

Adherence to Guidelines for Management of Children Hospitalized for Acute Diarrhea

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Background: The major burden of acute gastroenteritis (AGE) in childhood is related to its high frequency and the large number of hospitalizations, medical consultations, tests and drug prescriptions. The adherence to evidence-based recommendations for AGE management in European countries is unknown. The purpose of the study was to compare hospital medical interventions for children admitted for AGE with recommendations reported in the European Societies of Pediatric Gastroenterology, Hepatology and Nutrition and Pediatric Infectious Diseases guidelines.

Methods: A multicenter prospective study was conducted in 31 Italian hospitals. Data on children were collected through an online clinical reporting form and compared with European Societies of Pediatric Gastroenterology, Hepatology and Nutrition and Pediatric Infectious Diseases guidelines for AGE. The main outcomes were the inappropriate hospital admissions and the percentage of compliance to the guidelines (full >90%, partial >80% compliance) based on the number and type of violations to evidence-based recommendations.

Results: Six-hundred and twelve children (53.6% male, mean age 22.8 ± 15.4 months) hospitalized for AGE were enrolled. Many hospital admissions (346/602, 57.5%) were inappropriate. Once admitted, 20.6% (126/612) of children were managed in full compliance with the guidelines and 44.7% (274/612) were managed in partial compliance. The most common violations were requests for microbiologic tests (404; 35.8%), diet changes (310; 27.6%) and the prescription of non-recommended probiotics (161; 14.2%), antibiotics (103; 9.2%) and anti-diarrheal drugs (7; 0.6%).

Conclusions: Inappropriate hospital admissions and medical interventions are still common in the management of children with AGE in Italy. Implementation of guidelines recommendations is needed to improve quality of care.

Key Words: gastroenteritis, diarrhea, guidelines, adherence, hospital

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Acute gastroenteritis (AGE) is a major cause of medical visits and hospitalizations in developed countries and leads to approximately 1.5 million outpatient visits and 220,000 hospitalizations per year in the United States, before the introduc-

tion of the Rotavirus vaccine.¹ In Europe, AGE is among the 3 most frequent causes of hospital admission^{2,3} with an estimated annual incidence that ranges between 4% and 17%.⁴ In Italy, where the incidence of AGE is slightly higher (between 4.5% and 19.6%),^{4,5} the rate of hospital admission for AGE is about 0.8% in children <5 years.⁵

AGE is a self-limiting and typically mild disease, whose management is, in most cases, simple and based on consistent and straightforward recommendations. According to high quality and authoritative guidelines,^{6–8} the management consists of the replacement of fluids losses. Antidiarrheal drugs, changes in diet or laboratory investigations are not routinely needed. In addition to treatment recommendations, selected guidelines also report the indications for hospital admission for AGE.⁷ However, those recommendations are usually based on expert opinion, as there are no controlled trials that specifically study this outcome.

The burden of AGE, mainly related to its high incidence, may be further increased in terms of costs by variability in procedures and excess of medical interventions.^{9,10}

Good compliance to guidelines recommendations for AGE may improve child clinical outcomes¹¹ and significantly affect the economic burden of the disease¹² by reducing complications and unnecessary interventions.

However, low adherence to guideline recommendations for AGE has been reported both in developed^{12,13} and developing countries.¹⁴ A rate up to 30% of inappropriate hospital admissions has been reported for common acute illnesses in children, such as influenza-like illness,¹⁵ but to date, no specific data are available on AGE in European children.

The aim of this study was to estimate the rate of inappropriate hospital admissions for AGE in children ≤5 years of age and to assess physicians' compliance with guideline recommendations for the management of children admitted for AGE.

PATIENTS AND METHODS

Ethics Statement

This prospective multicenter observational study was approved by the Scientific Committee of the Italian Society of Pediatrics and conducted in close collaboration with the Working Group for the Accreditation and Quality Improvement and the Italian Society of Pediatric Research.

