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Evaluation of Cases Developing Sepsis After Acute Gastroenteritis: A Single Center Experience

Akut Gastroenterit Sonrasında Sepsis Gelişen Vakaların Değerlendirilmesi: Tek Merkez Deneyimi

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Abstract

Objective: Acute gastroenteritis (AGE) is among the most common reasons for admission to healthcare institutions in the world and is the second most common cause of death in children under the age of five. Life-threatening complications such as seizures, encephalitis, aseptic meningitis and sepsis may occur during AGE. It is thought that sepsis may develop due to bacterial translocation after AGE, but the mechanism is not clear. In our study, pediatric patients who were hospitalized and treated with the diagnosis of AGE were evaluated retrospectively. It was aimed to evaluate the clinical and laboratory findings of the patients included in the study, possible etiological agents, duration of hospitalization and affecting factors, and the risk of sepsis development.

Material and Methods: Our study was designed as a single-center, retrospective study. Patients aged between one month and 16 years who were treated as inpatients with the diagnosis of AGE in the Pediatric Infection Clinic of our hospital between January 2015 and December 2019 were included in the study.

Results: Of the 924 patients included in the study, 503 (54.4%) were male and 421 (45.6%) were female, and the average age was 27.82 (1-190 months). The most common clinical findings were diarrhea (99.4%), vomiting (67.2%) and fever (55.1%), respectively. Sepsis was observed to develop in 237 of 924 patients included in our study (25.6%). Patients who developed sepsis were hospitalized for longer periods of time than those who did not develop sepsis, and the rate of vomiting, fever and hyponatremic dehydration was higher ($p< 0.05$), and laboratory findings showed that C-reactive protein (CRP) and procalcitonin PCT values

Öz

Giriş: Akut gastroenterit (AGE), dünyada sağlık kurumlarına başvuruların en sık nedenleri arasında yer almakta olup, beş yaş altı çocuklarda ölümlerin en sık ikinci nedenidir. Akut gastroenterit sırasında nöbet, ensefalit, aseptik menenjit ve sepsis gibi hayatı tehdit eden komplikasyonlar görülebilmektedir. Sepsisin, AGE sonrasında bakteriyel translokasyona bağlı olarak gelişebildiği düşünülmektedir; ancak bu mekanizma net değildir. Bu çalışmada, AGE tanısıyla hastaneye yatırılarak tedavi edilen çocuk hastalar retrospektif olarak değerlendirilmiştir. Çalışmaya dahil edilen hastaların klinik ve laboratuvar bulguları, muhtemel etiyolojik ajanlar, hastanede yatış süresi ve buna etki eden faktörler ile sepsis gelişim riskinin değerlendirilmesi amaçlanmıştır.

Gereç ve Yöntemler: Çalışmamız, tek merkezli ve retrospektif olarak tasarlanmıştır. Ocak 2015-Aralık 2019 tarihleri arasında, hastanemiz Çocuk Enfeksiyon Kliniği'nde AGE tanısıyla yatarak tedavi edilen 1 ay-16 yaş arası hastalar çalışmaya dahil edilmiştir.

Bulgular: Çalışmaya dahil edilen 924 hastanın 503 (%54.4)'ü erkek, 421 (%45.6)'i kız olup yaş ortalaması 27.82 (1-190 ay) idi. En sık görülen klinik bulgular sırasıyla ishal (%99.4), kusma (%67.2) ve ateş (%55.1) olarak tespit edildi. Çalışmamıza dahil edilen 924 hastanın 237 (%25.6)'sinde sepsis geliştiği görüldü. Sepsis gelişen hastaların, sepsis gelişmeyenlere kıyasla hastanede daha uzun süre yattığı; kusma, ateş ve hiponatremik dehidratasyon gelişme oranlarının daha yüksek olduğu belirlenmiştir ($p< 0.05$). Ayrıca, bu gruptaki hastalarda laboratuvar bulgularından C-reaktif protein (CRP) ve prokalsitonin (PCT) değerlerinin istatistiksel olarak anlamlı yüksek olduğu ($p< 0.05$) görüldü. Sepsis gelişen ve

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were statistically significantly higher in those who developed sepsis. ($p< 0.05$) was seen. When the cases with and without sepsis were examined with Receiver Operating Characteristic (ROC) analysis, it was determined that the two best parameters in determining sepsis were CRP and PCT. According to this analysis, sensitivity for CRP was 54.04% and specificity was 71.03%. For PCT, sensitivity was found as 60.98% and specificity as 72.64%.

Conclusion: In our study, it was determined that sepsis developed in 25.6% of the patients treated as inpatients with a diagnosis of AGE. CRP and PCT values are seen to be superior to other laboratory parameters in predicting sepsis. Careful monitoring of pediatric patients diagnosed with AGE in terms of sepsis as well as fluid-electrolyte balance is important in terms of the development of morbidity and mortality.

