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Characteristics of brief resolved unexplained events at a pediatric medical care center in Venezuela

Omar Naveda Romero[1,a], Mariangel Fonseca Colina[1,b], Talmary Parra Castellano[1,b], Dangely Luis Santana[1,b], Fabiola Linares Cárdenas[1,b], Roseelena Moiz[1,b], Yeirsinia Yépez[1,b], Teomarys Lagos Rodríguez[1,b], Shirlye Balza Tovar[1,b], Josmary Mejías Vega[1,b]

[1] Clínica "Santa Cruz", Barquisimeto, Venezuela.
[a] Pediatrician specializing in Pediatric and Neonatal Intensive Care Medicine.
[b] Pediatrician specializing in child health care.

Keywords:
brief resolved unexplained event; recurrence; diagnosis; hospitalization; gastroesophageal reflux (source: MeSH-NLM).

ABSTRACT

Objective. To describe the characteristics of brief resolved unexplained events (BRUE) at a pediatric medical care center in Venezuela between January 2021 and October 2025. **Methods.** An observational study with descriptive analysis of 178 patients meeting BRUE criteria, selected through consecutive non-probability sampling, who presented to the emergency department or outpatient clinic. Pearson's chi-square test and the Mann–Whitney U test were used. **Results.** 9 % of patients developed an underlying disease. Recurrence occurred in 33.1 % of cases, and 48.9 % were classified as high risk. The most frequently diagnosed underlying disease was gastroesophageal reflux. 5.1 % were hospitalized, and additional diagnostic tests were performed in 57.9 % of cases. Factors associated with recurrence included altered level of consciousness, high-risk BRUE, abnormal perinatal history, and subsequent diagnosis of an underlying disease. Factors associated with an underlying disease were age under 60 days, high-risk BRUE, recurrence of the event, prematurity, and frequent regurgitation. **Conclusions.** BRUE accounted for 1.3 % of emergency visits; 9 % of patients developed an underlying disease, one-third experienced recurrence, and half were classified as high risk. 5.1 % were hospitalized, and no deaths were recorded.

Características del evento breve, resuelto e inexplicable en un centro médico de atención pediátrica en Venezuela

Palabras clave:
evento breve; resuelto e inexplicable; recurrencia; diagnóstico; hospitalización; reflujo gastroesofágico (fuente: DeCs-BIREME).

RESUMEN

Objetivo. Describir las características del evento breve, resuelto e inexplicable (BRUE) en un centro médico de atención pediátrica en Venezuela, entre enero del 2021 y octubre del 2025. **Métodos.** Estudio observacional con análisis descriptivo de 178 pacientes con criterios para BRUE, seleccionados por muestreo no probabilístico consecutivo, que acudieron a sala de emergencia o consulta ambulatoria. Se utilizó chi-cuadrado de Pearson y la prueba U de Mann-Whitney. **Resultados.** El 9 % de los pacientes desarrolló enfermedad subyacente. Hubo recurrencia en el 33,1 % de los casos y el 48,9 % fue de alto riesgo. La enfermedad subyacente más frecuentemente diagnosticada fue el reflujo gastroesofágico. El 5,1 % fue hospitalizado y en el 57,9 % de los casos se realizaron estudios complementarios. Los factores asociados a la recurrencia fueron: nivel de conciencia alterado, BRUE de alto riesgo, historia perinatal anormal y diagnóstico posterior de enfermedad subyacente. Los factores asociados a la enfermedad subyacente fueron: edad menor de 60 días, BRUE de alto riesgo, recurrencia del evento, prematurez y regurgitación frecuente. **Conclusiones.** El BRUE tuvo una incidencia del 1,3 % de las visitas a emergencia; además, el 9 % desarrolló una enfermedad subyacente, una tercera parte presentó recurrencia y la mitad fue de alto riesgo. El 5,1 % fue hospitalizado y no se registraron defunciones.

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Correspondence:
Omar Eugenio Naveda Romero
omarnavedamd@yahoo.com

INTRODUCTION

The term ALTE (*apparent life-threatening event*) originated at the 1986 consensus conference on apnea held by the National Institutes of Health of the United States of America, with the aim of replacing the term "sudden infant death syndrome" [1]. However, the imprecise nature of its original definition made its application difficult, both in clinical practice and in research, which prompted the need to replace it with a more specific and operational concept [2].

In 2016, the American Academy of Pediatrics (AAP) introduced the term BRUE (brief resolved unexplained event), known in Spanish as "evento breve, resuelto e inexplicable," to describe a sudden clinical event that may occur in neonates and infants younger than one year of age. It is characterized by being brief, resolved at the time of evaluation, and lacking an identifiable cause after an appropriate clinical assessment, which reflects its transient nature and the absence of a clear etiology. Unlike ALTE, the BRUE concept explicitly incorporates the information obtained through a structured history evaluated by a qualified health professional. Likewise, it establishes the first year of life as the age limit and defines minimum diagnostic criteria, thereby constituting a more precise and internationally standardized definition [3].

Several studies have shown that between 5 % and 9 % of BRUE cases are attributable to underlying diseases, without this being associated with a higher risk of mortality or sudden infant death syndrome [4,5]. Despite these findings, approximately 63 % of patients with BRUE are hospitalized and up to 82 % undergo diagnostic testing, most of which may be unnecessary [6].

