Acute Gastroenteritis During Childhood in Bolu, Turkey: 3 years of experience

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ABSTRACT
We evaluated 6563 children with the complaint of diarrhea. 29.1% were below 2 years of age, 37.4% were 2-5 years of age and 33.3% were over 5 years of age. 22.3% were admitted during spring, 33.5% were admitted during summer, 23.6% were admitted during autumn and 20.4% were admitted during winter. Rotavirus antigen was found in 16.1% cases. 7.6% of the patients were hospitalized. The direct medical cost for out-patient's clinic was $18.7 and for hospitalized patients was $74.3. The most common agent in the childhood gastroenteritis was rotavirus. Viral agents were identified frequently during winter and bacterial and parasitic agents were identified frequently during summer.

Keywords: Acute gastroenteritis, child, etiological agents, cost

INTRODUCTION
Acute gastroenteritis is an important problem and ranks the second after respiratory infections depending on frequency of the disease around the world[1]. Acute diarrhea is common in all age groups; however, it is more common in the "0-5 years of age" group than other ages. In developing countries attack rates range from 2-5 episode/child/year in this age group[2]; in the developed countries, attack rates range from 1-2,5 episode/child/year[3]. Generally, these infections resolve spontaneously. However, they can be fatal for young children. Approximately 1,7 million children die annually due to acute diarrhea [4]. Most of these cases are seen in the developing countries.

Volume of fluid lost through gastroenteritis can vary from 5 ml/kg/day to 200 ml/kg/day[5]. Severe fluid loss observed during gastroenteritis increases morbidity and mortality. This severe picture is associated with the virulence of the agent, age of the host, nutrition state, and immunization state. Gastroenteritis-induced dehydration, acid-base disturbance, electrolyte imbalance and malnutrition is the most important cause of childhood mortality. In our country, gastroenteritis is the fifth common cause of childhood mortality[6].

Childhood diarrhea has many causes and infection is the most common cause. Many different types of microorganisms can cause gastroenteritis. Viral agents are frequently observed during winter while bacterial agents are frequently observed during summer. The acute gastroenteritis agents are associated with the study site, time and population. It is possible to reduce the bacterial and parasitic gastroenteritis through providing clean water and correction of the infrastructure systems in the settlement areas. However these measures do not prevent viral gastroenteritis[7]. In addition to the high annual costs[8], it causes emotional trauma for the child and family[9].

In order to control the problems associated with acute gastroenteritis the etiological agents shall be identified accurately based on age groups. In this study, we present the characteristics of the acute gastroenteritis patients (1 month to 16 years old) consulting the gastroenteritis clinic, identified agents and information regarding respective costs for our country.

MATERIALS AND METHODS

Bolu is a province located in the north-west of Turkey. We retrospectively evaluated 6563 acute gastroenteritis cases who had consulted the children emergency service and children's polyclinics of Bolu İzzet Baysal Gynecology and Pediatric Hospital with a complaint of diarrhea and who were subject to fecal examinations between 1 January 2007 and 31 December 2009 using the automations system of the hospital. In this study, acute gastroenteritis was considered as "3 or more watery stools daily[10]". The age of the patients was divided into 3 groups: under 2 years old, 2-5 years old and over 5 years old. The patient's age and gender, complaints, direct microscopic fecal assessment, viral antigens in feces, fecal cultures, number of hospitalized patients, number of hospitalized days and the cost imposed on the government by the patients were evaluated. Fecal assessments were performed within 15 minutes following defecation in the microbiology laboratory of the hospital. Rotavirus and adenovirus were assessed by immunochromatographic (Rida Quick, r-biopharm) method. Fecal samples were cultivated into 5% sheep blood agar, Eosine Methylene Blue (EMB) agar, Salmonella Shigella (SS) agar medium and Selenit F agar medium, and they were then incubated at 37 °C. Following 8-hours of incubation period, passages were made from Selenit F liquid medium into EMB agar and SS agar medium. Each agar medium contained one colony. And then they were incubated at 37 °C. Following 24-hours of incubation period, all agar mediums were evaluated. Lactose negative colonies produced from EMB agar and SS agar mediums were tested by conventional biochemical methods. The slide agglutination was used by Salmonella and Shigella antiserums to identify the bacteria with the biochemical characteristics of Salmonella and shigella. Data was evaluated by Package for the Social Sciences (SPSS, Inc., Chicago, IL), version 17.0 for Windows statistical program. Chi-square (χ^2) and one way Anova tests were used for statistical assessment and $p<0.05$ was considered as significant.

