

# An Association of Iron Deficiency Anemia with Acute Gastroenteritis among Children: A cross-sectional study

Sana Nafis<sup>1</sup>, Rabbia Shaheen<sup>2</sup>, Sohail Akhtar<sup>3</sup>, Hameed Ullah<sup>4</sup>

<sup>1</sup>Senior Registrar, Peshawar Medical College, Peshawar, Pakistan

<sup>2</sup>Senior Registrar, Mercy Teaching Hospital, Peshawar, Pakistan

<sup>3</sup>Assistant Professor, Pak International Medical College, Peshawar, Pakistan

<sup>4</sup>Assistant Professor Paeds, Kuwait Teaching Hospital Peshawar, Pakistan

## Correspondence:

Dr Sana Nafis

Email [sananafis@hotmail.com](mailto:sananafis@hotmail.com)

## Abstract

**Background:** Iron deficiency anemia (IDA) and acute gastroenteritis (AGE) are prevalent conditions among children globally, affecting health outcomes significantly.

**Objective:** To determine the association between iron deficiency anemia and acute gastroenteritis among children through a cross-sectional study.

**Material and Methods:** In this six-month cross-sectional study, a total of 180 children presenting with symptoms of acute gastroenteritis (AGE) at Al Syed Children Hospital, Mardan, KP, Pakistan were included. Associations between IDA and various factors were analyzed using chi-square tests, with a significance level set at  $p < 0.05$ .

**Results:** Significant associations were observed across several parameters among acute gastroenteritis (AGE) and iron deficiency anemia (IDA) patients. The majority of children with AGE were aged less than 2 years (60.8%), while children with IDA showed a similar distribution (59.8%), with a statistically significant p-value of 0.03. Male children were more prevalent in both AGE (69.7%), and IDA (54.7%) groups, though gender distribution did not show statistical significance ( $p=0.98$ ). Family income levels below 20,000 BDT were more common among children with AGE (63.5%), and IDA (62.4%), although not statistically significant ( $p=0.16$ ). Cow's milk ingestion was significantly associated with IDA (48.7%) compared to AGE (80%), with a p-value of 0.001. Furthermore, children with moderate malnutrition exhibited a significantly higher prevalence of IDA (50.4%) compared to AGE (82.2%), also with a p-value of 0.001.

**Conclusion:** Iron deficiency anemia (IDA) is prevalent among children with acute gastroenteritis (AGE), with notable contributing factors including age below 2 years, cow's milk ingestion, and moderate malnutrition.

**Keywords:** Iron deficiency anemia, acute gastroenteritis, children, cow's milk ingestion, malnutrition

Cite this article: Nafis S, Shaheen R, Akhtar S, Ullah H.I. An Association of Iron Deficiency Anemia with Acute Gastroenteritis Among children; across sectional study. BMC J Med Sci. 2024; 5(2): 95-101. <https://doi.org/10.70905/bmci.05.02.0429>

## Introduction

Anemia is a major public health issue among children, with a global prevalence of 43% among those aged 6 to 59 months<sup>1</sup>. Anemia affects almost two-thirds of children in Southeast Asia, with iron deficiency accounting for half of the cases. In iron deficiency anemia (IDA), hemoglobin synthesis in the bone marrow is reduced, resulting in low hemoglobin levels in the

blood. Iron deficiency is diagnosed in children aged 6 months to 5 years with serum ferritin levels  $< 7$  ng/ml and hemoglobin levels  $< 11$ g/dl<sup>2</sup>.

The prevalence of IDA in underdeveloped countries ranges from 50 to 60% and 10 to 20%, respectively<sup>3</sup>. The frequency of child anemia is estimated to be around 52.10%. Iron deficiency (ID) is widely recognized as the

Authorship Contribution: <sup>1,4</sup>Substantial contributions to the conception or design of the work; or the acquisition, Data analysis, Literature review, <sup>2</sup>Drafting the work or revising it critically for important intellectual content, <sup>3,4</sup>Final approval of the version to be published, Topic Selection & Supervision

Funding Source: none

Conflict of Interest: none

Received: May 30, 2024

Accepted: Sept,26, 2024

Published: Dec30, 2024

leading cause of anemia and the most common form of micronutrient malnutrition<sup>4</sup>. Children under 5 years old are especially vulnerable to anemia and ID due to increased iron requirements during growth, inadequate iron intake from supplemental foods, and recurrent infections<sup>5,6</sup>.