All physicians who agreed to participate in the study and report their practice and prescriptions signed a written informed consent. Each participating institution received a private username and password to access the Pediatric Network website. Any physician might review his/her own data, but did not have access to information recorded by other institutions.

Study Design

The Pediatric Network for the Accreditation and Quality Improvement Working Group is a nationwide network that involves 126 hospitals admitting children (aged <16 years) and is aimed at improving the quality of health care by the promotion of standardized

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practice. All centers involved in the Pediatric Network received an invitation to participate in this study. From November 1, 2011, to June 30, 2012, all participant physicians reported their practice about children ≤ 5 years of age accessing their institution because of AGE. Gastroenteritis was defined according to guidelines developed by the European Societies of Pediatric Gastroenterology, Hepatology and Nutrition and Pediatric Infectious Diseases (ESPGHAN/ESPID).⁷ Physicians were invited to enroll at least 5 consecutive cases.

Data were recorded at the time of discharge by 1 operator for each hospital and loaded into an anonymous electronic Case Report Form available on the pediatric network website (<http://network-pediatrico.sip.it/>; see Appendix, Supplemental Digital Content 1, <http://links.lww.com/INF/B910>).

Outcomes

The primary outcomes were as follows:

1. Appropriateness of the hospital admission, based on the specific criteria for hospitalization.
2. Compliance with the indications for the assessment of dehydration, diagnostic tests and recommended treatments in accordance with the guidelines.

In addition, the number and types of violations of the guideline recommendations were considered as secondary outcomes.

Assessment of Adherence to the Guideline Recommendations

The evidence-based ESPGHAN/ESPID guidelines were used as the standard to assess the physicians' compliance to evidence-based recommendations.⁷ Adherence to recommendations for admission was assessed by comparing the child's conditions reported by the physician with the criteria of the guidelines. The presence of at least 1 of these conditions was considered as an appropriate indication to admit a child with AGE. Severe clinical conditions, such as shock, suspected surgical conditions and bilious vomiting, were always considered appropriate. The other conditions needed to be specifically described by the physician in the Case Report Form to be checked for appropriateness.

Medical interventions applied during child's hospital stay, including prescriptions and procedures, were similarly compared with those recommended in the guidelines. The following 10 items were considered to evaluate the appropriateness of medical interventions during hospitalization:

1. Evaluation of the main signs/symptoms to assess dehydration (Did the physician report the capillary refill time, skin turgor, respiratory pattern, etc.?)
2. Concordance between the objective assessment of dehydration and the physician's estimate (Was the physician able to adequately assess the reported signs?)
3. Nutritional interventions (eg, withdrawal, changes in diet or feeding)
4. Prescription of blood tests (other than electrolytes)
5. Rehydration route (eg, oral, nasogastric or intravenous)
6. Prescription of microbiological investigations
7. Prescription of probiotics (indications and strains)
8. Prescription of antiemetics (indications and drugs)
9. Prescription of antibiotics (indications and drugs)
10. Prescription of anti-diarrheal drugs

The overall compliance was calculated based on the presence of major and minor violations of each of the domains reported

above (see Appendix, Supplemental Digital Content 2, <http://links.lww.com/INF/B911>).

A major violation was defined as follows:

1. A medical intervention inconsistent with guideline recommendations that might negatively affect the course of the disease and/or might be associated with unnecessary costs or inappropriate interventions, or
2. Any violation to "high grade" recommendations in the guidelines (strength of evidence I and II according to the Muir-Gray score).^{16,17}

A minor violation was defined as follows:

1. A violation that did not substantially change the outcome but was generally considered inappropriate or any violation to "low grade" recommendations in the referral guidelines (strength of evidence III, IV and V according to Muir-Gray).

In our model, any major violation reduced the overall compliance by 10% and any minor violation by 5%; the final score (percentage) was calculated by the sum of the results reported for each domain, with an ideal maximum of 100%. We considered full compliance for scores $>90\%$ and partial compliance for scores $>80\%$.