Keywords: Children, acute gastroenteritis, sepsis

gelişmeyen olgular, Receiver Operating Characteristic (ROC) analiziyle incelendiğinde, sepsisi belirlemede en iyi iki parametrenin CRP ve PCT olduğu saptandı. Bu analize göre CRP için sensitivite %54.04, spesifisite %71.03; PCT için ise sensitivite %60.98, spesifisite %72.64 olarak bulundu.

Sonuç: Çalışmamızda, AGE tanısıyla yatarak tedavi edilen hastaların %25.6'sında sepsis geliştiği saptandı. Sepsisi öngörmede ise CRP ve PCT değerlerinin diğer laboratuvar parametrelerine göre daha üstün olduğu görülmektedir. AGE tanısıyla izlenen çocuk hastaların, sıvı-elektrolit dengesi yanında sepsis açısından da dikkatli bir şekilde takip edilmesi; morbidite ve mortalite gelişimini önemlemek açısından önem arz etmektedir.

Anahtar Kelimeler: Çocuk, akut gastroenterit, sepsis

Introduction

Acute gastroenteritis (AGE) is one of the most common reasons for seeking medical care worldwide and is the second leading cause of death in children under five years of age (1,2). It accounts for approximately 1.7 billion cases and 525.000 deaths annually, with 80% of deaths occurring in children under two years of age (2).

Diarrhea is defined as three or more loose or watery stools per day, or more frequent and watery stools than usual in breastfed infants (3). Globally, viruses are the most common infectious cause of AGE in children, with rotavirus being the most frequently identified viral pathogen (1). In children under five years of age, in addition to viral infections, moderate to severe diarrhea may also be caused by pathogens such as *Cryptosporidium, Shigella,* and enterotoxigenic *Escherichia coli* (4,5). Fluid and electrolyte imbalances resulting from dehydration in patients with AGE are the most common cause of death, and therefore rehydration and replacement therapy are the primary treatment methods (1).

Extragastrointestinal complications such as seizures, encephalitis, aseptic meningitis, neutropenia, and sepsis may occur during and after AGE. Among these, sepsis is a life-threatening organ dysfunction that develops due to an inappropriate host response to infection (6). Although the mechanism of sepsis developing after AGE is not fully understood, it is thought to be caused by bacteremia resulting from mucosal damage and bacterial translocation in the intestinal wall. Studies have shown that rotavirus causes intestinal epithelial metaplasia and dysfunction, thereby rendering enterocytes vulnerable to bacterial invasion (7). Additionally, the immature intestinal barrier in infants contributes to susceptibility to bacterial translocation following AGE, thereby increasing the incidence of sepsis (7).

There are few studies on the development of sepsis during AGE. In this study, the demographic characteristics, clinical and laboratory features of patients hospitalized with a diagnosis of AGE in our clinic were investigated, and patients who developed sepsis during follow-up were evaluated.

Materials and Methods

Our study included 924 patients aged 1 month to 16 years who were hospitalized and treated with AGE between January 1, 2015, and December 31, 2019. Patients with underlying diseases and immunodeficiency were excluded from the study. Laboratory values of the patients [white blood cell count (WBC), C-reactive protein (CRP), procalcitonin (PCT), hemoglobin, neutrophil count, platelet count, urea, creatinine, sodium, potassium, chloride, aspartate aminotransferase (AST), alanine aminotransferase (ALT), blood gas, stool microscopic examination, stool culture, stool viral antigen tests], clinical findings, length of stay, treatment initiated during hospitalization, and prognosis, as well as clinical and laboratory results of the patients who developed sepsis, were retrospectively recorded from patient files.

AGE was defined as a decrease in stool consistency followed by watery stools, accompanied by fever and vomiting, and three or more bowel movements within 24 hours. Diarrhea was defined as three or more loose or watery bowel movements per day, or more frequent and watery bowel movements than usual in breastfed infants (3,4). A high fever was defined as an axillary temperature of 38.5 °C or higher.

Pediatric sepsis was defined as the presence of Systemic Inflammatory Response Syndrome (SIRS) with suspected or proven infection, while septic shock was defined as sepsis with cardiovascular dysfunction.

SIRS: At least one of the following: increased/decreased body temperature or leukocyte count; tachycardia without external stimulation, pain or chronic drug use or, in children under one year of age, external vagal stimulation, beta-blocker medication use, congenital heart disease, or unexplained cardiac depression resulting in bradycardia, tachypnea with an average respiratory rate at least two standard deviations above the normal range for age, or the need for mechanical ventilation not due to neuromuscular disease or anesthesia (8).

