

Predictor Factors for Emergency Department revisiting of children with acute gastroenteritis: case-control study

Factores predictores de reconsulta por Gastroenteritis Aguda en Urgencias Pediátricas: estudio de casos y controles

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Abstract

The objective of this work is to describe risk factors for reconsultation in patients with an acute gastroenteritis diagnosis, identifiable in their first visit to the Emergency Department. **Patients and Method:** Case-control study, including patients aged between 0-16 years who consulted in the Emergency Department (ED) of a tertiary hospital for 4 years. The case is defined as the episode with a gastroenteritis diagnosis that reconsulted within 72 hours. A control was selected for each case, which was the first patient to consult after each case with the same diagnosis and not reconsulted later. Epidemiological and clinical variables, and diagnostic-therapeutic interventions carried out during the first visit were studied. Univariate and multivariate analyses of the reconsultation risk were performed using logistic regression models. **Results:** Gastroenteritis diagnoses accounted for 5.3% of all ED visits. 745 patients (6.2%) reconsulted within 72 hours. Multivariate analysis found association between reconsultation with each year of increasing age (OR 0.94, 95% CI 0.91-0.97), absence of rotavirus vaccination (OR 1.47, 95% CI: 1.11-1.95), no prior assessment in primary care (OR 1.55, 95% CI 1.09-2.19), increased stool output in the last 24 hours (OR 1.06, 95% CI 1.02-1.10), and stool collection in the ED (OR 1.54, 95% CI 1.05-2.24). **Conclusions:** Younger patients with an increased stool output are especially susceptible to return to the ED for consultation. Rotavirus vaccination could reduce reconsultation. None of the diagnostic-therapeutic actions carried out seems to reduce the number of visits to the ED.

Keywords:

Gastroenteritis;
vomiting;
diarrhea;
emergency department;
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Introduction

Acute gastroenteritis (AGE) is a highly prevalent pathology in pediatric age that entails a significant morbidity and mortality rate worldwide¹. This is a frequent diagnosis in the Pediatric Emergency Department (PED)², resulting in a high number of repeated consultations³⁻⁵.

These repeated consultations in the PED are a little-analyzed phenomenon in Spain, where there are no specific studies on AGE. In the study by Mintegui et al⁷, in which the repeated consultations rate reports 13.4%, gastrointestinal pathology is the third cause of repeating consultation and represents 12% of that rate. These data are similar to those of Rivas et al, although in this case, the study was carried out in a population of frequent users of health services (patients with at least 10 visits to the Emergency Department in a year) and the proportion of repeated consultations was 27%⁸.

The only published studies on repeated consultations in pediatric patients with AGE^{9,10} focus on evaluating the association of certain therapeutic measures with repeated consultations. To date, there are no studies evaluating the association with demographic or clinical characteristics.

Given the high rate of visits due to this pathology, it would be useful to know which variables can predict repeated consultation, in order to influence them, anticipate and prevent a possible bad course and thus optimize resources.

Therefore, the objective of this study is to suggest identifiable risk factors in a first visit to the Emergency Department (ED) that may increase the risk of repeating consultation due to the same reason.

Patients and Method

A single-center case-control study was designed, including patients under 16 years of age who consulted in the PED of a tertiary hospital in the *Comunidad de Madrid*, Spain, which see 55,000 emergencies annually. The study period covered 4 years (April 2013-March 2017). The study was approved by the local clinical research and ethics committee.

Population and sample

The study included patients with an AGE diagnosis at discharge, defined according to the diagnostic coding of the *Sociedad Española de Urgencias de Pediatría* (SEUP) as the increased daily volume and frequency of stools and watery ones, associated or not with vomiting and/or fever² (code A09 of the International Classification of Diseases, ICD-10).

All cases were selected during the study period, defined as case the first visit to the ED of each patient with AGE diagnosis at discharge who came to the PED during the study period and who repeat the consultation at least once, with the same diagnosis at discharge, and within 72 hours of the first visit. The control sample was selected through systematic sampling of patients who visited the ED with an AGE diagnosis at discharge, pairing them with the cases temporarily in order to ensure a homogeneous distribution of the etiological agents. In this way, the control was defined as the first patient who visited the PED after each case, with the same diagnosis at discharge and who did not repeat consultation later. Other variables were not included in the pairing to analyze their impact as risk factors, thus controlling their influence on other variables through multivariate analysis.