RESULTS

The mean age of the patients was identified to be 6.5 ± 5.1 years (median: 5 years). 1916 (29.1%) of the patients were under the age of 2, 2460 (37.4%) were 2-5 years old and 2187 (33.3%) were over the age of 5. (Table 1) A significant difference with respect to the age groups was observed in the gastroenteritis admissions ($p<0,001$). 3545 of the patients were males (54%) and 3018 were females (45.9%). 1465 (22,3%) of the patients were admitted during spring, 2203 (33.5%) were admitted during summer, 1550 (23.6%) were admitted during autumn and 1345 (20.4%) were admitted during winter. A significant difference was observed between the patients who had consulted the hospital due to gastroenteritis depending on seasons ($p<0.001$). 2133 of the patients complaining about diarrhea had abdominal pain (%32.5), 2389 (36.4%) had fever and 3295 (50.2%) had nausea-vomiting. 504 patients (7.6%) were hospitalized in the pediatric service. No exitus case was reported.

Table 1 Patient Distribution by Age Groups and Admission Season

	<2 years (n)		2-5 years (n)		>5 years (n)		Total
	Male	Female	Male	Female	Male	Female	
Autumn	254	213	307	251	242	205	1472
Summer	345	268	454	405	386	346	2204
Spring	212	166	304	237	327	297	1543
Winter	247	211	262	240	205	179	1344
Total	1058	858	1327	1133	1160	1027	6563

In the viral fecal assessment, 1058 cases (16.1%) were tested positive with respect to rotavirus antigen and 158 cases (2.4%) were tested positive with respect to adenovirus antigen. 521 (49.2%) of the rotavirus cases were under the age of 2, 361 (34.1%) were 2-5 years old and 176 (16.6%) were over the age of 5. (Table 2) Incidence of rotavirus gastroenteritis in the patients under the age of 2 was significantly higher than the patients with the age of over 5 ($p<0.001$). 392 cases with rotavirus (37%)

were admitted during winter, 303 (28.6%) cases were admitted during spring, 226 (21.3%) cases were admitted during summer and 137 (12.9%) were admitted during autumn. When the age groups were taken into consideration, cases developing rotavirus gastroenteritis during summer were significantly less than the cases developed during winter (p=0.002) and spring (p<0.001). 50 (31.6%) of adenovirus cases were under the age of 2, 55 (34.8%) cases were 2-5 years old and 53 (33.5%) were over 5

years old. No significant difference was observed between the age groups when the adenovirus positive cases were taken into consideration (p>0.05). 55 (34.8%) cases with adenovirus were admitted during winter, 37 (23.4%) cases were admitted during spring, 46 (29.1%) during summer and 23 (14.5%) were admitted during autumn. No significant difference was found between age groups based on seasons. (p>0.05).

Table 2 Distribution of the cases with positive fecal virus test based on virus type and age group

	<2 years (n)		2-5 years (n)		>5 years (n)		Total
	Rota V	Adeno V	Rota V	Adeno V	Rota V	Adeno V	
Autumn	162	12	108	16	33	9	340
Summer	94	8	72	18	60	20	272
Spring	67	7	38	5	32	8	157
Winter	198	23	143	16	51	16	447
Total	521	50	361	55	176	53	1216

In the direct microscopic fecal assessment, leukocyte was identified in 1135 (17.2%) cases, erythrocyte in 106 (1.6%) of cases, entemoeba

histolitica cyst or trofozoit in 53 (0.8%) cases and giardia lamblia cyst or trofozoit was identified in 33 (0.5%) of cases (Table 3).

Table 3 Distribution of the cases with positive fecal pathological finding based on age group

	<2 years (n)	2-5 years (n)	>5 years (n)	Total (n)	%
Lökosit	139	383	613	1135	17.2
Eritrosit	10	37	59	106	1.6
E histolitica	5	21	27	53	0.8
Giardia İntestinalis	-	3	30	33	0.5
Salmonella	2	7	11	20	0.3
Shigella	-	1	-	1	0.01

Fecal culture was requested from 93 patients (1.4%). In the fecal cultures, salmonella spp was produced in 20 cases (0.3%) and shigella spp was produced in 1 case (0.01%). 15 of these bacterial agents (68.1%) were identified in the patients admitted during summer.

According to direct smear or culture, the incidence of bacterial or parasitic acute gastroenteritis is significantly higher in summer than in autumn and winter (p<0.001). Viral acute gastroenteritis is

significantly higher in winter than other seasons (p<0.001). No pathology was identified in 5239 patients (79.9%).