Dehydration was classified as mild, moderate, or severe. Mild dehydration was defined as fluid loss of less than 3% of body

weight, moderate dehydration as fluid loss between 3% and 9%, and severe dehydration as fluid loss of more than 9% (3).

Ethics approval for our study was obtained from the Ethics Committee on April 6, 2019, with approval number 1224.

Statistical Analysis

SPSS 24 software was used for statistical analysis. Descriptive statistics were presented as number (n) and percentage (%) for categorical variables, and mean, standard deviation, median, minimum, and maximum for numerical variables. Comparisons between two independent groups for numerical variables were performed using the Mann-Whitney U test, Kruskal-Wallis test, and chi-square test for data that did not follow a normal distribution. Multivariate logistic regression analysis and ROC analysis were used to predict sepsis. Specificity, sensitivity, and likelihood ratios were calculated for significant parameters. The statistical significance level was set at p= 0.05.

Results

Our study included a total of 924 patients aged between one month and 16 years, comprising 503 (54.4%) males and 421 (45.6%) females. Mean age was 27.82 ± 31.55 months, and the proportion of patients under two years of age was 63.5% (n= 587). The demographic and clinical characteristics of the patients are summarized in Table 1.

Table 1. Demographic and clinical characteristics of patients

		n	%
Sex	Male	503	54.44
	Female	421	45.56
Age groups	0-24 months	587	63.5
	24-48 months	183	19.8
	48-60 months	48	5.2
	Older than 60 months	106	11.5
Age (median)	15.8 (IQR)		
Birth weight (reached)	Very low birth weight	13	2.1
	Low birth weight	88	14.1
	Normal birth weight	525	83.9
Low birth weight	Present	61	6.60
Birth time (reached)	Premature birth	112	37.8
	Mature birth	184	62.2
Prematurity (history)	Present	91	9.8
Previous history of hospitalization due to gastroenteritis	Present	65	7.14
Admission time due to previous gastroenteritis	1 week ago	8	0.9
	1-2 weeks ago	12	1.3
	2-4 weeks ago	7	0.8
	1-6 months ago	6	0.6
	6-12 months ago	11	1.2
Concurrent accompanying disease	Present	247	26.75
Accompanying diseases	LRTI	114	12.3
	URTI	73	7.90
	Anemia	21	2.27
	UTI	20	2.16
	Surgical diseases*	18	1.95
	Gastroenterologic diseases**	8	0.87
	Conjunctivitis	6	0.65
	Aphthous stomatitis	6	0.65
	Cellulitis	3	0.32

LRTI: Lower respiratory tract infection, URTI: Upper respiratory tract infection, UTI: Urinary tract infection.
*Invagination, ileus.
**Mallory Weiss syndrome, rectal prolapse.

When the symptoms of the patients at admission were examined, diarrhea (99.4%) and vomiting (67.2%) were the most common, while fever (55.1%) was present in 509 patients, 73 (7.9%) had abdominal pain, 30 (3.2%) had fatigue, 17 (1.84%) had rash, and 16 (1.73%) had irritability.

When comparing the degree of dehydration among the patients, 822 (88.9%) had mild dehydration, 96 (10.3%) had moderate dehydration, and 6 (0.65%) had severe dehydration. When examining the characteristics of dehydration, isonatremic dehydration was observed in 700 (75.7%) patients, hyponatremic dehydration in 181 (19.59%) patients, and hypernatremic dehydration in 43 (4.65%) patients. When comparing the severity of dehydration with laboratory values, statistically significant differences were observed between WBC, neutrophil count, platelet count, urea, and creatinine. Patients with severe dehydration had statistically significantly higher WBC, neutrophil count, platelet count, urea, and creatinine values compared to other patients (Table 2).

When the stool characteristics of the patients were examined, 881 (95.4%) had watery and mucous stools, and 43 (4.6%) had bloody stools. Among the 365 (39.5%) patients who underwent stool culture, viral pathogens were the most common, followed by bacterial pathogens in 11 (1.1%) patients and parasitic pathogens in 7 (0.75%) patients. No growth was observed in the stool cultures of 195 (21.2%) patients. Among the viral pathogens, rotavirus was the most common in 145 (15.6%) patients, adenovirus in 6 (0.64%) patients, and both rotavirus and adenovirus in 1 (0.10%) patient. Among bacterial pathogens isolated from stool cultures, the most common were *Salmonella enteritidis* (0.24%), *Campylobacter jejuni* (0.16%), *Salmonella typhi* (0.16%), *Salmonella* (0.08%), and *Salmonella* species (0.08%) (Table 3).

