



Online ISSN (2789-3219)

Research Article

Viral Etiology and its Association with Demographics and Clinical Characteristics in Children Hospitalized for Watery DiarrheaMushriq Abdullah Hussein* , Nabeeha Najatee Akram 

Department of Pediatrics, College of Medicine, Mustansiriyah University, Baghdad, Iraq

Received: 10 January 2025; Revised: 22 February 2025; Accepted: 24 February 2025

Abstract

Background: Acute infectious gastroenteritis (AG) stands for one of the commonest causes of death in children under 5 years of age. **Objective:** To assess the prevalence of viral etiology in children hospitalized for watery diarrhea and identify the relation between patients' characteristics and the underlying viral etiology of AG. **Methods:** A cross-sectional study included children hospitalized with AG who presented with watery diarrhea. Three sets of data were collected: the sociodemographic characteristics (age, gender, residence, type of feeding, method of sterilization, number of family members, and socioeconomic status), the clinical characteristics (duration of illness, frequency of diarrhea per day, presence of vomiting, degree of dehydration, fever, and napkin rash), and the laboratory result (white blood cell count, C-reactive protein, pus on general stool exam, and the type of viral etiology detected in the stool by immunoassay). **Results:** A total of 216 children aged less than 5 years were included, with 170 (78.7%) who were less than 1 year of age. Less than two-thirds of the patients (59%) had identified viral etiology, in which 102 children (47%) had rotavirus in their stool and 26 (12%) adenoviruses were detected. Four sociodemographic factors were significantly related to the viral etiology: age less than 1 year, male sex in adenovirus and female in rotavirus, formula feeding, and socioeconomic status. **Conclusions:** The study highlights an increasing frequency of viral detection in children hospitalized with watery diarrhea, with rotavirus remaining the most identified pathogen, followed by adenovirus.

Keywords: Adenovirus, Children, Gastroenteritis, Rotavirus, Watery diarrhea.

المسببات الفيروسية وارتباطها بالتركيبة السكانية والخصائص السريرية لدى الأطفال المقيمين في المستشفى بسبب الإسهال المائي

الخلاصة

الخلفية: التهاب المعدة والأمعاء المعدني الحاد (AG) هو أحد أكثر أسباب الوفاة شيوعاً لدى الأطفال دون سن 5 سنوات. **الهدف:** تقييم انتشار المسببات الفيروسية لدى الأطفال المصابين بالإسهال المائي في المستشفى وتحديد العلاقة بين خصائص المرضى والمسببات الفيروسية الأساسية لـ AG. **الطرائق:** شملت دراسة مقطعية الأطفال الذين تم إدخالهم إلى المستشفى مع AG والذين يعانون من الإسهال المائي. تم جمع ثلاث مجموعات من البيانات: الخصائص الاجتماعية والديموغرافية (العمر، الجنس، الإقامة، نوع التغذية، طريقة التعقيم، عدد أفراد الأسرة، والحالة الاجتماعية والاقتصادية)، والخصائص السريرية (مدة المرض، وتواتر الإسهال في اليوم، ووجود القيء، ودرجة الجفاف، والحمى، والطفح الجلدي بالمناديل)، والنتيجة المختبرية (تعداد خلايا الدم البيضاء، البروتين التفاعلي C، القيق في فحص البراز العام، ونوع المسببات الفيروسية المكتشفة في البراز عن طريق المقايضة المناعية). **النتائج:** تم تضمين ما مجموعه 216 طفلاً تقل أعمارهم عن 5 سنوات، مع 170 (78.7%) كانوا أقل من عام واحد. حدد أقل من ثلثي المرضى (59%) مسببات فيروسية، حيث كان لدى 102 طفل (47%) فيروس روتا في البراز و 26 (12%) من الفيروسات الغدية. ارتبطت أربعة عوامل اجتماعية ديموغرافية ارتباطاً كبيراً بالمسببات الفيروسية: العمر أقل من عام واحد، وجنس الذكور في الفيروس الغدي والأنثى في فيروس الروتا، والتغذية الصناعية، والحالة الاجتماعية والاقتصادية. **الاستنتاجات:** سلطت الدراسة الضوء على زيادة وتيرة الكشف عن الفيروسات لدى الأطفال الذين يدخلون المستشفى بسبب الإسهال المائي، حيث يظل الفيروس العجلي هو العامل الممرض الأكثر تحديداً، يليه الفيروس الغدي.