Chart reviewing and assessment of violations and compliance were independently performed by 3 authors (A.L.V., I.L. and R.S.). Selected cases with peculiar clinical conditions were jointly assessed by all authors and dealt with using the Delphi method.

Statistical Analysis

Statistical analysis was performed using SPSS software (version 20.0; SPSS Inc., Chicago, IL) and R (version 2.5.0; The R Foundation for Statistical Computing, Vienna, Austria). Analyses included only available data, and missing values were not imputed. Data were summarized as means \pm SD [95% confidence interval (CI) of the mean] for continuous variables and as frequencies (%) for categorical variables. Concordance between the subjective (as reported by physicians) and objective (as evaluated by clinical signs) assessment of the severity of dehydration was based on the quadratic weighted Cohen's kappa statistics.

Univariate and multivariate logistic regression analysis was applied to identify the main factors associated with inappropriateness of hospital admission, noncompliance with management guidelines and inappropriate medical interventions. Hence, those factors showing a bivariate association with the dependent variable at a level of $P < 0.2$ were entered en bloc into a multivariate logistic regression model. All models were age-adjusted regardless of the P value. Associations were expressed as unadjusted and adjusted odds ratios (ORs) with 95% CI. All significance tests were 2-sided with the significance level set at 0.05.

RESULTS

We enrolled 612 children (328 male, mean age 22.8 ± 15.4 months) hospitalized for AGE in 31 hospitals who agreed to participate to the study. Most were hospitalized (91%, 555/612), whereas 9% (57/612) were managed in a brief observation period consisting of a temporary admission (<12 hours). The mean length of stay was 4.3 ± 2.0 days. The general characteristics of the children and their home management are reported in Table, Supplemental Digital Content 3, <http://links.lww.com/INF/B912>.

Clinical Conditions and Assessment of Dehydration

Eighty-eight percent of the children presented with a watery (311, 52%) or semiliquid (212, 36%) stool pattern and 7% reported

bloody diarrhea. Vomiting was reported in 79% of patients. About a quarter of the children (23%) had another illness together with AGE; of these children, 93/612 (15%) were admitted with a concomitant acute illness, and 49/612 (8%) children had an underlying chronic condition (Table, Supplemental Digital Content 3, <http://links.lww.com/INF/B912>).

Most patients (416; 68%) were labeled by the physician as mildly dehydrated, 165 (27%) as moderately dehydrated and only 10 (1.6%) as severely dehydrated or in shock at admission. However, the concordance between physicians' estimation of dehydration and the objective assessment was poor (weighted kappa 0.37, 95% CI: 0.46–0.56).

Many children (453/612, 74%) underwent IV rehydration. Of these, 180 (40%) received IV fluids for <24 hours and 273 (60%) received fluids for a longer period. A quarter of the children (159/612, 25%) received only oral rehydration. No child received rehydration through a nasogastric tube.

The mean percentage of weight gain during hospitalization, determined as the difference between the weight at discharge and at admission, was 0.66% (95% CI: 0.35–0.97; Table, Supplemental Digital Content 4, <http://links.lww.com/INF/B913>). Only 31 (7%) children gained >5% of their body weight compared with the weight at admission.

Appropriate Admission Rates

The main reported reasons for hospital admission were as follows: severe clinical conditions in 438 (73%) children, an explicit family request for hospitalization in 98 (16%), and logistical concerns or poor reliability of caregivers in 66 (11%) children. No reason for hospital admission was reported for 10/612 patients. Based on the discrepancy with the criteria in the guidelines, many of the hospital admissions (346/602, 57.5%) were inappropriate.