When the pathogens detected in the stool samples of the patients were analyzed according to seasons, bacterial, viral, and parasitic infections were found to be statistically significant and high in August ($p< 0.001$) (Figure 1).

When the clinical results of patients were examined according to pathogens, it was seen that patients with viral pathogens in their stool were younger than those with bacterial and parasitic agents and had longer vomiting periods than those with bacterial agents ($p= 0.025$, $p= 0.010$, respectively). Patients with parasitic pathogens had statistically longer vomiting durations compared to others. No statistically significant differences were found between the duration of hospitalization, vomiting frequency, diarrhea duration, diarrhea frequency, and fever duration based on the pathogen detected in stool. When the ages of the patients were compared according to the pathogen detected in stool examinations, the age at which viral pathogens were detected was 19 ± 18.44 months, which was younger than the age at which other bacterial and parasitic pathogens were detected.

When the patients were examined for the development of sepsis, it was found that sepsis developed in 237 (25.6%) of them. During hospitalization, 386 (41.8%) patients developed electrolyte imbalance, 38 (4.1%) patients developed convulsions, and 2 (0.2%) patients developed hemolytic uremic syndrome. Of the patients, 898 (97.2%) were discharged with complete recovery, whereas 26 (2.8%) required referral for further management; among these, 20 (2.17%) were transferred to other wards and 6 (0.65%) to the pediatric intensive care unit.

When the clinical course of the patients who developed sepsis was examined, it was observed that the length of hospital stay was statistically longer in patients who developed sepsis compared to those who did not ($p< 0.001$).

Table 2. Relationship between laboratory values and dehydration results in patients

	Mild n= 822	**Moderate n= 96**	**Severe n= 6**	**p**
White blood cell count (1/mm^3)	12.4 ± 6.4	13 ± 6.1	17.3 ± 5.2	**0.048**
Neutrophil count (1/mm^3)	7.2 ± 5.5	7.6 ± 4.4	10.7 ± 3.8	**0.021**
Hemoglobin (g/dL)	11.6	11.7 (7.8-12.3)	11.6 ± 1.1	0.905
Platelet count (x10^3/mm^3)	339.1 ± 13.2	394.1 ± 166.5	471.8 ± 270.7	**0.004**
Urea (mg/dL)	20.7 (IQR)	27.0 (IQR)	37.1 (IQR)	**<0.001**
Creatinine (mg/dL)	0.3 (IQR)	0.3 (IQR)	0.4 (IQR)	**0.002**
Sodium (mmol/L)	137.7 ± 4	138.1 ± 6.1	141.5 ± 11.7	0.662
Potassium (mmol/L)	4.4 ± 0.8	4.9 ± 1.3	4.9 ± 1.3	0.577
Chlorine (mmol/L)	102.4 ± 5.7	105.1 ± 9.3	108.2 ± 16.7	0.128
AST (U/L)	37.0 (IQR)	40.3 (IQR)	43.4 (IQR)	0.483
ALT (U/L)	19.8 (IQR)	22 (IQR)	19.1 (IQR)	0.417
C-reactive protein (mg/L)	8.9 (IQR)	8.6 (IQR)	3.9 (IQR)	0.295
Procalcitonin (ug/L)	0.5 (IQR)	0.6 (IQR)	1.1 (IQR)	0.762

ALT: Alanine aminotransferase, AST: Aspartate aminotransferase.

Table 3. Patients' stool culture and distribution of infectious agents

		n	%
Pathogen in stool culture	Not analyzed	559	60.4
	No pathogen	195	21.2
	Viral	152	16.4
	Bacterial	11	1.1
	Parasite	7	0.75
Leukocyte in stool	Not analyzed	504	54.55
	None	349	37.77
	Leukocyte	44	4.76
	Leukocyte and erythrocyte	24	2.60
	Erythrocyte	3	0.32
Pathogen that grew	*Salmonella enteritidis*	3	0.24
	Campylobacter jejuni	2	0.16
	Salmonella typhi	2	0.16
	Salmonella	1	0.08
	Salmonella species	1	0.08
Virus antigen	Not analyzed	480	51.9
	Negative	292	31.6
	Rotavirus	145	15.6
	Adenovirus	6	0.64
	Rotavirus and adenovirus	1	0.10
Other pathogens	Amoebic cyst	6	0.42
	Clostridium difficile Toxin-A/B	3	0.24
	Giardia antigen/cyst	1	0.16