* **Corresponding author:** Mushriq A. Hussein, Department of Pediatrics, College of Medicine, Mustansiriyah University, Baghdad, Iraq; Email: mushriq.abdullah@uomustansiriyah.edu.iq

Article citation: Hussein MA, Akram NN. Viral Etiology and its Association with Demographics and Clinical Characteristics in Children Hospitalized for Watery Diarrhea. *Al-Rafidain J Med Sci.* 2025;8(1):148-153. doi: <https://doi.org/10.54133/ajms.v8i1.1700>

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**INTRODUCTION**

Acute infectious gastroenteritis (AG) represents one of the commonest causes of death in children under 5 years of age, with increasing mortalities documented in developing countries [1]. The World Health Organization (WHO) declared it as an inevitable experience in almost every child during the first five years of life [2]. The prevalence of AG in Iraqi children is probably underreported, especially in cases with viral etiology as a result of the lack of widespread use of confirmatory tests [3]. However, it's well known that viruses are the culminating cause in the

majority, and rotavirus lies at the top of the list, while astrovirus and adenovirus come next in frequency [4]. Other viruses reported in children include norovirus, parechovirus A, sapovirus, Aichi virus, and bocavirus [5–8]. The viral profile of AG varies with season [9] and geography. The seasonal trend had been confirmed with increasing cases reported during the cold season, with rotavirus infection peaks in April while adenovirus and astrovirus peak in the last 2 months of the year [9]. In addition to the season, several risk factors had been linked to viral gastroenteritis, especially caused by rotavirus, including not receiving the Rota vaccine, female

gender, rural residency, and lack of breastfeeding [10]. Hospitalization from rotavirus was linked to low birth weight, daycare centers, maternal age less than 25 years, and maternal education of less than a high school [10]. Identifying the risk factors of viral gastroenteritis is fundamental, as negative health consequences is related to acute gastroenteritis in pediatric patients, as in addition to increasing the death rate to more than 9 folds [11], it increases the risk of impaired linear growth as compared to unaffected children [12]. So, recognizing risk groups, including feeding behaviors that place a child at increased risk of viral gastroenteritis, may allow the development of targeted prevention strategies [13]. This study aims at assessing the prevalence of viral etiology in children hospitalized for watery diarrhea and to identify the association of the patient's demographic and clinical characteristics with the underlying viral etiology of acute gastroenteritis.

METHODS

Study design and setting

A cross-sectional study included children hospitalized with acute gastroenteritis who presented with watery diarrhea to Central Child Teaching Hospital for a 6-month period from 1st October 2023 to 31 March 2024. The ethical committee at the Department of Pediatrics, College of Medicine, approved the study with approval no. 9/2024.

Inclusion criteria

Patients were included in the study after matching the following inclusion criteria: patients aged within a range of 2 months to 5 years and presentation with watery diarrhea.

Exclusion criteria

The exclusion criteria include children with underlying chronic illness, including chronic diarrhea, immunodeficiency, receiving chemotherapy, those presenting with bloody diarrhea, and parents who refused to participate in the study.

Outcome measurements

For all patients included in the study, three sets of data were collected. First, the sociodemographic characteristics (age, gender, residence, type of feeding, method of sterilization, number of family members, and socioeconomic status). Secondly, the clinical characteristics (duration of illness, frequency of diarrhea per day, presence of vomiting, degree of dehydration, fever, napkin rash). Third, the laboratory result (white blood cell count WBC, C-reactive protein, pus on general stool exam GSE, the type of viral etiology detected in the stool). Stool testing for rotavirus, adenovirus, and astrovirus was done by using Certest®: a one-step-colored chromatographic immunoassay that contains 3 strips for simultaneous

detection of these three viruses' antigens in fresh stool samples. The stool samples were collected in sterile containers and examined immediately. A micropipette is used to collect 125 µL of liquid stool in the collection tube, then the stool sample from the collecting tube is added to the testing card, and the result is read after 10 minutes. The sample size was determined according to the following formula: $n = Z^2 P(1-P)/d^2$

Where: n is the sample size, Z is the statistic corresponding to the level of confidence, P is expected prevalence, and d is precision. According to previous studies, the prevalence of viral enteritis among Iraqi children was found to be about 18%. The sample size is $N = (1.96)^2 (0.18) (1-0.18) / (0.05)^2 = 226$.

However, during the study period, we did manage to recruit only 216 participants into the study.

Ethical consideration

The Ethical Committee at the Department of Pediatrics, College of Medicine approved the study with approval no. 9/2024.

Statistical analysis

Statistical analyses were performed by using SPSS software version 25.0 (SPSS, Chicago). Continuous data was presented as mean and standard deviation and analyzed using an analysis of variance (ANOVA) test. Categorical variables were expressed as numbers and percentages and analyzed with the Chi-square test. A p-value of less than 0.05 was considered to indicate a statistically significant difference.