IDA is linked to impaired motor development and cognitive performance, as well as weariness, sleep difficulty, irritability, and poor memory and academic performance. Our bodies require an appropriate balance of iron, and both excess and lack can be hazardous. Thus, additional population-based data on iron status in children is needed to establish an effective nutritional program to prevent iron insufficiency<sup>7,8</sup>. Acute gastroenteritis (AGE) is a severe public health concern and a common childhood infection that is associated with high morbidity and mortality. Childhood diarrhea creates a significant burden, killing 525,000 children under the age of five, accounting for about 8% of all child deaths worldwide<sup>9,10</sup>.

Numerous investigations on children indicated that episodes of diarrhea were associated with an increased likelihood of iron deficiency anemia (IDA). Another study revealed that anemia was a significant contributor to diarrheal disease. This constitutes a reciprocal interaction<sup>11,12</sup>. Individual tests commonly used to assess iron status in the body include inherent limitations due to their diminished specificity or sensitivity; therefore, a combination of multiple iron status indicators yields the most accurate evaluation of iron status. A complete blood count indicates diminished hemoglobin levels, whereas serum ferritin represents total body iron stores. The correlation between age and anemia in early childhood has not been thoroughly investigated<sup>13,14</sup>.

The purpose of this study is to investigate the relationship between iron deficiency anemia and acute gastroenteritis in children, considering their high prevalence and possibly overlapping symptoms. Understanding this link could lead to better diagnostic and therapeutic procedures, ultimately improving pediatric healthcare outcomes.

## **Material and Method:**

### **Study Design and Setting:**

This cross-sectional study was conducted at Al Syed

Children's Hospital a pediatric care center, Mardan, Pakistan from February 2023 to December 2023.

### **Study Population:**

The study included children aged 6 months to 5 years who presented with acute gastroenteritis. Children with chronic diseases, other causes of anemia, or those on iron supplementation were excluded from the study. A total of 180 children meeting the inclusion criteria were enrolled.

### **Data Collection Tools:**

The study protocol received approval from the Institutional Review Board (IRB) (NO.\_R/C 022) of Al syed Hospital Mardan. Informed consent was obtained from parents or guardians of participating children before any data collection procedures were initiated. The study adhered strictly to ethical guidelines outlined in the Declaration of Helsinki, ensuring confidentiality, voluntary participation, and respect for participants' rights throughout the research process.

Data were collected using structured questionnaires administered to parents or guardians. These questionnaires gathered demographic information (age, gender), family socioeconomic status (monthly income, parental education), and clinical history (symptoms, duration). Clinical assessments conducted by healthcare professionals included evaluating hydration status (categorized as no dehydration, some dehydration, or severe dehydration) and conducting physical examinations to assess for pallor and nutritional status (moderate malnutrition, well-nourished). Additionally, blood samples were collected from each participant for laboratory investigations, including measurement of hemoglobin levels to diagnose anemia, serum ferritin levels to assess iron stores, and total iron binding capacity to evaluate iron status.

### **Statistical Analysis:**

Data were analyzed using statistical software, SPSS version 26.0. Descriptive statistics were used to summarize the demographic and clinical characteristics of the study population. Continuous variables were expressed as means  $\pm$  standard deviations, and categorical variables as frequencies and percentages. The association between iron deficiency anemia and acute gastroenteritis was assessed using chi-square tests for categorical variables and t-tests for continuous variables. Logistic regression analysis was performed to

identify independent predictors of iron deficiency anemia among children with acute gastroenteritis. A p-value <0.05 was considered statistically significant.