The following criteria were considered for the exclusion of patients: patients who needed hospitalization, those whose baseline pathology conditioned the achievement of an adequate fluid and electrolyte balance (previous intestinal surgery, metabolic disorders, congenital adrenal hyperplasia) and those where the cause of the condition was not a gastrointestinal infection (appendicitis, diabetic ketoacidosis, antibiotic-associated diarrhea, cow's milk protein intolerance, inflammatory bowel disease, celiac disease, immunodeficiencies). The lack of access to the patient's medical history (protected, belonging to another autonomous community) is also considered an exclusion criterion.

Variables under study

The following variables were analyzed as potential risk factors: epidemiological ones, clinical picture characteristics, and diagnostic and therapeutic interventions performed during the first visit to the ED.

The impact on the general condition was defined as the alteration of the pediatric assessment triangle¹¹ at the time of emergency care. The dehydration degree was assessed according to the Gorelick scale¹².

In the case of patients who required additional tests, analytical data and results of such tests were collected. In the center, the current protocol indicates stool collection during severe diarrhea (which causes severe dehydration: Gorelick scale score ≥ 7) or more than 5 days in duration, bloody mucus in stools, epidemic outbreak, or need for hospitalization. The therapeutic interventions studied were: oral intake tolerance test, oral or intravenous rehydration, and ondansetron administration. Rehydration was indicated according to the center protocol and to a Gorelick scale score other than 0, where the intravenous route was used in those patients that oral rehydration failed, there was a general condition impact, severe dehydration, need for blood analysis, or risk factors such as convul-

sion, immunosuppression, underlying disease, and/or epidemic environment. Ondansetron administration depended on the presence of uncontrollable vomiting (uncontrollable vomiting with no tolerance to oral intake).

A retrospective data collection was carried out from the review of the patient's clinical history and the clinical records database of the *Comunidad de Madrid*. This includes information on both primary care (data on personal history and vaccination status) and specialized care.

Statistical analysis

The statistical software S.P.S.S. version 20 was used for data processing and analysis. Categorical variables are expressed as absolute frequency and percentage. the quantitative ones of symmetric distribution are presented as mean and standard deviation and those of asymmetric distribution as median and interquartile range.

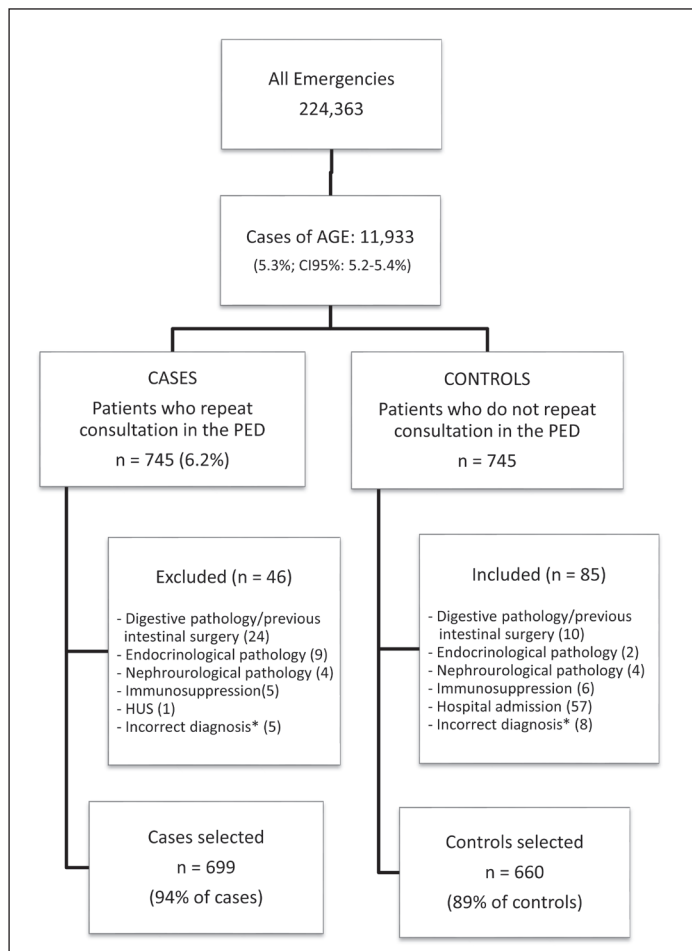


Figure 1. Sample Selection Flowchart. AGE: Acute gastroenteritis. PED: Pediatric Emergency Department. HUS: hemolytic uremic syndrome. *Patients diagnosed with AGE who do not meet the criteria established in the diagnostic coding of the Spanish Society of Pediatric Emergencies.