RESULTS

A total of 216 children were included in the study, with a majority of 170 (78.7%) being less than 1 year of age. Males outnumbered females with a male-to-female ratio of 1.16:1. Most studied patients reside in urban areas (64.81%) and come from families with low socioeconomic status (61.11%). The type of feeding was exclusive bottle feeding in 146 children (67.59%), and 162(75%) of included families practice improper methods of sterilization of the feeding bottle, as seen in Table 1. Most of the patients studied had illness durations ranging from 1 to 5 days and a frequency of bowel motions of 5-10 times per day. The presence of fever, vomiting, moderate dehydration, and napkin rash characterizes most of the patients. On laboratory testing, a trend of absence of pus in the stool, negative CRP, and normal WBC count was reported, as seen in Table 2. When testing the stool for viral etiology, less than two-thirds of the patients (59%) had identified viral etiology, in which 102 children (47%) had rotavirus in their stool and 26 children (12%) had adenovirus detected. Astrovirus was not detected in any stool sample, and in all the remaining 88 patients (41%), no viruses were detected in the stool sample, as demonstrated in Figure 1. Four sociodemographic factors were significantly related to the viral etiology: age less than 1 year ($p = 0.024$),

male sex in adenovirus and female in rotavirus ($p=0.012$), formula feeding ($p=0.01$), and socioeconomic status ($p<0.001$). All other factors were insignificantly related to the viral etiology of gastroenteritis, as seen in Table 3.

Table 1: Sociodemographic of studied children with acute gastroenteritis (n=216)

Variables	n(%)
Age (year)	
≤1	170(78.7)
>1	46(21.3)
Gender	
Male	116(53.7)
Female	100(46.3)
Residence	
Urban	140(64.81)
Rural	76(35.19)
Type of feeding	
Breast	40(18.52)
Formula	146(67.59)
Mixed	24(11.11)
Table food	6(2.78)
Sterilization	
Proper	54(25)
Improper	162(75)
Family members	
1-4	74(34.26)
5-8	66(30.56)
>8	76(35.19)
Family history of diarrhea	
No	166(76.85)
Yes	50(23.15)
Socioeconomic status	
Low	132(61.11)
Medium	64(29.63)
High	20(9.26)

Table 2: Clinical and laboratory characteristics of children with acute gastroenteritis (n=216)

Variables	n(%)
Illness duration (day)	
1-5	170(78.7)
>5	46(21.3)
Frequency of bowel motion	
5-10	154(71.3)
11-15	46(21.3)
>15	16(7.41)
Pus in GSE	
Nil	158(73.15)
Positive	58(26.85)
CRP	
Negative	174(80.56)
Positive	42(19.44)
WBC count	
≤15	126(58.33)
>15	90(41.67)
Vomiting	
No	18(8.33)
Yes	198(91.67)
Degree of dehydration	
Mild	86(39.81)
Moderate	110(50.93)
Severe	20(9.26)
Fever	
Absent	60(27.78)
Present	156(72.22)
Napkin rash	
Absent	70(32.41)
Present	146(67.59)

CRP: C- reactive protein, GSE: general stool examination, WBC: white blood cell.

Rotavirus was significantly associated with vomiting, fever, napkin rash, moderate dehydration, and an

average of 5-10 bowel motions per day. While adenovirus had no napkin rash in all patients. Elevated WBC >15 was significantly related to adenovirus detection in the stool, as seen in Table 4.

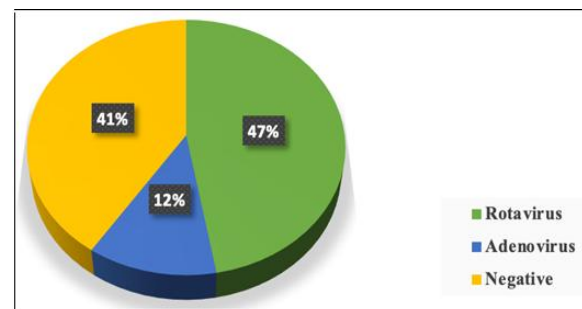


Figure 1: the type of viral infection in children with acute gastroenteritis.

