa</i>	4	33.3%

**Table VII. Comparison of Patient Characteristics Prior to Consultation Between Patients with Rotaviral Isolates vs. Patients with Bacterial Isolates**

	Patients with Rotaviral Isolates N=39			Patients with Bacterial Isolates N=12		
	No. of Cases	%	Mean	No. of Cases	%	Mean
Duration of diarrhea (hours)			2.5 days			2.8 days
Frequency of Stool Motions			7 times			5.3 times
Duration of vomiting	30	76.9%	1.9 days	8	66.7%	1.8 days
Duration of fever	25	64%	2.3 days	4	33.3%	4.3 days
Other infection						
URTI	9	23.7%		1	8.3%	
Pneumonia	2	5.3%				
Degree of Dehydration						
No	12	30.8%		1	8.3%	
Some	24	61.5%		6	58.3%	
Severe	3	7.7%		5	41.7%	

## DISCUSSION

With the improvement of laboratory techniques to detect rotavirus and other entropathogens, we were able to identify the various etiologic agents of diarrhea as shown in Table I. In our study we were able to isolate a single pathogen in 60.4% and mixed pathogens in 8.8% giving a total isolation rate of 69.3%, which is

comparable with the isolation rate of Bravo and her co-workers despite the use of antibiotics in 30.8% of the ninety-one patients<sup>16</sup>. The presence of mixed culture in 8.8% of cases is also a problem encountered by various researches on diarrhea<sup>16,17</sup>. Its significance is still unclear. All of the isolates in this group had rotavirus. Nevertheless, we cannot determine the actual causative agent in this group thus we did not include them in our study population.

The over all incidence of rotavirus infection noted in this study was 42.9% out of 91 children with diarrhea. In 1975, Davidson and his co-workers demonstrated that 57% of 378 ill children had rotavirus<sup>18</sup>. From 1987 to 1996 in Germany, Berner and his co-workers noted rotavirus to occur in 25% out of 3,615 patients in the community and 22% out of 8,383 hospitalized patients<sup>19</sup>. While a study done in Austria from December 1997 to May 1998 by Fruwirth and his co-workers, which involved 144 children with community acquired acute gastroenteritis showed rotavirus to be positive at 34%<sup>20</sup>. In our local studies, Paje-Villar was able to isolate rotavirus at rate of as high as 65.7% out of 236 infants and young children, Bravo at 32% out of 172 patients and Rogacion was able to isolate it at a low rate of 16.6% out of 126 patients<sup>6,16,9</sup>. Thus, the 42.9% isolation rate of rotavirus in this study is quite high compared to the usual isolation rate of rotavirus for the past 10 years which was from 15-30%. Does this means that bacterial cause of diarrhea in the Philippines is decreasing? Since patients on antibiotics were included in this study the true incidence of a bacterial cause of diarrhea cannot be determined since antibiotic can affect isolation of bacteria in 24-48 hours after intake, thus only 12 (13.2%) was positive for pure bacterial isolate without intake of antibiotic. Countries in Europe noted a high incidence of rotavirus infection with the decline in the bacterial cause of diarrhea. Thus, a new study regarding the etiology of diarrhea maybe needed to further prove that indeed the bacterial cause of diarrhea is decreasing in our country and then we can note that our population are better educated in the hygienic way of handling our food.

Rotavirus is the single most important cause of acute diarrhea particularly under the age of 2 years<sup>3,6,8,9</sup>, while bacterial causes of diarrhea are common above two years of age and older<sup>3,6</sup>. This study also showed that rotavirus is most commonly seen in children aged 7-12 months with a mean age of 11.5 months while bacterial isolates had a mean age of 20 ±19.9 months. In both developing and developed countries some 90%



of infants and young children, regardless of socioeconomic status or environmental conditions, will contract rotavirus infection by the end of the third year of life<sup>21</sup>. It is also important to note that rotavirus infection in the neonate occurs but of the 6 (6.5%) stool specimens included in the study from patients less than 1 month old rotavirus antigen was found to be negative in all them. In a study by Perez-Schael, rotavirus is being shed by newborn children mostly without symptoms<sup>22</sup>.