Only 188 out of the 438 children (43%) who were admitted for severe clinical conditions, as reported by the physicians, actually had an indication for hospital admission according to guidelines. We considered as appropriate those cases (66/602, 11%) in which the caregivers could not provide adequate care at home or

in which there were social/logistical concerns that might pose a risk for the child's health conditions. No relevant difference was observed among institutions according to geographical location and type of training (university vs. general hospital). Although, inappropriate hospital admissions were more frequent in large hospitals (>15 beds or 1000 inpatients/yr) than in small institutions (OR: 1.59, 95% CI: 1.04–2.44, *P* = 0.034).

Compliance With Recommendations During Hospital Stay

Once admitted to the hospital, 2/3 of the patients were managed in some agreement with evidence-based recommendations. A total of 21% (126/612) and 45% (274/612) of the children were managed in full or partial compliance with guideline recommendations, respectively (Fig. 1).

No difference in compliance was observed between children managed in a brief observation regimen or regular hospitalization (mean compliance 86 ± 9.1 vs. 84.7 ± 9.8; *P* = 0.37).

Inappropriate requests for microbiological tests (404, 35.8%) and nutritional interventions (310; 27.6%) were the 2 most frequent violations. The administration of antidiarrheal drugs not included in the guidelines was the third most common violation (271, 24%), with 161 prescriptions for non-indicated probiotics (14.2%), 103 for non-indicated antibiotics (9.2%) and 7 for other non-indicated antidiarrheal drugs (0.6%).

Children who were admitted because of poor family reliability (OR = 0.31; 95% CI: 0.15–0.60) or based on an explicit request by the caregiver (OR = 0.47; 95% CI: 0.28–0.79) had a significantly lower risk of being managed inappropriately (*P* = 0.001 and *P* = 0.004, respectively; Table 1). The major factors associated with the most common violations are reported in Table 2.

The presence of >5 diarrheal stools was the only feature linked with the request for microbiological investigations (OR = 1.66, 95% CI: 1.06–2.61). Antibiotics were prescribed more frequently in children with bloody diarrhea (OR = 3.34, 95% CI: 1.51–7.39), in those who showed increased levels of inflammatory markers (OR = 5.9; 95% CI: 3.19–10.9) and in

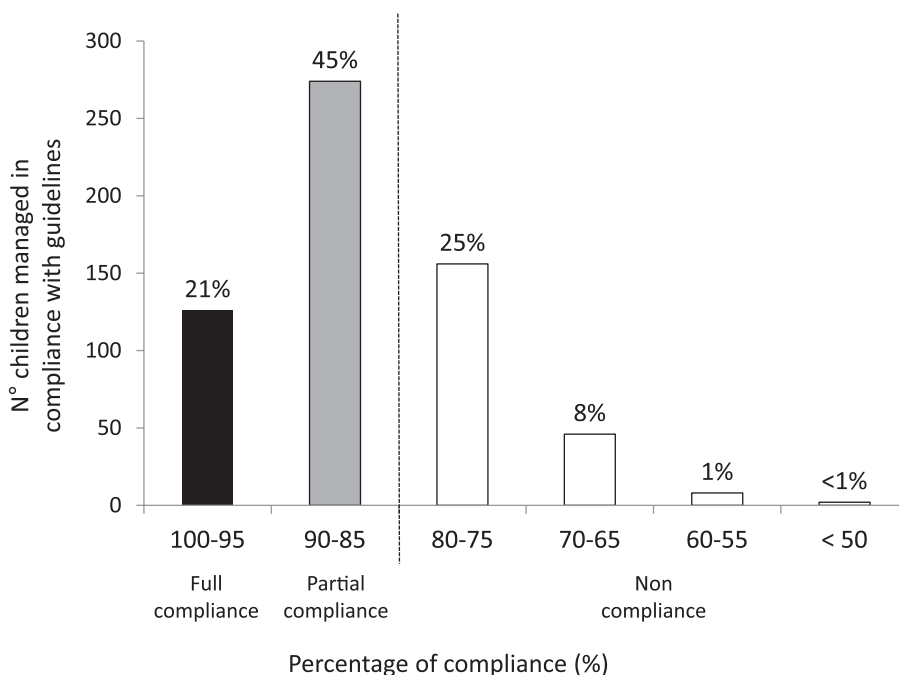


FIGURE 1. Compliance to guideline recommendations among children hospitalized for AGE. Note: Compliance was calculated according to the presence of major and/or minor violations committed by physicians during the hospital stay (see Appendix, Supplemental Digital Content 2, <http://links.lww.com/INF/B911>).