The association among qualitative variables was analyzed using the Chi-square test, and for quantitative variables, the Student's t-test or Mann-Whitney U test were used as a non-parametric test. The risk level of repeating consultation was established with OR and 95%CI through binary logistic regression models for both univariate and multivariate analysis. A $p < 0.05$ value was considered statistically significant.

Results

Figure 1 shows the flowchart of patient selection. 745 patients repeated consultation within 72 hours, generating 856 repeated consultations (7.2% of all AGEs; 95%CI 6.7-7.6%). 1,490 patients were selected (745 cases and 745 controls) and after applying the exclusion criteria, 699 cases and 660 controls were analyzed.

Univariate analysis

Table 1 shows the epidemiological characteristics of both groups. An association between repeating consultation and age in years was found, in which the younger patients repeated consultation the most, especially those younger than 2 years (57.3% compared with 44.3% of those older than 2 years, OR 1.69, 95%CI 1.36-2.09), decreasing that risk for each year of age increase. It was also observed a risk increase of repeating consultation as the number of depositions reported in the previous 24 hours raised, where this difference is more pronounced in those patients with 5 or more depositions (57.2% compared with 47.5% with fewer depositions, OR 1.48; 95%CI 1.17-1.86). There was no severe dehydration among the analyzed patients. Tables 2 and 3 show the association between repeating consultation and clinical and management variables.

Multivariate analysis

All variables with statistically significant associations determined in univariate analysis were included in a multiple logistic regression model. The result of this multivariate analysis reflected a decrease in the risk of repeating consultation for each year that age increases (OR 0.94, 95%CI 0.91-0.97), as well as the lack of rotavirus vaccination (OR 1.47, 95%CI 1.11-1.95) and no prior assessment in primary care (OR 1.55, 95%CI 1.10-2.19). The increased number of stools in the last 24 hours (OR 1.06, 95%CI 1.02-1.10) and microbiological stool sampling in the ED (OR 1.54, 95% CI 1.05-2.24) were also independently associated with returning to ED. There was no association with the presence of pathological agents in stools (OR 1.36, 95% CI 0.87-2.15), the subsequent primary care visit (OR 1.21, 95%CI 0.81-1.81) or the presence of abdominal pain (OR 1.29, 95%CI 0.99-1.67), although in abdominal pain there was a significant trend ($p = 0.057$).

Table 1. Epidemiological characteristics of the study groups

	Revisit		No Revisit		p Value	OR		Total analyzed N
	n	%	n	%		OR	CI95%	
Sex male	392	56.1	368	55.8	0.905			1,359
Age (years) ^a	1.5	0.9-3.4	2.1	1.0-5.3	< 0.001	0.94	0.91-0.96	1,359
Corresponding hospital ^b	265	37.9	232	35.2	0.291			1,359
Underlying disease	606	86.7	572	86.7	0.988			1,359
No history of prematurity	669	95.7	623	94.4	0.263			1,359
No chronic treatment	674	96.4	644	97.6	0.215			1,359
Previous admissions	130	18.6	122	18.5	0.957			1,359
Previous hospitalizations for AGE	36	5.2	23	3.5	0.132			1,359
non-vaccinated rotavirus	535	78.1	417	69.4	< 0.001	1.57	1.22-2.02	1,286
Epidemic environment	99	22.3	103	20.3	0.436			951
No prior assessment in PC	607	86.8	546	82.7	0.035	1.38	1.02-1.86	1,359
No referral from PC ^c	73	85.9	94	82.5	0.515			199

The values in the table are expressed in absolute frequencies (N) and percentages (%). ^aThe values are expressed in median and interquartile interval; risk is indicated for each year of increasing age. ^bCorresponding hospital within the health area in which the patient resides. ^cIncludes only those previously valued in primary care. OR: Odds ratio. CI95%: 95% confidence interval. AGE: acute gastroenteritis. PC: primary care.