## Results:

In this study of 180 children with acute gastroenteritis, the majority were aged between 6 months and 1 year (50%), with a mean age of  $17 \pm 0.56$  months. The sample consisted of more males (60%) than females (40%). Most families had a monthly income of less than 20,000 BDT (61.7%), and maternal education levels varied, with 35% having primary education, 31.7% SSC, 20% HSC, and 13.3% university education. Paternal education showed 23.3% with primary, 36.7% SSC, 23.3% HSC, and 16.7% university education. The majority of families were extended (62.5%), and mixed feeding was the predominant mode of feeding (55.8%), while 33.3% of the children had a history of cow's milk ingestion.

Parameter	Number (%)
Age	
6 months - 1 year	90 (50%)
1 - 2 years	63 (35%)
>2 years	27 (15%)
Mean $\pm$ SD (months)	$17 \pm 0.56$
Gender	
Male	108 (60%)
Female	72 (40%)
Monthly Family Income	
<20,000 BDT	111 (61.7%)
>20,000 BDT	69 (38.3%)
Maternal Education	
Primary	63 (35%)
SSC	57 (31.7%)
HSC	36 (20%)
University	24 (13.3%)
Paternal Education	
Primary	42 (23.3%)
SSC	66 (36.7%)
HSC	42 (23.3%)
University	30 (16.7%)
Family Type	
Nuclear	68 (37.5%)
Extended	113 (62.5%)
Mode of Feeding	
EBF	80 (44.2%)
Mixed feeding	100 (55.8%)
Cow's milk ingestion	60 (33.3%)

In children diagnosed with acute gastroenteritis, clinical findings revealed that a significant portion experienced vomiting (78.3%), while fever was also prevalent (45.6%). Other symptoms such as cough (14.4%) and passage of blood in stool (10%) were less common. Hydration status

indicated that a majority of children exhibited some level of dehydration, with 62.8% showing some dehydration and 16.7% severe dehydration, while 20.6% were without dehydration. Physical examination findings showed that a substantial number of children were well nourished (62.2%), with others presenting with moderate malnutrition (37.8%) and pallor (33.3%). These findings underscore the varied clinical presentation and severity of acute gastroenteritis in the studied population.

Clinical Parameter	Number (%)
Symptoms	
Fever	82 (45.6%)
Vomiting	141 (78.3%)
Cough	26 (14.4%)
Passage of blood in stool	18 (10%)
Hydration Status	
No dehydration	37 (20.6%)
Some dehydration	113 (62.8%)
Severe dehydration	30 (16.7%)
Physical Examination	
Pallor	60 (33.3%)
Moderate Malnutrition	68 (37.8%)
Well-nourished	112 (62.2%)

Among the 180 children studied, laboratory findings revealed that a significant majority had anemia, with 65% having hemoglobin levels below 11 g/dl. Serum ferritin levels were below 7 ng/ml in 58.3% of cases, indicating low iron stores, while 41.7% had serum ferritin levels within the normal range of 7-140 ng/ml. Total iron binding capacity was elevated (>450  $\mu$ g/dl) in 58.3% of children, suggesting potential iron deficiency, whereas 41.7% had levels within the normal range (<450  $\mu$ g/dl). These results highlight a high prevalence of anemia and potential iron deficiency among children with acute gastroenteritis in this study.

Lab Parameters	Number (%)
Hemoglobin	
>11 g/dl (normal)	63 (35%)
<11 g/dl (anemia)	117 (65%)
Serum Ferritin Level	
<7 ng/ml	105 (58.3%)
>7 ng/ml (normal: 7-140)	75 (41.7%)
Total Iron Binding Capacity	

>450 µg/dl	105 (58.3%)
<450 µg/dl (normal)	75 (41.7%)

In this study involving 120 children with acute gastroenteritis (AGE) and 117 children with iron deficiency anemia (IDA), several significant associations were observed. Children aged less than 2 years constituted a higher proportion in both AGE (60.8%) and IDA (59.8%) groups compared to older children (>2 years). Gender distribution showed a higher prevalence of males in both AGE (69.7%) and IDA (54.7%) groups. Family income levels below 20,000 BDT were more prevalent among children with AGE (63.5%) and IDA (62.4%), though not statistically significant (p=0.16). Family type (extended vs. nuclear) did not significantly differ in its distribution between AGE and IDA groups (p=0.47). Notably, cow's milk ingestion was significantly associated with a higher.