TABLE 1. Determinants of Inappropriate Hospital Admissions and Compliance to Guidelines During Hospitalization

Determinants of Inappropriate Admission Rates	Univariate Analysis		Multivariate Analysis	
	OR (95% CI)	P	OR (95% CI)	P
Age	1.00 (0.99–1.01)	0.288	1.00 (0.99–1.01)	0.985
First medical assessment	—	0.555		
Primary care pediatrician	1		*	*
Other hospital	1.85 (0.74–4.58)	0.182	*	*
Emergency department	1.47 (0.79–2.75)	0.22	*	*
Emergency medical service	1.67 (0.47–5.95)	0.424	*	*

Determinants of noncompliance with guidelines during hospital stay	Univariate Analysis		Multivariate Analysis	
	OR (95% CI)	P	OR (95% CI)	P
Age	1.00 (0.99–1.01)	0.898	0.99 (0.98–1.01)	0.641
Underlying chronic conditions (Yes vs. No)	0.83 (0.44–1.56)	0.57	*	*
Concomitant acute illnesses (Yes vs. No)	1.32 (0.84–2.08)	0.228	*	*
Reasons for admission		<0.001		
Severe clinical conditions	1		1	<0.001
Explicit family request	0.47 (0.28–0.79)	0.004	0.20 (0.11–0.38)	<0.001
Logistical concerns or poor caregiver reliability	0.31 (0.15–0.60)	0.001	0.25 (0.11–0.54)	<0.001
Appropriateness of hospital admission (no vs. yes)	1.29 (0.92–1.81)	0.142	1.55 (1.00–2.39)	0.047

*Not entered in the multivariate model (univariate $P > 0.2$) because of an univariate association.

those children with a concomitant acute illness (OR = 3.05; 95% CI: 1.59–5.83).

DISCUSSION

This is the first prospective study specifically assessing physicians' compliance with guideline recommendations for hospital admissions and management of children with AGE. Our results indicate that more than 50% of children with AGE were admitted without meeting the criteria for hospitalization reported in the reference guidelines. Once admitted, about 2/3 of inpatient children were managed in compliance with evidence-based recommendations.

Medical interventions in discordance with evidence-based criteria are strongly associated with higher costs and worse clinical outcomes,^{11,12} and the clinical and economic burden steadily

rises when the inappropriateness is related to common diseases, such as AGE.

In developed countries, the burden of AGE is huge because of the high number of hospitalizations, outpatient consultations and medical interventions. A widespread rotavirus vaccination campaign might significantly reduce costs and hospitalization,¹⁸ but it is not applied in all countries,¹⁹ and even when routinely applied it is expected to decrease the AGE rate by only 25–28%.²⁰

Severe dehydration is the major indication for hospital admission in those children; a weight loss of at least 5% is reported as the most reliable index of dehydration,⁷ but in our population, only a minority of children experienced a significant weight gain after rehydration. Even if during hospitalization some children might have a weight loss because of lack of appetite, blood samples and other physical and psychological factors, it is highly probable that most children were not significantly dehydrated at admission.