Table 2. Clinical characteristics of study groups

	Revisit		No Revisit		p Value	OR		Total analyzed N
	n	%	n	%		OR	CI95%	
PAT non-stable	67	9.6	67	10.2	0.726			1,359
Evolution period (hours) ^a	24	18-72	24	24-72	0.961			1,321
Pathological products in stools	89	13.4	55	8.9	0.011	1.59	1.11-2.26	1,286
Number of depositions in last 24 hours ^a	5	3-7	4	3-7	0.001	1.07	1.03-1.10	1,158
Vomiting	481	68.8	466	70.6	0.472			1,359
Uncontrollable vomiting	46	10.2	62	12.6	0.257			
Vomiting in last 24 hours ^a	4	2-6	4	2-5	0.678			763
Fever	334	49.3	294	46.7	0.335			1,307
Highest temperature ^b	38.8	0.6	38.6	2.4	0.166			604
Abdominal pain	258	36.9	202	30.6	0.014	1.33	1.06-1.66	1,359
Dehydration	73	10.4	77	11.7	0.472			1,359
Moderate dehydration	25	3.6	19	2.9	0.468			1,359

The values in the table are expressed in absolute frequencies (N) and percentages (%). ^aThe values are expressed in median and interquartile interval. ^bThe values are expressed in mean and standard deviation. OR: Odds ratio. CI95%: 95% confidence interval. PAT: pediatric assessment triangle.

Table 3. Diagnostic-therapeutic management of study groups

	Revisit		No Revisit		p Value	OR		Total analyzed N
	n	%	n	%		OR	CI95%	
Blood analysis	57	8.2	56	8.5	0.826			1,359
Microbiological stool analysis	109	15.6	71	10.8	0.009	1.53	1.11-2.11	1,359
Stool culture (+)	47	43.1	24	33.8	0.211			180
Virus (+)	15	22.4	11	25.6	0.700			110
Oral tolerance test	277	41.3	280	43.0	0.524			1,322
Oral Rehydration	41	5.9	49	7.8	0.176			1,316
Ondansetron administration	135	19.4	132	20.3	0.685			1,345
Intravenous rehydration	46	6.7	50	8.1	0.337			1,311
No subsequent PC visit	638	91.3	566	88.4	0.085			1,339
Glycemia ^a	93.9	29.1	94.9	24.9	0.806			167
Ketonemia (mmol/l) ^b	2.0	0.8-4.0	2.1	0.7-4.2	0.916			65
pH ^a	7.35	0.05	7.35	0.1	0.973			94
Bicarbonate ^a	21.5	3.8	22.6	4.6	0.198			94
Sodium ^a	135.4	4.0	135.3	2.9	0.906			98
Potassium ^a	4.0	0.6	4.0	0.6	0.965			98
Chlorine ^a	105.2	5.8	103.8	3.8	0.256			67
Leukocytes ^b	10,400	8,700-14,000	11,400	7,400-16,425	0.910			97
Neutrophils ^b	6,600	3,900-10,656	7,150	3,750-11,625	0.730			95
CRP ^b	0.5	0.1-3.6	0.5	0.1-2.9	0.953			93
Time in PED (hours) ^b	1	0-2	1	0-2	0.527			1,359

The values in the table are expressed in absolute frequencies (N) and percentages (%). ^aThe values are expressed in mean and standard deviation. ^bThe values are expressed in median and interquartile interval. OR: Odds ratio. CI95%: 95% confidence interval. PC: primary care. CRP: c-reactive protein. PED: pediatric emergency department.

Discussion

The AGE is a frequent diagnosis in the PED, reaching in our case 5.3% of all diagnoses at discharge, a figure slightly lower than other studies conducted in our country^{13,14}. In our study period, 1 out of every 14 patients who consulted in the ED due to AGE, had consulted for the same reason in the previous 72 hours. Proposing risk factors that can be related to repeat consultation will help to design strategies aimed at optimizing resources in the ED. Most of the studies previously conducted focus on the efficacy of the different therapeutic measures^{9,10}, while ours is the first with a high number of pediatric patients, which analyze clinical and epidemiological variables.