Prevalence of IDA (48.7%) compared to AGE (80%), with a p-value of 0.001. Similarly, children with moderate malnutrition showed a significantly higher prevalence of IDA (50.4%) compared to AGE (82.2%), also with a p-value of 0.001. These findings underscore the demographic and dietary factors influencing the prevalence of iron deficiency anemia among children with acute gastroenteritis in the studied population.

**Table 4. Association of IDA with different variables**

Variables	Children with AGE (N=120)	Children with IDA (N=117)	p-value
Age			
< 2 years (N=102)	62 (60.8%)	70 (59.8%)	0.03
> 2 years (N=78)	40 (33.3%)	47 (40.2%)	
Gender			
Male (N=108)	43 (69.7%)	64 (54.7%)	0.98
Female (N=72)	27 (56.3%)	53 (45.3%)	
Family Income			
< 20,000 BDT (N=111)	47 (63.5%)	73 (62.4%)	0.16
> 20,000 BDT (N=69)	23 (50%)	44 (37.6%)	
Family Type			
Extended (N=113)	48 (64%)	68 (58.1%)	0.47
Nuclear (N=68)	22 (48.9%)	49 (41.9%)	
Feeding History			
Cow's milk ingestion present (N=60)	32 (80%)	57 (48.7%)	0.001
Cow's milk ingestion absent (N=120)	38 (47.5%)	60 (51.3%)	
Nutritional Status			

Moderate malnutrition (N=68)	37 (82.2%)	59 (50.4%)	0.001
Well Nourished (N=112)	33 (44%)	58 (49.6%)	

The multivariate analysis reveals significant associations between certain variables and the prevalence of acute gastroenteritis (AGE) and iron deficiency anemia (IDA) among children. Age under two years was significantly associated with both conditions (p = 0.03), indicating a higher vulnerability in this age group. Cow's milk ingestion showed a strong association with both AGE and IDA, with children who consumed cow's milk being more affected (p = 0.001). Similarly, moderate malnutrition was significantly linked to these conditions, with a higher proportion of affected children being malnourished (p = 0.001). Other variables, including gender, family income, and family type, did not show statistically significant associations, suggesting their limited impact in this context. These findings highlight the importance of addressing age-specific dietary and nutritional interventions to reduce the burden of AGE and IDA in children.

**Table: 5 Multivariate analysis**

Variable	Children with AGE (N=120)	Children with IDA (N=117)	p-value
Age			
< 2 years (N=102)	62 (60.8%)	70 (59.8%)	0.03
> 2 years (N=78)	40 (33.3%)	47 (40.2%)	
Gender			
Male (N=108)	43 (69.7%)	64 (54.7%)	0.98
Female (N=72)	27 (56.3%)	53 (45.3%)	
Family Income			
< 20,000 BDT (N=111)	47 (63.5%)	73 (62.4%)	0.16
> 20,000 BDT (N=69)	23 (50%)	44 (37.6%)	
Family Type			
Extended (N=113)	48 (64%)	68 (58.1%)	0.47
Nuclear (N=68)	22 (48.9%)	49 (41.9%)	
Feeding History			
Cow's milk ingestion present (N=60)	32 (80%)	57 (48.7%)	0.001
Cow's milk ingestion absent (N=120)	38 (47.5%)	60 (51.3%)	
Nutritional Status			
Moderate malnutrition (N=68)	37 (82.2%)	59 (50.4%)	0.001
Well-nourished (N=112)	33 (44%)	58 (49.6%)	

## Discussion:

Diarrhea and iron deficiency anemia remain frequent health problems around the world, increasing the

financial strain on healthcare systems, particularly in poor nations. IDA has a negative impact on mental health, resulting in poor educational achievement and employment capability, reducing earning potential, and harming the country. In addition, it increases the risk of complications and death from infectious diseases such as AGE<sup>11,12</sup>. In this study, almost two-thirds (65%) of children were anemic (hemoglobin <11 g/dl), and more than half (58.3%) had iron deficiency, which is

similar to another study done by Ranjha AA et al, where 53.0% were anemic. The current study demonstrated that half of the children (50%) were one year old, which was consistent with the findings of Ranjha AA et al.,<sup>13,14</sup> who found that 51% of the infants were under the age of one year<sup>6</sup>. More than half of the children with IDA were under the age of two, which is consistent with the study conducted by Semba RD et al.