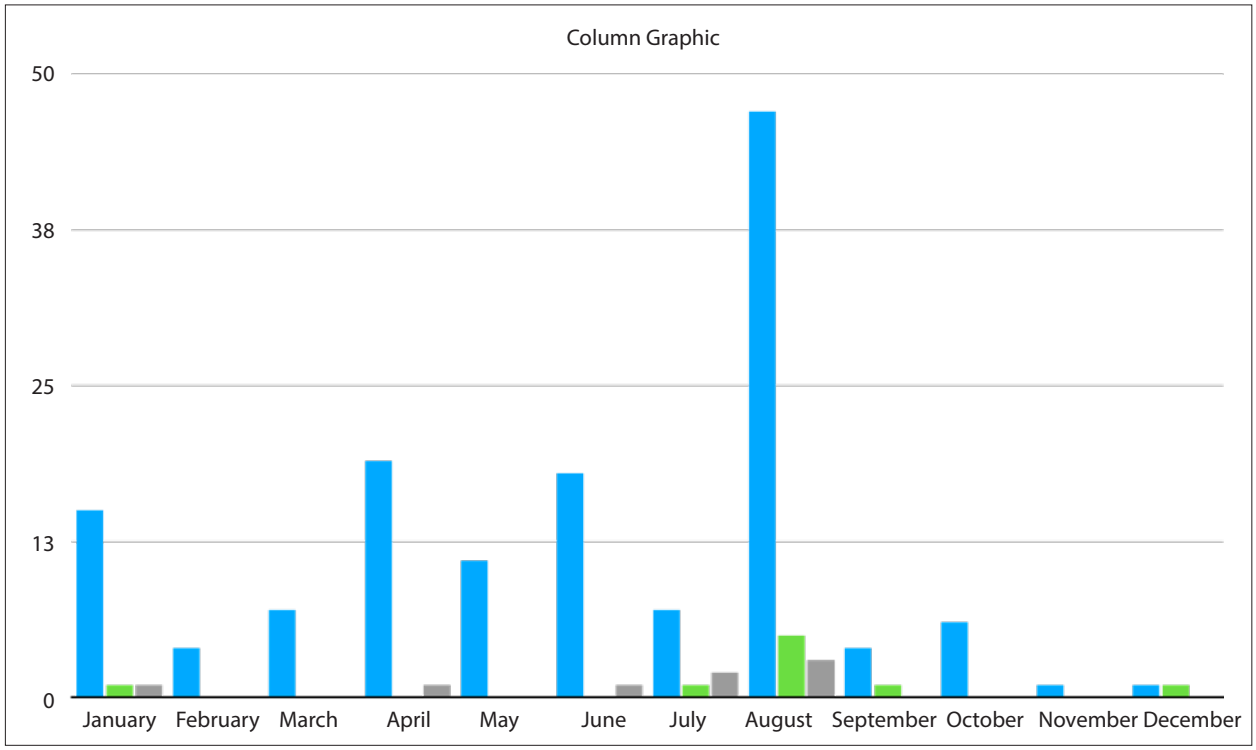

Figure 1. Seasonal distribution of diarrhea pathogens (blue: viral agents, green: bacterial agents, gray: parasitic agents).

Table 4. Clinical course and laboratory parameters of patients developing sepsis

	Sepsis absent	Sepsis present	
	Median (min-max)	Median (min-max)	p
Length of stay	4.0 (2-30)	6.0 (2-30)	**<0.001**
Age	6 (1-11)	6 (1-12)	0.880
Vomiting duration	2.0 (1-20)	2.0 (1-20)	0.124
Vomiting frequency	5.0 (1-20)	5.0 (1-15)	0.053
Diarrhea duration	2.0 (1-14)	2.0 (1-15)	0.883
Diarrhea frequency	6.0 (1-15)	6.0 (1-20)	0.444
Fever duration	2.0 (1-14)	2.0 (1-15)	0.983
White blood cell count (1/mm^3)	12910 (7600-27090)	12475 (5400-32870)	0.194
Neutrophil count (1/mm^3)	8250 (2500-10220)	7120 (1000-15640)	**0.024**
Hemoglobin (g/dL)	12.3 (8.3-15.7)	11.4 (6.8-15.7)	**<0.001**
Platelet count (x10^3/mm^3)	320000 (19000-807000)	322000 (24000-531000)	**0.032**
C-reactive protein (mg/L)	53.4 (0.21-228)	36.7 (0-346)	**<0.001**
Procalcitonin (ug/L)	0.52 (0-24)	1.7 (0.650-138)	**<0.001**

No significant differences were found in age, duration of vomiting, frequency of vomiting, duration of diarrhea, or frequency of diarrhea among the patients. In patients who developed sepsis, all of the neutrophil, hemoglobin, platelet, CRP, and PCT values were found to be statistically significantly higher than in patients who did not develop sepsis (Table 4).

In patients who developed sepsis, the incidence of vomiting, fever, and hyponatremic dehydration was higher compared to those who did not develop sepsis (p= 0.003, p< 0.001, p= 0.004) (Table 5).