The younger patients presented the highest risk of repeating consultation due to AGE, especially those younger than 2 years, as is the case when we study consultations¹⁵ and repeated consultations³ related to

any pathology. These patients are especially susceptible to dehydration, generating great anxiety in the family. This dehydration risk may be even more severe in newborns and young infants exclusively breastfed because of, among other factors, the inability to have adequate intake control. However, there are studies that refer to the protective role of breastfeeding against AGE^{17,18}.

Rotavirus is responsible for up to 30% of AGE cases, which is the main cause of hospitalizations due to acute diarrhea in our country¹⁹⁻²¹. It is also associated with high use of health resources (emergency and primary care visits). Since 2006, in Spain, there are two types of rotavirus vaccines, not financed by the Public Health System²². Effectiveness studies have been carried out in Spain with favorable outcomes, despite an average coverage lower than 50%. These outcomes are related to a decrease in hospitalizations due to rotavirus-related AGE between 67% and 71%²³. Based on these data, our study proves that rotavirus vaccination

is a protective factor against repeat consultation. This is one more argument for recommending this vaccination since it could reduce the number of visits to the ED due to AGE, as had already been suggested²⁴.

Abdominal pain is a frequent symptom in AGE pictures, which sometimes is difficult to manage. According to our data, 37% of the patients who repeated consultation, presented abdominal pain in the first visit, compared with 30% of those who did not, however, pain was considered present as referred by the patient or his/her family, without using validated scales for the pain assessment²⁵, or gathered information about the analgesic procedures performed in the ED. The presence of blood or pus in stools is sometimes associated with enteroinvasive gastroenteritis that tends to occur more aggressively¹⁶, it is, therefore, one of the reasons for collecting microbiological stool samples²⁶. This sample collection was another factor that was independently associated with repeating consultation, but not with the presence of the pathological agents before mentioned. The expectation of a possible treatment based on the outcome of the stool culture and worries over a high rate of stool emission could have influenced the increased risk detected of repeating consultation.

Despite AGE is a very common disease, there are significant variations in the management of it²⁷. There are studies that evaluate the efficacy of different treatments. Freedman et al conducted a systematic review of the interventions most frequently used in the AGE management in developed countries, including repeated consultations as one of the variables analyzed. In their results, there was no association between the use of intravenous rehydration or antiemetics, and less repeated consultations¹⁰, however, they found a relation between the ondansetron administration with optimization of rehydration and reduction of the hospitalization risk. Another review by Tamasik et al which compared the use of ondansetron versus placebo found no significant difference between the two options regarding repeated consultations²⁸.

Our results seem to confirm what has been described before^{9,10,28}, and, although oral and intravenous rehydration has demonstrated to be effective in reversing dehydration^{29,30}, in our sample, none of the therapeutic actions performed reduced the risk of repeating consultation.

Most of the patients who are frequent users of PEDs come directly without an appointment to primary care^{7,8}, this data may be extrapolated to the rest of the ED visits as it is evident in our sample. However, those who previously visited their pediatrician repeat consultation less than those who did not, regardless of whether or not they were referred from their healthcare center. The criteria coincidence or the accessibility to their health center that denotes this previous visit,

may have an effect of confidence and peace in the parents and prevent repeating consultation. In most cases, in our sphere, AGE is a mild pathology that does not require complementary tests or hospital treatment. For this reason and due to its intrinsic characteristics, Primary Care must be promoted and vindicated as a system capable of resolving most of the health problems of its population, thus regenerating patients' confidence in this essential care level.

There are several limitations in our study, among which we can point out the lack of recording of some data in clinical records that with a larger sample size could be improved. The Gorelick scale score was not registered in all the clinical records, however, it has been calculated retrospectively with the data obtained in the physical examination. It has not been possible to check if all indications for treatment or complementary studies comply with the center's protocols, however, it has been verified that they will reflect normal clinical practice. As well as other works with similar objectives such as that of Freedman (2013)¹⁰, the clinical situation of patients at the time of repeating consultation is not analyzed and it is therefore not known if that visit is motivated by worsening and/or persistence of symptoms, or other psychosocial aspects that are difficult to measure. Thus, the risk of repeating consultation measures (OR) will not be accurate. However, repeated consultation is identified as a marker of bad course and the objective of the study is not to point out natural aspects of the disease that condition such bad course, but to propose risk factors present in the first visit on which we can influence and therefore prevent repeating consultation regardless of why it occurs. Thus, when these potential factors are identified, they should be confirmed with tests that provide more information. Also, it has not been possible to study the feeding type of small infants since this data was frequently not recorded. As mentioned before, we think that the diet of this group of patients may influence the risk of repeating consultation, so it would be interesting to include this variable in future studies. Neither have socio-cultural or psychological aspects been considered which might influence the decision to repeat consultation.