In terms of male to female ratio, male children were impacted more (69.7%) than females, which is similar to the study conducted by Ranjha AA et al., whereas Ahmad et al. indicated that the majority of the children were female.<sup>15</sup> The reason for this disparity could be that most cultures do not care for female offspring. High monthly family income is frequently reflected in improved child health since it indirectly prevents children from a variety of infectious disorders including diarrhea<sup>16</sup>.

This study also found that a vast majority of children had family incomes of up to 20,000 BDT (61.7%) per month, which is consistent with the study conducted by Ranjha AA et al. Monthly family income, education, mother's occupation, and family type were all associated with children's health. This survey found that 35% of moms studied up to grade 5, 31.7% studied up to SSC, 20% studied up to HSC, and 13.3% went to university, which is substantially identical to Dagneu et al.'s findings<sup>17,18</sup>.

The role of the extended family structure is particularly crucial because it has been discovered that children from extended families do not receive better care. The current study found that nearly two-thirds (62.5%) of the children lived in an extended family system, with 64% having IDA. Din and Fellows published similar findings, confirming that 63% of children lived in the extended family system.

Our study found that 44.2% of children had a history of EBF, which is consistent with the findings of Hossain M et al. In this study, 78.3% of children vomited, 45.8% had a fever, 14.2% coughed, 10% had blood in their stool,

and 16.7% had severe dehydration. The findings of this study are consistent with previous research on dehydration, fever, and vomiting related to diarrhea.<sup>24</sup> This study found that more than half of the children (58.3%) had reduced Hb, serum ferritin levels, and higher TIBC levels, which is consistent with the findings of Ranjha AA et al<sup>19,20</sup>.

In this study, we discovered that IDA is substantially linked with characteristics such as age under two years, history of cow's milk intake, and moderate malnutrition in children (p values 0.03, 0.001, and 0.001, respectively). However, there is no significant connection between IDA and gender, family income, or family type (p values of 0.98, 0.16, and 0.47, respectively). The study's findings are consistent with previous research conducted by Ranjha AA et al. and Abdel-Rasoul et al<sup>21,22</sup>.

A cross-sectional study of Palestinian refugee toddlers found that having a current bout of fever or diarrhea increased the likelihood of anemia<sup>23,24</sup>. Another longitudinal study showed that anemia is an independent predictor of diarrheal illness. It is also plausible that the relationship is reciprocal, with diarrhea raising the risk of anemia and anemia increasing the risk of diarrhea, similar to the link between vitamin A deficiency and diarrheal illness.<sup>25</sup> Anemia is caused by underlying inflammation, changes in iron homeostasis, poor proliferation of erythroid progenitor cells, a blunted erythropoietin response, and a shorter erythrocyte half-life. Infection-related anemia has been linked to pro-inflammatory cytokines such as IL-1, TNF-a, and IL-6.

## **Conclusion:**

In conclusion, this study highlights the demographic, clinical, and laboratory profiles of children with acute gastroenteritis (AGE) and iron deficiency anemia (IDA). Most participants were under two years old, with common symptoms like fever, vomiting, and dehydration. Laboratory findings revealed a high prevalence of anemia and low ferritin levels, with significant associations between IDA, young age, cow's milk consumption, and moderate malnutrition.

## **Limitation:**

This study has a few limitations as it is a cross-sectional design, single-center setting, and small sample size.