Table 5. Clinical results of patients who developed sepsis

		Sepsis Absent		Sepsis Present		
		n	%	n	%	p
Sex	Male	377	54.88	126	53.16	0.208
	Female	310	45.12	111	46.84	
Vomiting	Absent	206	30.03	96	40.51	**0.003**
	Present	480	69.97	141	59.49	
Diarrhea	Absent	4	.58	1	.42	0.784
	Present	683	99.42	236	99.58	
Fever	Absent	360	52.48	54	22.78	**<0.001**
	Present	326	47.52	183	77.22	
Abdominal pain	Absent	629	91.56	222	93.67	0.298
	Present	58	8.44	15	6.33	
Fatigue	Absent	664	96.65	230	97.05	0.768
	Present	23	3.35	7	2.95	
Restlessness	Absent	674	98.11	234	98.73	0.524
	Present	13	1.89	3	1.27	
Rash	Absent	675	98.25	232	97.89	0.720
	Present	12	1.75	5	2.11	
Degree of dehydratation	Mild	615	89.52	207	87.34	0.322
	Moderate	69	10.04	27	11.39	
	Severe	3	.44	3	1.27	
Character of dehydratation	Hyponatremic	117	17.03	64	27.00	**0.004**
	Isonatremic	536	78.02	164	69.20	
	Hypernatremic	34	4.95	9	3.80	

In 32 of the 237 (9.72%) patients suspected of sepsis, bacterial growth was detected in blood cultures, with the most common pathogen being *Klebsiella pneumoniae*, followed by *Staphylococcus hominis, Staphylococcus aureus, and E. coli*.

In a multivariate regression analysis of laboratory values in patients with sepsis, PCT (p< 0.001, R^2: 0.17), CRP (p= 0.024, R^2: 0.17), neutrophil (p< 0.001, R^2: 0.17), and hemoglobin (p< 0.001, R^2: 0.17) values were found to be significant predictors of sepsis. When ROC analysis was performed between the groups with and without sepsis using parameters with significant differences, the two best parameters were found to be CRP and PCT. The area under the curve for the CRP parameter was 0.661, and the cutoff value was determined as 21.34. With the determined cutoff value, sensitivity was found to be 54.04%, and specificity was 71.03%. The area under the curve for the PCT parameter was 0.694, and the cutoff value was determined as 81.97. With the determined cutoff value, sensitivity was found to be 60.98%, and specificity was 72.64% (Figure 2) (Table 6).

When the treatments administered to the patients were examined, all patients received intravenous fluid therapy, 306 (33.1%) patients received antibiotic therapy, and 238 (25.8%) patients received probiotic therapy.

When the patients who received antibiotic treatment were examined, 233 (76.1%) were treated with ceftriaxone, and 26 (8.5%) were treated with ampicillin. Twenty-four (7.9%) patients received multiple antibiotic treatments.

When the length of hospital stay was compared with the administration of probiotic and antibiotic therapy, statistically significant differences were found (p= 0.027, p> 0.001). Patients who required probiotic and antibiotic therapy had longer hospital stays compared to those who did not. Six patients were admitted to the Pediatric Intensive Care Unit due to septic shock, and two patients were admitted to the Pediatric Surgery Clinic due to intussusception and ileus. All transferred patients were discharged with full recovery.