The large size of our sample, the group selection, and large number of controlled variables represent the main strengths of our study. However, prospective studies would be necessary to provide a higher degree of evidence and multicentric ones in order to extrapolate the conclusions outside our sphere.

We can conclude that in our sphere, the AGE causes a large number of repeated consultations in the ED, that younger patients (especially those under 2 years of age) and high defecation rates are especially susceptible to repeat consultation in the ED. In addition, vaccination against rotavirus in these patients could reduce

repeating consultations and, except for the number of depositions and the request for microbiological stools study, none of the clinical findings or diagnostic-therapeutic actions carried out seems to reduce the number of these repeated consultations in the ED.

Ethical Responsibilities

Human Beings and animals protection: Disclosure the authors state that the procedures were followed according to the Declaration of Helsinki and the World Medical Association regarding human experimentation developed for the medical community.

Data confidentiality: The authors state that they have followed the protocols of their Center and Local regulations on the publication of patient data.

Rights to privacy and informed consent: The authors state that the information has been obtained anonymously from previous data, therefore, Research Ethics Committee, in its discretion, has exempted from obtaining an informed consent, which is recorded in the respective form

Conflicts of Interest

Authors declare no conflict of interest regarding the present study.

Financial Disclosure

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References

- Guarino A, Ashkenazi S, Gendrel D, et al. European Society for Pediatric Gastroenterology, Hepatology, and Nutrition/European Society for Pediatric Infectious Diseases evidence-based guidelines for the management of acute gastroenteritis in children in Europe: update 2014. *J Pediatr Gastroenterol Nutr.* 2014;59:132-52.
- Benito Fernández J, Luaces Cubells C, Gelabert Colomé G, et al. Actualización del sistema de codificación diagnóstica de la Sociedad Española de Urgencias de Pediatría. *An Pediatr (Barc).* 2015;82:442.
- Neuman MI, Alpern ER, Hall M, et al. Characteristics of recurrent utilization in pediatric emergency departments. *Pediatrics.* 2014;134:1025-31.
- Alpern ER, Clark AE, Alessandrini EA, et al. Recurrent and high-frequency use of the emergency department by pediatric patients. *Acad Emerg Med.* 2014;21:365-73.
- Pines JM, Asplin BR, Kaji AH, et al. Frequent users of emergency department services: Gaps in knowledge and a proposed research agenda. *Acad Emerg Med.* 2011;18:64-9.
- Bertoli-Avella AM, Haagsma JA, Van Tiel S, et al. Frequent users of the emergency department services in the largest academic hospital in the Netherlands: a 5-year report. *Eur J Emerg Med.* 2017;24:130-5.
- Mintegui Raso S, Benito Fernández J, Vázquez Ronco MA, et al. Los niños que repiten consulta en urgencias de pediatría. *An Pediatr (Barc).* 2000;52:542-7.
- Rivas García A, Manrique Martín G, Butragueño Laiseca L, et al. Hiperfrecuentadores en urgencias. ¿Quiénes son? ¿Por qué consultan? *An Pediatr (Barc).* 2017;86:67-75.
- Freedman SB, Thull-Freedman JD, Rumantir M, et al. Emergency department revisits in children with gastroenteritis. *J Pediatr Gastroenterol Nutr.* 2013;57:612-8.
- Freedman SB, Ali S, Oleszczuk M, et al. Treatment of acute gastroenteritis in children: an overview of systematic reviews of interventions commonly used in developed countries. *Evid Based Child Health.* 2013;8:1123-37.
- Pediatric assessment. Dieckmann RA. En: Fuchs S, Yamamoto L, editors. *American Academy of Pediatrics. APLS: The Pediatric Emergency Medicine Resource.* Sudbury, MA: Jones & Bartlett Pub; 2012. p2-37.
- Gorelick MH, Shaw KN, Murphy KO. Validity and reliability of clinical signs in the diagnosis of dehydration in children. *Pediatrics.* 1997;99:E6.
- Sendarrubias M, Carrón M, Molina JC, et al. Clinical impact of rapid intravenous rehydration with dextrose serum in children with acute gastroenteritis. *Pediatr Emerg Care.* 2017 May 1 [Epub Ahead of Print].
- Muñoz Vicente E, Bretón Martínez JR, Ros Díez A, et al. Gastroenteritis aguda infecciosa en urgencias de un hospital urbano. *An Pediatr (Barc).* 2008;68:432-8.
- Crilly J, Cameron CM, Scuffham PA, et al. Emergency department presentations in infants: Predictors from an Australian birth cohort. *J Paediatr Child Health.* 2017;53:981-7.
- Gavilán Martín C, García Avilés B, González Montero R. Gastroenteritis aguda. Protocolos diagnóstico-terapéuticos de la AEP: Infectología pediátrica. 2011. [consultado el 20 de marzo de 2018]. Disponible en: <http://www.aeped.es/documentos/protocolos-infectologia-en-revision>
- Bentley JP, Simpson JM, Bowen JR, et al. Gestational age, mode of birth and breastmilk feeding all influence acute early childhood gastroenteritis: a record-linkage cohort study. *BMC Pediatr.* 2016. 27:16:55.
- Ladomenou F, Moschandreas J, Kafatos A, et al. Protective effect of exclusive breastfeeding against infections during infancy: a prospective study. *Arch Dis Child.* 2010;95:1004-8.
- Burnett E, Parashar U, Tate J. Rotavirus vaccines: Effectiveness, Safety and Future Directions. *Paediatr Drugs.* 2018 Jan 31. doi: 10.1007/s40272-018-0283-3.
- Burnett E, Jonesteller CL, Tate JE, et al. Global Impact of Rotavirus Vaccination on Childhood Hospitalizations and Mortality From Diarrhea. *J Infect Dis.* 2017;215:1666-72.
- Comité Asesor de Vacunas (CAV-AEP). Rotavirus. Manual de vacunas en línea de la AEP [Internet]. Madrid: AEP; 2018. [consultado el 20 de marzo de 2018]. Disponible en: <http://vacunasaep.org/documentos/manual/cap-35>
- European Centre for Disease Control and Prevention. Expert opinion on rotavirus vaccination in infancy. 2017. [consultado el 20 de marzo de 2018]. Disponible en: <https://ecdc.europa.eu/sites/portal/files/documents/rotavirus-vaccination-expert%20opinion-september-2017.pdf>
- Castilla J, Beristain X, Martínez-Artola V,