## **Recommendation:**

This study recommends conducting larger, multicenter, and longitudinal research to establish causal relationships between iron deficiency anemia (IDA) and

acute gastroenteritis (AGE) and improve generalizability. Early screening for IDA in children with AGE is crucial to facilitate timely diagnosis and management

#### Conflict of Interest:

All Authors declare that there is no conflict-of-interest  
financial support: N/A

#### References:

1. Aihara M. Infectious disease in Kenya--epidemiological study of diarrhoeal disease in children. *Rinsho byori. The Japanese Journal of Clinical Pathology*. 1997 May 1;45(5):421-6.
2. Zulu G, Sikasunge CS, Welte TM, Simuunza MC, Stelzle D, Schmidt V, Hachangu A, Mutale W, Masuku M, Chembensofu M, da Costa CP. Epidemiology of intestinal helminthiasis with an emphasis on taeniasis in Chipata district of the Eastern province of Zambia. *PLoS Neglected Tropical Diseases*. 2023 Nov 20;17(11):e0011561.
3. Arnipalli S. Iron Deficiency Anemia: Efficacy and Limitations of Nutritional and Comprehensive Mitigation Strategies.
4. Bauhofer AF, Cossa-Moiane IL, Marques SD, Guimarães EL, Munlela BA, Anapakala EM, Chiláule JJ, Cassocera M, Langa JS, Chissaque A, Sambo JA. Intestinal protozoa in hospitalized under-five children with diarrhea in Nampula—a cross-sectional analysis in a low-income setting in northern Mozambique. *BMC Infectious Diseases*. 2021 Dec;21:1-8.
5. Saeed A, Abd H, Sandstrom G. Microbial etiology of acute diarrhea in children under five years of age in Khartoum, Sudan. *Journal of medical microbiology*. 2015 Apr;64(4):432-7.
6. Ghoshal U, Dey A, Ranjan P, Khanduja S, Agarwal V, Ghoshal UC. Identification of opportunistic enteric parasites among immunocompetent patients with diarrhea from Northern India and genetic characterization of *Cryptosporidium* and *Microsporidia*. *Indian journal of medical microbiology*. 2016 Jan 1;34(1):60-6.
7. Samie A, Guerrant RL, Barrett L, Bessong PO, Igumbor EO, Obi CL. Prevalence of intestinal parasitic and bacterial pathogens in diarrhoeal and non-diarrhoeal human stools from Vhembe district, South Africa. *Journal of health, population, and nutrition*. 2009 Dec;27(6):739.
8. Mothiba DP, Khabo-Mmekoa CM, Ngobeni-Nyambi R, Momba MN. Assessing the Occurrence of Host-Specific Faecal Indicator Markers in Water Systems as a Function of Water, Sanitation and Hygiene Practices: A Case Study in Rural Communities of Vhembe District Municipality, South Africa. *Pathogens*. 2023 Dec 23;13(1):16.
9. Badawi MM, SalahEldin MA, Idris AB, Idris EB, Mohamed SG. Diarrheal diseases prevalence among children of Sudan and socio-cultural risks related; systematic review and meta-analysis. *BMC Infectious Diseases*. 2024 Jan 2;24(1):30.
10. Alelign A, Mulualem N, Tekeste Z. Prevalence of intestinal parasitic infections and associated risk factors among patients attending Debarq Primary Hospital, northwest Ethiopia. *Plos one*. 2024 Mar 7;19(3):e0298767.
11. Balachandran N, Cates J, Kambhampati AK, Marconi VC, Whitmire A, Morales E, Brown ST, Lama D, Rodriguez-Barradas MC, Moronez RG, Domiguez GR. Risk factors for acute gastroenteritis among patients hospitalized in 5 Veterans Affairs medical centers, 2016–2019. In *Open Forum Infectious Diseases* 2022 Aug 1 (Vol. 9, No. 8, p. ofac339). Oxford University Press.
12. Friesema IH, De Boer RF, Duizer E, Kortbeek LM, Notermans DW, Norbruis OF, Bezemer DD, van Heerbeek H, van Anel RN, van Enk JG, Fraaij PL. Etiology of acute gastroenteritis in children requiring hospitalization in the Netherlands. *European journal of clinical microbiology & infectious diseases*. 2012 Apr;31:405-15.