A key epidemiologic feature of rotavirus is its seasonality, seen in monthly fluctuations of hospital admissions for rotavirus disease all over the world. Seasonality is most apparent in climates with marked seasonal changes. In developing countries, like the Philippine with a tropical climate, the rotavirus infection appears endemic throughout the year with no peak months. Although most rotavirus infection could be noted during the rainy season when diarrheal diseases is at its peak<sup>23</sup>, which was proven in our study when we were able to get a high isolation of rotavirus during the rainy months of August and September. However, Rogacion noted that half of her rotavirus admissions (10 out of 21) were seen during the months of January to March. Thus, the reason for this seasonal variation is unknown. Rotavirus spread via the fecal-oral route and the rapidity of spread has been explained by aerosol formation. The movement of the rotavirus season in time and place indicates that neither temperature nor humidity alone can explain the trend. Laboratory studies have suggested that each community may have its own local reservoir of strains, since there is no single epidemic strain<sup>24</sup>.

Rotavirus infections are common throughout life, but significantly the disease is limited for the most part to early childhood, which would suggest development of immunity. The immunological mechanisms controlling rotavirus infection and illness are not fully understood. The presence of IgA in serum correlates with protection against rotavirus infection and more severe illness. Since colostrum is rich in IgA, one should expect that purely breastfed infant would rarely develop rotavirus diarrhea and studies have shown that IgA rotavirus antibody in breastmilk has been detected for as long 2 years after the onset of lactation. Yolken et al measured the secretory antibody directed against rotavirus in human milk by means of enzyme-linked immunoabsorbent assay and showed that human milk contains significant concentration of antibody against rotavirus. The level is highest in colostrums and decreases to lower but

detectable levels in most breastmilk for up to 24 months of lactation<sup>25</sup>. However, the study done by Gelera in 1992 showed that there was equal percentage of rotavirus infection among breastfed and non-breastfed infants<sup>26</sup>. The study of Ruuska and Vesikari, showed prolonged breastfeeding had no significant effect on the incidence of diarrhea but a trend towards a higher incidence of diarrhea in the age period of 7-12 months in infants breastfed for a short time was noted<sup>13</sup>. Unfortunately, this study was not able to compare this two population since there was no patient that was purely breastfed.

The nutritional status of most of the patients in study positive for rotaviral antigen in the stool, had no wasting and stunting (23.1%) which is comparable with the findings of Rogacion and Villa<sup>9,15</sup>. While patients with bacterial isolates had mild to severe wasting.

Diarrhea, vomiting, fever and dehydration are the major findings in diarrhea caused by rotavirus. This study showed a duration of diarrhea of  $2.5 \pm 1.8$  days which is the same as foreign and local studies<sup>9,13,15</sup>. Stools were mostly described as watery with a mean frequency of 7 times a day compared to 8.42 times in the study by Rogacion and 1.2-5.6 times by Ruuska and Vesikari.

The presence of vomiting is much higher in this study for patients positive for rotaviral antigen occurring at 76.9% of the patients compared to only 66% in the study by Rogacion. Compared to patients with bacterial isolates vomiting is more common in rotavirus diarrhea.

The presence of fever at 64% prior to consultation is comparable to the findings of Rogacion at 62% in patients positive for rotavirus antigen in the stool and more common compared to patients with bacterial isolates. On the day of consultation fever was still present in 51.3% of the patients with a mean of  $38.6^{\circ}\text{C}$  was seen in patients positive for rotaviral infection. The duration of fever is also shorter at 2.3 days compared to 4.3 days to patients with bacterial isolates. Thus, one should consider a possible bacterial cause of diarrhea if fever is more than 3 days.