The cost per patient imposed on the government is approximately $28.80, ranging from$9.1 to $991.60. The cost of the out-patient clinic is $18.70 (ranging from $9.10 to $87.20) and the cost of the hospitalized patient was $74.30 (ranging from $12.20 to $991.6).

DISCUSSION

Acute gastroenteritis is a major cause of morbidity and mortality among children in the developing countries[11]. In developed countries, mortality associated with acute gastroenteritis is decreased; however, it remains to be a major cause of morbidity[12]. The etiological agents for acute infectious diarrhea are: 70-80% viruses, 10-20% bacteria and 10% parasites[13]. The etiology of acute gastroenteritis is very important for treatment and prognosis.

According to the literature, acute gastroenteritis is generally more common in children under the age of 5[14,15]. Children under the age of 5 are not aware of toilet cleaning and hygiene rules. Therefore, gastrointestinal infections are more common among children than adults due to fecal-oral contamination. In our study, 66.5% of the cases were under the age of 5.

The acute gastroenteritis agent may depend seasons. Viral agents are common during winter and bacterial agents are common during summer[16]. In a study performed by Caprioli et al[17], it was observed that viral agents were common during winter and bacterial agents were common during autumn. In Koçak's study in which the entire childhood period was included[15], it was observed that 32.8% of the acute gastroenteritis cases happened during summer and 21.8% happened during winter. In our study, 33.5% of the cases were admitted during summer and 20.4% of them were admitted during winter. In our study, viral agents were more common during winter (p<0.001) and bacterial and parasitic agents were more common during summer than autumn and winter (p<0.001).

Clinical symptoms are associated with etiological agent and patient's age. The complaints include diarrhea, nausea-vomiting, loss of appetite, fever, fatigue and abdominal cramps[18]. In a study performed by Nguyen et al[19], 43.6% of the patients had fever accompanied with diarrhea and 53.8% had nausea-vomiting accompanied with diarrhea. In a study performed by Aydın et al[14], 70% had vomiting, 22.9% had fever and 32.7% had abdominal pain. In our study, 32.5% had abdominal pain, 36.4% had fever and 50.2% had nausea-vomiting.

According to literature, the incidence of hospitalization due to acute gastroenteritis is 3.3-6%[13,14]. In the developed countries, the patients are hospitalized frequently as a result of dehydration due to acute gastroenteritis to ensure peace of mind for families and to facilitate treatment. This also helps with safe administration of intravenous fluid[20]. In our study, 7.6% of the cases were hospitalized. Insistence of the families in hospitalization of the children was another factor that increased the ratio of hospitalization in our study because the families indicated that their attempts to feed liquids to the children were unsuccessful[21].

Feces shall definitely be assessed in the patients with diarrhea; it shall be examined for blood and mucus. Then leukocyte, erythrocyte, cyst and parasites should be assessed by microscopy. Identifying leukocyte in feces provides information regarding diarrhea agent, anatomic localization and mucosal inflammation. Leukocytes are identified in feces generally during bacterial gastroenteritis. In a study performed by Koçak[15], leukocyte was found in 31.4% of the cases and E histolitica was found in 1.5% of the cases. In a study performed by Aydın et al[14], leukocyte was identified by direct feces smear in 18% of the cases. Giardia lamblia-induced acute gastroenteritis was identified in 0.5 %[9] to 1%[22] of the cases. In our study, leukocyte was identified in 17.2% of the cases, erythrocyte in 1.6%, E histolitica in 0.8% and giardia in 0.5% of the cases by direct feces microscopy. Different results may be obtained by direct feces microscopy depending on the experience of the one implementing the assessment.

Viruses are the etiological agent in 87% of the acute diarrhea cases[12]. According to literature, rotavirus is the etiological agent in 78.3% of the viral gastroenteritis cases and adenovirus is the etiological agent in 17.8% of the viral gastroenteritis cases[23]. Only in a study conducted in Guatemala that has a different climate, enteric adenovirus was the most common etiology in children[24]. In our study, rotavirus was the etiological agent in 87% of the viral gastroenteritis cases while adenovirus was the etiological agent in 12.9% of the viral gastroenteritis cases.

In developing countries, bacteria and parasites are more prevalent than viruses[25]; in developed countries viruses are more prevalent than other

agents[17,26]. Virus was identified in watery stool in 1972 for the first time. Up to now, several viruses have been identified in diarrhea through direct or indirect methods[27]. The most common aetiological agent is rotavirus and it is the most important acute gastroenteritis agent in the developing and developed countries[28]. Rotavirus incidence in children with acute gastroenteritis is 2-49% in the developing countries and 8-50% in the developed countries[29]. In our country, rotavirus incidence in children with diarrhea is 15.5 % to 21%[1,30]. In our study, rotavirus antigen was positive in 16.1% of the cases. This result is concordant with the literature published in our country.