13. Karsten C, Baumgarte S, Friedrich AW, Von Eiff C, Becker K, Wosniok W, Ammon A, Bockemühl J, Karch H, Huppertz HI. Incidence and risk factors for community-acquired acute gastroenteritis in north-west Germany in 2004. *European journal of clinical microbiology & infectious diseases*. 2009 Aug;28:935-43.
14. Lugauer S, Überall MA, Schmitt-Grohé S, Stehr K, Cherry JD, Heininger U. Incidence and symptoms of gastroenteritis in hospitalized children out of a cohort of 10271. *Monatsschrift Kinderheilkunde*. 2000 Feb;148:119-22.
15. Spina A, Kerr KG, Cormican M, Barbut F, Eigentler A, Zerva L, Tassios P, Popescu GA, Rafila A, Eerola E, Batista J. Spectrum of enteropathogens detected by the FilmArray GI Panel in a multicentre study of community-acquired gastroenteritis. *Clinical Microbiology and Infection*. 2015 Aug 1;21(8):719-28.
16. Durepaire N, Pradie MP, Ploy MC, Mounier M, Ranger-Rogez S, Martin C, Denis F. Adenoviruses from stool samples in hospital units. Comparison with main pathogens in gastroenteritis (rotavirus, *Campylobacter*, *Salmonella*). *Pathologie-biologie*. 1995 Sep 1;43(7):601-10.
17. Qi X, Alifu X, Chen J, Luo W, Wang J, Yu Y, Zhang R. Descriptive study of foodborne disease using disease monitoring data in Zhejiang Province, China, 2016–2020. *BMC Public Health*. 2022 Sep 28;22(1):1831.
18. Gonzalez-Galan V, Sánchez-Fauquier A, Obando I, Montero V, Fernandez M, Torres MJ, Neth O, Aznar-Martin J. High prevalence of community-acquired norovirus gastroenteritis among hospitalized children: a prospective study. *Clinical microbiology and infection*. 2011 Dec 1;17(12):1895-9.
19. FRÜHWIRTH M, Heininger U, Ehlken B, Petersen G, Laubereau B, MOLL-SCHÜLER IN, Mutz I, Forster J. International variation in disease burden of rotavirus gastroenteritis in children with community-and nosocomially acquired infection. *The Pediatric Infectious Disease Journal*. 2001 Aug 1;20(8):784-91.
20. Karsten C, Baumgarte S, Friedrich AW, Von Eiff C, Becker K, Wosniok W, Ammon A, Bockemühl J, Karch H, Huppertz HI. Incidence and risk factors for community-acquired acute gastroenteritis in north-west Germany in 2004. *European journal of clinical microbiology & infectious diseases*. 2009 Aug;28:935-43.
21. Jansen A, Stark K, Kunkel J, Schreier E, Ignatius R, Liesenfeld O, Werber D, Göbel UB, Zeitz M, Schneider T. Aetiology of community-acquired, acute gastroenteritis in hospitalized adults: a prospective cohort study. *BMC infectious diseases*. 2008 Dec;8:1-7.
22. Mammias IN, Koutsaftiki C, Nika E, Vagia F, Voyatzis A, Spandidos DA, Theodoridou M, Myriokefalitakis N. Prospective study of human norovirus infection in children with acute gastroenteritis in Greece. *Minerva pediatrica*. 2012 Jun 1;64(3):333-9.

23. Jewkes J, Larson HE, Price AB, Sanderson PJ, Davies HA. Etiology of acute diarrhea in adults. *Gut*. 1981 May 1;22(5):388-92.
24. Durepaire N, Pradie MP, Ploy MC, Mounier M, Ranger-Rogez S, Martin C, Denis F. Adenoviruses from stool samples in hospital units. Comparison with main pathogens in gastroenteritis (rotavirus, Campylobacter, Salmonella). *Pathologie-biologie*. 1995 Sep 1;43(7):601-10.
25. Johnstone SL, Erasmus L, Thomas J, Groome MJ, du Plessis NM, Avenant T, de Villiers M, Page NA. Epidemiology and etiology of moderate to severe diarrhea in hospitalized patients  $\geq$  5 years old living with HIV in South Africa, 2018–2021: A case-control analysis. *PLOS Global Public Health*. 2023 Sep 8;3(9):e0001718.