In this study, most of the patients rotaviral isolates presented with no signs (30.8%) and some signs of dehydration (61.5%) upon consultation, which is the same as the finding of Rogacion in 1987. This could be attributed to the awareness of the mother to seek consult early in the course of the disease although, this study was still able to detect 3 patients (7.7%) with severe dehydration. The severe dehydration could not be due to the diarrhea whose mean frequency is only at  $7 \pm 4.2$

times in 24 hours which is below the definition of severe diarrhea, that is, passage of one stool in two hours, but maybe due to vomiting which is quite prominent in patients with rotavirus infection.

Concomitant illness of upper or lower respiratory tract infection was noted in almost 29% of the patients with rotaviral diarrhea. Foreign studies have also detected rotavirus in the respiratory tract<sup>27</sup>, blood and cerebrospinal fluid in conjunction with febrile seizures<sup>28</sup>. However none of our patient had febrile seizures.

This study further proved that a stool exam which is positive for rotavirus is negative for pus and RBC while patients with bacterial diarrhea had pus in their stool exam. Thus, if a pediatrician or a physician would not rely on the clinical picture of rotavirus diarrhea, a simple stool exam would greatly help in further diagnosing the patient and evaluate the need for an antibiotic. As shown in this study 38.5% of this patients were given unwarranted antibiotics by some physicians. The use of antibiotics specially in children less than 5 years old with diarrhea has no benefit since the most common etiologic agent is still rotavirus. This is a self-limiting disease with aggressive fluid and electrolyte therapy as the main mode of management.

Because of the increasing magnitude of the disease associated with rotavirus infections public health interventions to provide clean water and improved sanitation are unlikely to decrease the incidence of the disease. Thus the need for a vaccine is the first strategy for prevention. The first approach to rotavirus vaccines was the use of live, animal strains, termed Jennerian vaccines, that were believed to be naturally attenuated for humans, but when given orally, would mimic the immune response to natural infection and protect children against disease. The first vaccine tested was the bovine strain, RIT 4237 (serotype G6), followed by another bovine strain, (WC3) (serotype G6), a rhesus rotavirus vaccine (RRV) (serotype G3) and recently a lamb strain (LLR) (serotype GII)<sup>29</sup>. The first field trial of a rotavirus vaccine was conducted in 1983 in Finland by Vesikari and colleagues with RIT strain 4237. In August 31, 1998, the first rotavirus vaccine RotaShield (Wyeth-Lederle Vaccines and Pediatrics, Philadelphia, PA) was licensed by the Food and Drug Administration for oral administration to infants at 2, 4 and 6 months of age.

However, the effectivity of rotavirus vaccine combined with oral polio virus and with effect of breastfeeding were raised which are two very important matters in the developing countries since oral polio virus

vaccine is still being used in these countries and breastfeeding as part of the program against diarrhea. Studies have shown that this oral rotavirus vaccine maybe given concurrently with oral polio virus vaccine but infants given OPV concurrently with rotavirus vaccine may have slightly decreased serum antibody responses to rotavirus antigens and serotype 1 poliovirus, but this possible interference is not evident after 3 doses of rotavirus vaccine and polio vaccines<sup>30,31</sup>. Breastfeeding, however, showed a significant adverse effect to rotavirus vaccine seroconversion<sup>32</sup>. Despite these factors the vaccine was then recommended for use by the American Academy of Pediatrics in December 1998, with the aim of preventing mortality because of diarrhea which was not achieved from the programs of oral rehydration therapy, breastfeeding or improving sanitary and water infrastructures. But in July 1999, the Center for Disease Control (CDC) recommended that health care providers and parents postpone the use of the rhesus rotavirus vaccine tetravalent (RotaShield) for infants because of 15 cases with intussusception who received rotavirus vaccine. The withdrawal of the vaccine is big setback in our fight against diarrhea. Fortunately, our scientist were not disheartened and presently another rotavirus vaccine is now on its clinical trial in Finland and in the United States. With this study we were able to note the high incidence of rotavirus diarrhea in our country after which, a recent epidemiologic study regarding the prevailing serotypes will be needed before the vaccine trial can start in our country.