DISCUSSION

The prevalence of viral etiology in hospitalized children with watery diarrhea was 59%, which consisted of only two viruses: rotavirus and adenovirus. The sociodemographic factors that significantly related to the viral etiology are patient's age less than 1 year ($p=0.024$), male sex in adenovirus and female in rotavirus ($p=0.012$), formula feeding ($p=0.01$), and socioeconomic status ($p<0.001$). Rotavirus was significantly associated with age less than 1 year, female gender, formula feeding, and coming from a low socioeconomic family. On the other hand, adenovirus is associated with male gender and high socioeconomic status. Both the adeno and rotavirus groups had a significantly low frequency of bowel motion per day ($p<0.012$) and duration of illness ($p=0.012$). In the current study, the prevalence of enteric viruses detected in the stool sample of children hospitalized with watery diarrhea is 59%. This is higher than previously reported by multiple studies conducted in Iraq [9], Europe, and India [14,15]. The highest previous frequency in Iraq was reported in Samawah children, in which 56.7 percent of stool samples collected from children with acute diarrhea contained at least one enteric virus. In Europe, 35% to 40% prevalence rates have been reported, with 43.6% in India and 53.7% in Africa [12–14]. The increasing detection of enteric viruses in children with gastroenteritis may be attributed to several factors, including advancements in diagnostic techniques, improved surveillance, and epidemiological changes [16,17]. In addition, multiple countries, including the developing ones, applied strategies to control bacterial and parasitic causes of gastroenteritis, resulting in decreased prevalence, but no parallel decrease was documented in the viral etiology of gastroenteritis [17,18]. Rotavirus was the leading cause of watery diarrhea in the sample studied, and adenovirus came next as the second most common viral cause of watery diarrhea, and this matches previous studies from different parts of the world [19]. On the other hand, astrovirus were not detected in any stool sample from admitted children, and no co-infections were detected.

Table 3: the association of demographic characteristics with viral infection

Variables	Negative (n=88)	Rotavirus (n=102)	Adenovirus (n=26)	p-value
<i>Age (year)</i>				
≤1	58(65.91)	88(86.27)	48(92.31)	0.024
>1	30(34.09)	14(13.73)	4(7.69)	
<i>Sex</i>				
Male	112(63.64)	40(39.22)	20(76.92)	0.012
Female	64(36.36)	62(60.78)	6(23.08)	
<i>Residence</i>				
Urban	74(84.09)	46(45.1%)	20(76.92)	<0.001
Rural	14(15.91)	56(54.9)	6(23.08)	
<i>Type of feeding</i>				
Breast	26(29.55)	10(9.8)	4(15.38)	0.010
Formula	44(50)	86(84.31)	16(61.54)	
Mixed	12(13.64)	6(5.88)	6(23.08)	
Table	6(6.82)	0(0.0)	0(0.0)	
<i>Sterilization</i>				
Proper	18(20.45)	24(23.53)	12(46.15)	0.162
Improper	70(97.55)	78(76.47)	14(61.54)	
<i>Number of Family members</i>				
1-4	30(34.09)	26(25.49)	18(69.23)	0.065
5-8	30(34.09)	34(33.33)	2(7.69)	
>8	28(31.82)	42(41.18)	6(23.08)	
<i>Family history of diarrhea</i>				
No	60(68.18)	80(78.43)	26(100)	0.054
Yes	28(31.82)	22(21.57)	0(0.0)	
<i>Socioeconomic status</i>				
Low	62(70.45)	64(62.75)	6(23.08)	<0.001
Medium	24(27.27)	38(37.25)	2(7.69)	
High	2(2.27)	0(0.0)	18(69.23)	

Table 4: the Association of clinical and laboratory characteristics with viral etiology

Variables	Negative (n=88)	Rotavirus (n=102)	Adenovirus (n=26)	p-value
<i>Illness duration, (day)</i>				
1-5	58(65.91)	86(84.31)	26(100)	0.012
>5	30(34.09)	16(15.69)	0(0.0)	
<i>Bowel motion</i>				
5-10	70(79.55)	62(60.78)	22(82.62)	<0.001
11-15	6(6.82)	40(39.22)	0(0.0)	
>15	12(13.64)	0(0.0)	4(7.69)	
<i>Pus in GSE</i>				
Nil	64(72.73)	68(66.67)	26(100)	0.053
Positive	24(27.27)	34(33.33)	0(0.0)	
<i>CRP</i>				
Negative	68(77.27)	80(78.43)	26(100)	0.166
Positive	20(22.73)	22(21.57)	0(0.0)	
<i>WBC count</i>				
≤15	46(52.27)	80(78.43)	0(0.0)	<0.001
>15	42(47.73)	22(21.57)	26(100)	
<i>Vomiting</i>				
No	12(13.64)	0(0.0)	6(23.08)	0.007
Yes	38(86.36)	102(100)	20(76.92)	
<i>Degree of dehydration</i>				
Mild	44(50)	22(21.57)	20(76.92)	0.002
Moderate	36(40.91)	68(66.67)	6(23.08)	
Severe	8(9.09)	12(11.76)	0(0.0)	
<i>Fever</i>				
Absent	34(38.64)	6(5.88)	20(76.92)	<0.001
Present	54(61.36)	96(94.12)	6(23.08)	
<i>Napkin rash</i>				
Absent	22(25)	22(21.57)	26(100)	<0.001
Present	66(75)	80(78.43)	0(0.0)	

CRP: C- reactive protein, GSE: general stool examination, WBC: white blood cell.