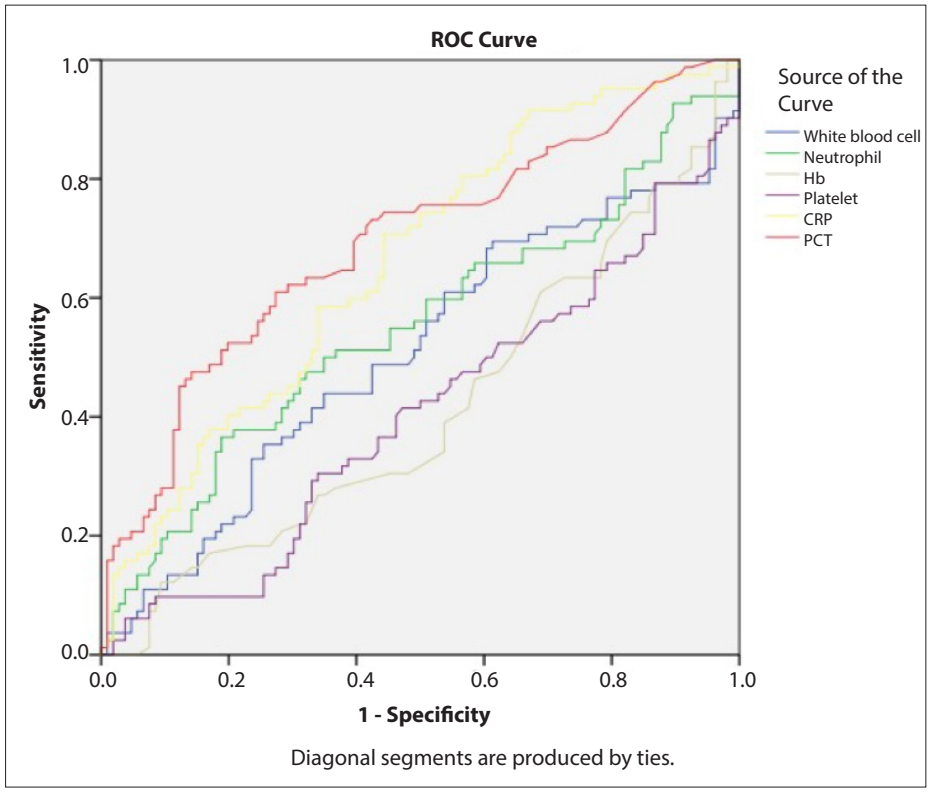

Figure 2. ROC analysis.

Table 6. Cut-off values of CRP and PCT

	Cut-off	Youden index J	Sensitivity (95% CI)	Specifity (95% CI)	+LR (95% CI)	-LR (95% CI)
CRP (mg/L)	>21.34	0.250	54.04 (47.4-60.5)	71.03 (67.5-74.7)	1.87 (1.6-2.2)	0.65 (0.6-0.7)
PCT (ug/L)	>0.73	0.332	60.98 (49.6-71.6)	72.64 (63.1-80.9)	2.23 (1.6-3.2)	0.54 (0.4-0.7)

CI: Confidence interval, CRP: C-reactive protein, PCT: Procalcitonin.

Discussion

AGE is one of the leading causes of mortality and morbidity in children under five years of age in developing countries, and it ranks second among the causes of death in this age group (2).

Studies have shown that AGE is most common in children aged 0-48 months, with a prevalence of 60-86% (9). In our study, mean age of the patients was 27.82 ± 31.55 months, and consistent with the literature, it was most common in the 0-24 month age group (63.5%). In studies conducted in our country, no relationship has been found between sex and hospitalization due to gastroenteritis, and no statistically significant difference was observed in our study (10,11).

In the literature, the rate of identification of the causative agent of AGE varies between 30% and 65%. In a study by Olesen et al., the rate of identification of the causative agent in patients presenting with diarrhea was 54% (12). When looking at patients followed up for acute diarrhea in the first five years of life, rotavirus is the most common cause of diarrhea in children under five years of age, and its incidence decreases with age. It has been reported that 40% of AGEs are caused by rotaviruses and 30% by other viruses (norovirus, adenovirus) (11). In our study, the cause of diarrhea was identified in 58.2% of patients, and viral agents were the most common cause, accounting for 49.6% of cases. The most common viral agent was rotavirus, which is consistent with the literature.

Rotavirus epidemics generally occur between late fall and mid-spring in regions with temperate climates (12). Giaquinto et al. have reported that AGE associated with rotavirus infection is most commonly seen during the winter months (13). In our country, various studies have shown that the peak period of the disease occurs during similar times, between January and March (14-17). In our study, however, unlike the literature, the incidence of rotavirus and other viral agents was found to be higher in August. While multiple etiological agents may coexist in gastroenteritis, virus-virus coinfection is more commonly observed (18). In our study, rotavirus and adenovirus coinfection was observed in 0.10% of the cases. Bacterial agents are less common than viral agents but are more prevalent in countries with temperate climates and during the summer months. In the studies by Olesen et al., *Salmonella* was detected in 5% of patients, enterohemorrhagic *E. coli* (STEC) in 3%, enteropathogenic *E. coli* (EPEC) in 2%, enteroaggregative *E. coli* (EAggEC) in 2%, enteroinvasive *E. coli* (EIEC) in 2%, and *Campylobacter* spp. in 4% of patients. (12). In studies conducted in our country, *Salmonella* species were found in 0.5-5% of cases, and *Shigella* species in 0-9.8% of cases (19). In our study, bacterial pathogens were detected in 6% of the 170 patients, with *Salmonella* accounting for 4.1% and *Campylobacter* for 1.1% of the bacterial pathogens. Children are more prone to dehydration than adults when gastroenteritis develops due to their higher basal fluid and electrolyte requirements (18). In a study by Salim et al., 91.4% of hospitalized patients under the age of five with rotavirus infection had mild to moderate dehydration, 3.4% had severe dehydration, and 5.2% had no dehydration (19). In our study, mild dehydration was detected in 88.9% of patients, moderate dehydration in 10.4%, and severe dehydration in 0.7%.