TABLE 2. Factors Associated With Inappropriate Medical Interventions and With Prolonged Hospitalization

Determinants	Antibiotics		Change in Diet		Stool Culture	
	aOR (95% CI)	P	aOR (95% CI)	P	aOR (95% CI)	P
Age (months)	1.01 (0.99–1.03)	0.247	1.02 (1.01–1.04)	0.002	0.99 (0.98–1.01)	0.286
N episodes of diarrhea/day	*					
0–3 episodes	*		1		1	
3–5 episodes	*		1.34 (0.86–2.08)	0.191	1.47 (0.94–2.28)	0.088
> 5 episodes	*		1.48 (0.96–2.30)	0.076	1.66 (1.06–2.61)	0.028
Episodes of vomiting	*					
No vomiting	*		1		—	
1–3	*		0.44 (0.27–0.74)	0.002	—	
3–5	*		0.83 (0.47–1.45)	0.511	—	
> 5	*		0.78 (0.44–1.40)	0.413	—	
Underlying chronic conditions	*		*		—	
Concomitant acute illness	3.05 (1.59–5.83)	0.001	—		0.77 (0.47–1.26)	0.3
Bloody diarrhea	3.34 (1.51–7.39)	0.003	—		—	
Inflammatory markers (high vs. normal)	5.90 (3.19–10.9)	<0.001	—		*	
White blood count (altered vs. normal)	1.83 (1.07–3.15)	0.064	—		0.81 (0.53–1.24)	0.335
Antibiotics	—		—		—	
Antiemetics	—		—		—	
Acetorphan	—		—		—	

*Not entered in the multivariate model (univariate $p > 0.2$) because of an univariate association.

—not in the set of predictors; aOR, adjusted OR.

In our population, although 16% of children were moderately severely dehydrated, about 2/3 underwent IV rehydration.

Although the rate of inappropriate admissions was high, the compliance with guidelines in hospitalized children was fairly good (66%) and similar to that reported in United States (69%).¹² Physicians' compliance was strongly related to the reason for admission; compliance was better in those patients with no real indications for admission (explicit family request or poor caregiver reliability). Therefore, there was a trend of not applying excessive invasive interventions in children who were in relatively good clinical condition.

The most common violations to the guidelines were inappropriate requests for microbiological investigations, nutritional interventions and antibiotic prescriptions. Microbiological tests are not recommended by the guidelines, unless in specific conditions, as these tests have no impact on medical interventions.⁷

Antibiotics were more likely prescribed in children with signs of inflammation (eg, high C-reactive protein or white blood cells). However, blood tests are not routinely recommended by the guidelines and are not predictive of a bacterial intestinal infection.

Although 70% of the children presented with vomiting, only a minority of the patients received antiemetics. The use of antiemetics is a very controversial issue in AGE. There is recent consistent evidence that ondansetron may reduce hospitalization and IV rehydration in children who access the emergency department.^{21,22} However, this beneficial effect must be considered in light of concern related to a warning of FDA reporting the association of ondansetron with severe cardiac side effects (FDA: Zofran [ondansetron]: Drug Safety Communication-Risk of Abnormal Heart Rhythms, 2011. from <http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm272041.htm>). It should be noted that these severe side effects were reported at doses and routes that differ from those suggested for AGE. Discussion among experts is still active on this issue; currently only 1 guidelines²³ worldwide recommend the use of ondansetron in selected cases, but a large use in the United States and Canada has been reported.^{21,22}

The significant variability in clinical practice and the lack of adherence to the standard of care might be linked to differences in clinical outcomes and health care expenses in industrialized countries.²⁴ In addition, it has been demonstrated that an educational intervention focused on guidelines may significantly reduce the number of inappropriate hospital admissions for other common pediatric illnesses.¹⁵ This result highlights the importance of medical education and retraining to influence clinical practice.

The main limit of this study was related to the bias of including data reported by physicians. However, the inclusion of a large number of institutions and the identification of a single referent person reporting the interventions of colleagues might have partially reduced this bias. Differently from other studies based on a retrospective analysis of medical prescriptions,^{12,14} our study was the first that has been designed on purpose to prospectively assess medical interventions in a European country.

Inappropriate hospital admissions and medical interventions are still common in the management of children with AGE. Our results are in line with previous findings indicating that effective treatment for AGE is poorly applied by physicians in various European countries and is still far from being optimal even compared with those published >10 years ago.²⁵

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