The under detection of astrovirus could be attributed to the low sensitivity of immunoassays; some immunoassays might exhibit cross-reactivity with other viral or bacterial pathogens in the stool [20]. This can obscure the presence of astrovirus or result in ambiguous results. Studies proved that immunoassays have significantly lower sensitivity for astrovirus, leading to underreporting compared to molecular methods [21,22]. The frequency of rotavirus detection in the current study is 47%, which represents the

highest frequency reported in an Iraqi study. Previous studies reported a prevalence range from 18% to 46% depending on the study design and settings [9,23–25]. The prevalence reported in studies published during the last five years [26–29] is about double the previously reported 10 years ago, which clearly indicates an increase in infections in children below 5 years of age, which could be attributed to the effect of the COVID-19 era [30]. It has been 5 years since the pandemic, and there was a dramatic decrease in

vaccination coverage with a resultant increased incidence of the disease in children under 5 years of age who were delivered after the pandemic [30–32]. The younger age was linked to rotavirus infection in post-COVID-19 [33,34], this matched the result in our study as more than two of the children with rotavirus were aged less than one year with a statistical significance ($p=0.024$). Regarding gender, there was a significant gender disparity in viral etiology causing watery diarrhea in the current study ($p=0.012$). The predominance of females in rotavirus cases and males in adenovirus cases may reflect underlying biological or behavioral differences. For instance, exposure patterns influenced by caregiving roles might contribute to these disparities [35]. Statistical significance underscores the importance of considering gender in designing prevention and treatment strategies. The role of gender in the viral etiology of gastroenteritis is a conflict issue, as some studies have not recognized gender as a significant factor for human adenovirus infection, while others identified male children to be more affected than females [36,37]. The predominance of formula feeding in children with viral etiology of gastroenteritis with a significant P value = 0.01 can be attributed to several factors, including immune protection, gut microbiota composition, and exposure pathways. Breastfeeding is proven to be protective against viral gastroenteritis due to the abundance of maternal antibodies and other bioactive components in breast milk [38,39]. Formula feeding is linked to a different gut microbiota composition compared to breastfeeding, since breastfeeding promotes the growth of beneficial bacteria, such as *Bifidobacterium* and *Lactobacillus*, which are known to enhance gut immunity and create an environment less favorable for rotavirus replication [40]. In contrast, formula feeding is linked to a more diverse but less protective microbiota, which may increase susceptibility to infections [40–42]. The clinical characteristics analyzed indicate that children infected with adenovirus and rotavirus had a significantly shorter duration of illness than children in whom no viral etiology was detected ($p=0.012$). This goes with the self-limited nature of the viral etiology of gastroenteritis and may indicate that cases with negative results for viral etiology are, in fact, misdiagnosed as viral based on clinical judgment while they are caused by bacterial or parasitic causes [43]. A constellation of clinical and laboratory characteristics consists of absent fever or napkin rash, presence of mild-moderate dehydration, vomiting, and 5–10 bowel motions per day together with a WBC count of $>15 \times 10^9$ indicative of adenovirus etiology of watery diarrhea. Children with rotavirus are presented similarly except for a tendency to have a lower WBC count and showing a napkin rash; this goes with previously published studies [44,45].

Limitations of the study

The study was conducted in hospital settings, so only admitted children were included. This will carry a chance of missing cases with not severe presentations

that do not need hospitalization [46]. Another limitation is that the vaccination status against rotavirus and the seasonal variation was not included in the study data, both of which represent a major determinant for viral gastroenteritis in children [47]. Future large-scale multicentric studies conducted in a community setting are needed to validate the clinical importance of our results, contributing to identifying diagnostic clinical and laboratory characteristics that can improve patient management.

Conclusion

The frequency of detecting viral etiology in children hospitalized with watery diarrhea is increasing. Rotavirus is still the predominant virus detected, and adenovirus comes next frequently. A constellation of clinical characteristics and laboratory findings can help to suggest the underlying viral etiology in children with watery diarrhea.

Conflict of interests

No conflict of interest was declared by the authors.

Funding source

The authors did not receive any source of funds.

Data sharing statement

Supplementary data can be shared with the corresponding author upon reasonable request.

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