- et al. Effectiveness of rotavirus vaccines in preventing cases and hospitalizations due to rotavirus gastroenteritis in Navarre, Spain. *Vaccine*. 2012;30:539-43.
24. Aristegui J, Ferrer J, Salamanca I, et al. Multicenter prospective study on the burden of rotavirus gastroenteritis in children less than 3 years of age in Spain. *BMC Infect Dis*. 2016;16:549.
 25. Santos JL. Escalas de valoración del dolor. En: *Manual de analgesia y sedación en urgencias de Pediatría*. Madrid: Ergon; 2009. p. 12-7.
 26. Polanco Allué I, Mellado Peña MJ. Gastroenteritis aguda. En: Polanco Allué I (ed). *Atlas de gastroenterología pediátrica*. Madrid: Ergón; 2014. p. 1-13.
 27. Lo Vecchio A, Dias JA, Berkley JA, et al. Comparison of Recommendations in Clinical Practice Guidelines for Acute Gastroenteritis in Children. *J Pediatr Gastroenterol Nutr*. 2016;63 226-35.
 28. Tomasik E, Ziółkowska E, Kołodziej M, et al. Systematic review with meta-analysis: ondansetron for vomiting in children with acute gastroenteritis. *Aliment Pharmacol Ther*. 2016;44: 438-46.
 29. Passariello A, Nocerino R, Terrin G, et al. Acceptability and efficacy of a gel hypotonic oral rehydration solution in children with acute gastroenteritis. *Eur J Gastroenterol Hepatol*. 2015;27:523-6.
 30. Brady K. Acute gastroenteritis: evidence-based management of pediatric patients. *Pediatr Emerg Med Pract*. 2018;15:1-25.