Rotavirus causes severe diarrhea especially among 6 months-2 years old children[31]. 95% of children are infected with rotavirus worldwide and as a result, they produce rotavirus antibodies by the ages of 3 to 5. Therefore, the incidence of symptomatic rotavirus infection decreases with age[32]. According to literature, most of the rotavirus cases are observed in children under the age of 5 and particularly, prior to the age of 2[31]. In our study, 49.2% of the rotavirus cases were under the age of 2 while 83.3% of the rotavirus cases were under the age of 5.

In our country, just like in the countries with mild climate, rotavirus gastroenteritis is common in winter and early spring[33]. In our study, concordant with the literature, rotavirus gastroenteritis was more common in winter and spring than summer (p<0.05).

The second most common viral agent in the acute gastroenteritis is adenovirus[34]. Adenovirus causes milder infections compared to rotavirus. The clinical picture of adenovirus is self-limited. The incidence of adenovirus in the childhood gastroenteritis is 3.1%[34] to 15%[35]. In our country, the incidence of adenovirus in the childhood gastroenteritis is 1% to 4.5%[27,36]. In our study, adenovirus antigen was positive in 2.4% of the cases. This result is concordant with the literature in our country.

According to the literature, most of the adenovirus cases are patients under the age of 2 years[24]. There are studies reporting that development of the adenovirus does not depend on age distribution[37]. In our study, 31.6% of adenovirus cases were under the age of 2, 34.8% were 2-5 years old, and 33.5% were

over the age of 5. No significant difference was observed between the age groups when adenovirus development was considered (p>0.05).

Adenovirus gastroenteritis may be observed throughout the year[33]. But there are articles which state that adenovirus gastroenteritis is more common in winter[38]. In our study, 34.8% of the cases were admitted during winter, but this raise in the number of the patients is not statistically significant (p>0.05).

According to literature, bacteria are etiological agents in 14% of the acute gastroenteritis cases[26]. However, since most of the cases are viral, fecal culture is not required routinely. Fecal culture is required in case of bloody diarrhea, travel history or immune deficiency[12,39]. According to the literature published in our country, fecal culture is required in 11.8 % - 23.3% of the acute gastroenteritis cases[14,40]. In our study, fecal culture was required only in 1.4% of the cases. Our number of fecal culture was pretty low because the symptoms were not considered to be caused by bacterial etiological agent. Besides, there is no reimbursement for the fecal culture assessment in the out-patient clinic by the government therefore, the doctors rather not to ask for fecal culture assessment. The possibility of reproducing bacterial agent in fecal culture is 0 to 5%[14,40]. In our study, the agent was reproduced in 0.32% of the cases. The most common agents in the culture are salmonella, E coli and shigella[14], and this is concordant with our study. We associated small number of fecal cultures with few agents reproduced in our study.

According to literature, bacterial acute gastroenteritis is common during summer[26]. But some studies report that the possibility of observing the disease is equal throughout the year[17]. In our study, 68.1% of these bacterial agents were identified in the patients admitted during summer.

We used all test methods to identify the pathogen of acute gastroenteritis, but we could only identify 20.1% of the agents. This incidence is reported to be 46.3% in an article published in our country[41], and 40% in the study conducted by Caprioli et al[17]. The low incidence may be due to using only one fecal sample. There are other factors including antibiotic initiation in the early period[17], diarrhea associated

with parenteral infection, food intolerance[42] or unidentified agents.

Direct medical cost of an acute gastroenteritis case is \$4.30[43] to \$47.00[44] for the out-patients' clinic, and \$133.80[43] to \$2307.00[44] for the hospitalized patients. In our study, the cost of the out-patients clinic was \$18.70 and in the hospitalized patients was \$74.30.

In conclusion, the most common agent in the childhood gastroenteritis is rotavirus. Rotavirus is common in children under the age of 5, particularly, in winter. The second most common viral agent in the acute gastroenteritis is adenovirus. The most important bacterial agent in childhood gastroenteritis is salmonella. The most common parasitic agent is Giardia lamblia. The etiological agent identification is necessary for treatment planning. The diagnosis can be implemented by easy tests including direct microscopic fecal assessment and viral tests. This diagnosis avoids prescribing unnecessary drugs.

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