## SUMMARY AND CONCLUSION

After 13 years, a review of the clinical profile of rotaviral diarrhea in a hospital setting was described. Thirty-nine out of the ninety-one cases (42.9%) were positive for rotavirus, most of whom have some signs of dehydration. The isolation rate was noted to be higher by 10% than previous local studies. Rotaviral antigen was detected by the ELISA method. The mean age of the patient was 11.5 months, commonly found in 7-12 months old and mostly were well nourished. Generally, the stools were watery with no pus. Duration of diarrhea was  $2.5 \pm 1.8$  days and stool motion of 7 times a day. A history of vomiting was more frequent in rotavirus infection, while dehydration was noted in bacterial infections. Upper and lower respiratory tract infection were noted to be the concomitant illnesses seen with rotavirus diarrhea. Although rotavirus diarrhea does not need antibiotic treatment this study noted that 38.5% of

the cases were given antibiotic.

**Based on this study the following recommendations can be made:**

1. The increasing incidence of rotavirus diarrhea further emphasizes the need for an effective vaccine against it to prevent morbidity and mortality from diarrheal diseases.
2. Regular surveillance and updated information

should be made available with regards to the etiologic agents of diarrhea to document emergence or decrease in the incidence of bacterial or viral causes of childhood diarrhea.

3. It should be further emphasized that antibiotic treatment should not be a part of the routine treatment of diarrhea especially in children less than 5 years old.

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**References:**

1. Field Health Service Information System Annual 1999. Department of Health.
2. Benn, C & Glass R.I: Impact of Diarrheal Diseases Worldwide: In *Viral Infections of the Gastrointestinal Tract*. edited by Kapikin, A.Z., Marcel, Dekker. 1-26, 1994.
3. Saniel, M, Moriles, R. Monzon, O., Salazar \, N., et al: The Relative Importance of Various Pathogens in the Etiology of Acute Diarrhea: A Hospital Based Study in Urban Philippines. *SEAMIC Publication*, 1987.
4. De Witt, T. Humphrey, K & Mc Carthy, P. Clinical predictors of acute bacterial diarrhea in children. *Pediatrics* 1985;76:551-556
5. Black, RE & Lanata CF. Epidemiology of diarrheal disease in developing countries. *Infection of the Gastrointestinal Tract*. Editor. Blaser, MJ, Smith, PD, Ravadin, PDS et al. Raven Press Ltd. New York, 1995.
6. Paje-Vilar, Estrella et. al. Diarrheas Among Filipino Infants and Children: Clinical and Laboratory Correlations. *Philippine Journal of Pediatrics* 1993;42:1-22.
7. De Zoysa I, Faechem RV. Interventions for the control of diarrheal diseases among young children: rotavirus and cholera immunization. *Bull WHO* 1985; 63:569-583.
8. Adkins, HJ, Escmilla J, Santiago L et al: Two year survey of etiologic agents of diarrheal diseases at San Lazaro Hospital, Manila, Republic of the Philippines. *Journal of Clinical Microbiology* 1987;25:1143.
9. Rogacion J, Bravo L, et al. Rotavirus Diarrhea: Its Clinical Profile A Hospital Based Study. *Philippine Journal of Pediatrics* 1989;38:63-73.
10. Estes, Mk and Cohen J. Rotavirus Gene Structure and Function. *Microbiology Review*. 1989;53:410-449.
11. Bishop RF. Natural History of Human Rotavirus Infection. In: *Viral Infections in the Gastrointestinal Tract* Ed: Kapikian AZ, Marcel Dekker, Inc. NY. P131-167, 1994.
12. Bravo, LC, Araki, Kazuko et. al.; Rotavirus Infection Among Filipino Children: A study of its subgroups, serotypes and electropherotypes. *ICMR Annals* Vol 16, 1996.
13. Ruuska T and Vesikari T. A Prospective Study of Acute Diarrhea in Finish Children from Birth to 2 ½ Years of Age. *Acta Paediatrica Scandinavia*. 1997;80:500-507.
14. Soenarto Y, Sebodo T, et al. Bacteria, parasitic agents and rotaviruses associated with acute diarrhea in hospital in-patient Indonesian children. Diarrhea case management using research findings directly for case management and teaching in a teaching hospital in Yogyakarta, Indonesia. Pp. 39-50, 1997.
15. Villa, FHR. The prevalence and clinical profile of rotavirus diarrhea in Manila Doctors Hospital. *Philippine pediatric Researches Abstracts* 1992-199, 1:36.
16. Bravo LC, Saniel M, et al. Enteropathogens in Acute Diarrhea. *Clinical Indicators Philippine Journal of Pediatrics* 1989;38:74-83.
17. Saniel, MC, Santa Maria, A. Sanvectors E. et al: Prospective study of diarrhea in infants and young children of a peri-urban community: morbidity patterns and etiologies. In: Tzipori S. ed. *Infectious diarrhea in the young: strategies for control in humans and animals*. The Netherlands: Elsevier, 113, 1985.
18. Davidson GP. Viral Enteritis during infancy In: *Textbook of Gastroenterology and Nutrition in Infancy*. Leberthal, E. (ed). Raven Press, New York pp. 1058-1063, 1981.
19. Berner, R, Schumacher, RF, Hameister, S and Forster, J. Occurrence and impact of community-acquired and nosocomial rotavirus infections – a hospital – based study over 10 years. *Acta Paediatrica Suppl* 426:48-52, 1999.
20. Fruwirth, M, Karmaus, W, et al. A prospective evaluation of community acquired gastroenteritis in pediatric practices: impact and disease burden of rotavirus infection. *Archives Disease in Childhood*. 2001;84:393-397.
21. Kapikian, AZ, Hoshino Y, et al. Efficacy of quadrivalent rhesus rotavirus-based human rotavirus vaccine aimed at preventing severe rotavirus diarrhea in infants and young children *Journal of Infectious Diseases* 1996;174 (Suppl 1): S65-72.
22. Perez-Schael I, et al Rotavirus shedding by newborn children *Journal of Medical Virology*. 1984;14:127-136.
23. San Pedro, M and Walz, Stephen. A. Comprehensive Survey of Pediatric Diarrhea at a Private Hospital in Metro Manila. *Southeast Asian Journal Tropical Medicine Public Health*. 1991;22:203-210.