The literature indicates that probiotics are beneficial in AGE, and there are studies suggesting that probiotic use may shorten the duration of diarrhea (20). In our study, the duration of diarrhea was found to be longer in patients receiving probiotic treatment. This was thought to be due to the fact that probiotics were only administered to patients with prolonged diarrhea.

In a study, the duration of diarrhea in hospitalized patients was found to be 3.4 ± 0.1 days in viral cases and 6.1 ± 0.4 days in bacterial cases (21). In the same study, the daily frequency of diarrhea was found to be 3.8 ± 0.1 times in viral cases and 10.4 ± 0.5 times in bacterial cases (21). In another study conducted in our country, it was reported that the number of diarrhea episodes per day (average 8.7/day) and the number of days with diarrhea (average 3.5 days) were statistically significantly longer in patients with rotavirus and adenovirus detected in stool compared to those without viral causes. In the same study, it was found that the number of diarrhea episodes per day and the number of days with diarrhea were lower in cases with parasites compared to those with non-parasitic causes (11). In our study, the duration of diarrhea in hospitalized patients was 3.1 ± 2.1 days for viral causes and 2.6 ± 2.3 days for bacterial causes; the frequency of diarrhea was 8 ± 3.9 times for viral causes and 3 ± 2.8 times for bacterial causes. In patients with parasitic causes, the duration of diarrhea was shorter compared to those with non-parasitic causes.

Wiegering and colleagues reported the duration of vomiting associated with viral causes as 2.5 ± 0.1 days and with bacterial causes as 0.9 ± 0.3 days in their study. In the same study, daily vomiting frequency was reported as 2.6 ± 0.2 times for viral causes and 1 ± 0.4 times for bacterial causes (21). In our study, similar to the literature, vomiting duration associated with viral pathogens was found to be 3.1 ± 1.7 days, and vomiting duration associated with bacterial causes was 1.4 ± 0.9 days. The number of vomiting episodes was 6.7 ± 4.4 times for viral causes and 1 ± 0.2 times for bacterial causes.

In a study investigating extraintestinal complications of rotavirus, the incidence of bacteremia was found to be 2.83% (7). In a study by Gözmen and colleagues, which examined 376 patients with rotavirus gastroenteritis, blood cultures were taken in cases of fever lasting longer than 48 hours or recurrent fever, resulting in a 0.79% rate of gram-negative bacteria and a 0.26% rate of candida growth. The gram-negative bacteria isolated were *E. faecalis*, *Klebsiella*, and *S. aureus* (22). In our study, 509

patients (55%) had fever at the time of hospital admission. Of these patients, 142 (59.9%) had refractory fever, and 35 (14.7%) had fever lasting longer than 48 hours. In our study, sepsis developed in 25.6% (237 patients) of patients after AGE. Consistent with the literature, the incidence of sepsis was found to be higher in patients with persistent fever or fever lasting longer than 48 hours. In a study by Scheier et al., *Acinetobacter* species were isolated in patients with leukocytosis and *Klebsiella pneumoniae* in patients with leukopenia in rotavirus-associated sepsis (5). In our study, 32 (9.72%) of the 237 patients who developed sepsis had a positive blood culture, with *K. pneumoniae* being the most common pathogen.

In studies conducted in children, parameters such as CRP, PCT, leukocyte count, and erythrocyte sedimentation rate have been found to be statistically significant in predicting sepsis. Studies have shown that PCT is a better marker than other parameters (23,24). In a study including children hospitalized for diarrhea, the sensitivity of CRP and PCT was found to be 89% and 79%, respectively, and their specificity was 61% and 87%, respectively (25). In our study, ROC and regression analyses revealed that CRP and PCT were the best predictive parameters for sepsis, with sensitivity rates of 54.0% and 60.9%, and specificity rates of 71.0% and 72.6%, respectively. Consistent with the literature, platelet, neutrophil, and leukocyte values were found to have low diagnostic value, while CRP and PCT were found to have significant diagnostic value. In our study, PCT was found to be a better diagnostic marker than CRP in sepsis. The lower sensitivity and specificity compared to the literature were thought to be due to the wider age range in our study.

Conclusion

In this study, which examined the demographic characteristics, clinical and laboratory results, disease agents, complications, and treatments of patients diagnosed with AGE, the data obtained were found to be consistent with the literature.

It should be noted that careful attention should be paid to the development of sepsis in patients with AGE, and that the timely and appropriate use of acute phase reactors such as CRP and procalcitonin can help predict the development of sepsis in advance.

Ethics Committe Approval: This study has been approved by the Clinical Research Ethics Committee of Şişli Hamidiye Etfal Training and Research Hospital, Health Sciences University (Decision no: 1224, Date: 16.04.2019).

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