24. Glass RI et al. The Epidemiology of rotavirus diarrhea in the United States: surveillance and estimates of disease burden *Journal of Infectious Disease*. 1996;Suppl 1:S5-II.
25. Yolken R, Wyatt R. et al. Secretory antibody directed against rotavirus in human milk-measurement by means of enzyme-linked immunoabsorbent assay. *The Journal of Pediatrics*. 1978;93:916-921.
26. Gelera, JM, et al. The relationship of breastfeeding to development of acute diarrhea from rotavirus. *PCMC Journal* 1992;1:203.
27. Zheng BJ et al. Rotavirus infection of the oropharynx and respiratory tract in young children *Journal of Medical Virology* 1991;34:29-37.
28. Nishimura, S. et al. Detection of rotavirus in cerebrospinal fluid and blood of patients with convulsions and gastroenteritis by means of reverse transcriptase polymerase chain reaction. *Brain Review*. 1993;15:457-459.
29. Midthum K, Kapikian AZ. Rotavirus vaccines: an overview. *Clinical Microbiology Review*. 1996;1:423-434.
30. Rennels, MB, Ward, R. et al. Concurrent Oral Poliovirus and Rhesus-Human Reassortant Rotavirus Vaccination. Effects on Immune Responses to Both Vaccine and on Efficacy of Rotavirus Vaccines *Journal of Infectious Diseases*. 1996;173:306-313.
31. Ing D., Glass, R et al. Immunogenicity of Tetravalent Rhesus Rotavirus Vaccine Administered with Buffer and Oral Polio Vaccine. *American Journal of Disease Children*. 1991;145:892-897.
32. Pichichero, M. Effect of Breastfeeding on Oral Rhesus Rotavirus Vaccine Seroconversion. A Metaanalysis. *Journal of Infectious Diseases*. 1990;162:753-755.