On the other hand, the AAP established a risk stratification system and provided evaluation and management recommendations for patients at lower risk of recurrence or underlying disease [7]. In this regard, some studies have reported that the AAP high-risk criteria for BRUE have shown a low positive predictive value and may incorrectly classify most infants as high risk [8]. Under these terms, it is justified to continue research on BRUE because of the need to identify recurrence rates, underlying causes, and the risk stratification of serious diseases, as well as to optimize clinical management, in order to avoid routinely indicating hospital admission, medication administration, tests, consultations with subspecialists, or home cardiorespiratory monitoring.

The aim of the study was to describe the characteristics of BRUE at a pediatric care medical center in a city in Venezuela; for this purpose, events meeting BRUE criteria were identified according to AAP recommendations, and factors associated with two relevant aspects of BRUE were established: event recurrence and the development of underlying diseases.

METHODS

Study type and area

An observational, descriptive study was conducted at Clínica Santa Cruz in the city of Barquisimeto, Lara State, Venezuela, between January 2021 and October 2025, where neonates and infants younger than 1 year of age who presented to the emergency department or follow-up consultation with BRUE criteria within the first 24 hours after the initial event (*index event*) were identified.

Population and sample

Through consecutive non-probabilistic sampling, neonates and infants meeting BRUE criteria who attended the emergency room or outpatient clinic were selected from a total of 13,267 visits. The sample size was calculated for the estimation of a proportion, using as reference data from a previously published multicenter study [4], in which 267,368 visits to pediatric emergency services and a BRUE proportion of 0.76 % were reported. Based on this expected proportion, the minimum sample size was calculated using a 95 % confidence level (Z = 1.96) and an absolute precision of 1.3 %, through the formula for estimating proportions in large populations. According to these parameters, the required sample size was 171 patients. Epidat 3.1 software was used to perform the calculation.

Patients who presented more than 24 hours after the index event, or with a comorbid condition that contributed to the event, or with documentation of substantially abnormal vital signs at the time of clinical evaluation, as well as those lost to follow-up or whose legal guardians did not provide consent, were excluded. If a patient was admitted more than once for BRUE, only the first admission was included in the analysis. The remaining admissions were considered recurrences. The flowchart showing patient selection is presented in Figure 1.

Variables

BRUE was diagnosed according to the AAP criteria, and the AAP criteria for risk stratification were also used [7].

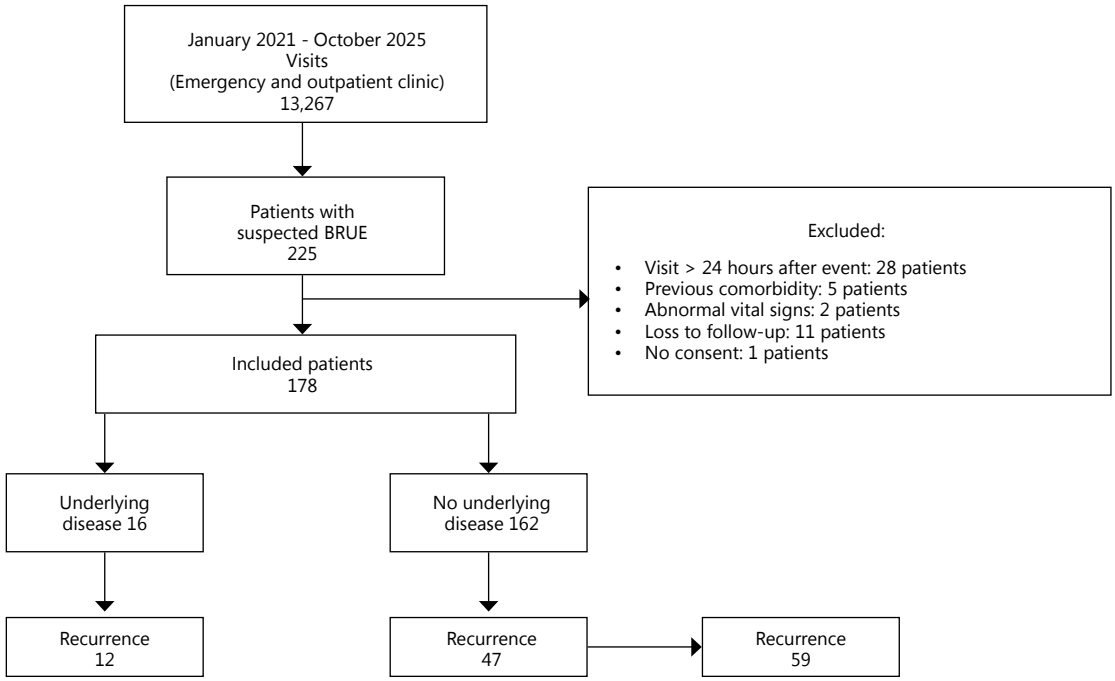

Figure 1. Flowchart of patient selection in the study

Recurrence was considered when the event was repeated two or more times before the diagnosis of an underlying disease or during the 90 days following the first consultation if no causal diagnosis had been established, including those cases in which the event was reported by caregivers via telephone.

Underlying disease was defined as a diagnosis requiring timely identification and that, otherwise, could potentially cause morbidity or mortality.

Underlying diseases included: gastroesophageal reflux (GER), lower respiratory tract infection, seizure disorder, congenital heart disease, laryngomalacia, and inborn error of metabolism. Once GER was suspected, it was diagnosed by a pediatric gastroenterologist. Lower respiratory tract infection included bronchiolitis, pneumonia, and pertussis-like syndrome. The diagnosis of bronchiolitis was based on the McConnochie criteria [9]. Pneumonia was radiologically confirmed. The definition of pertussis-like syndrome was based on the clinical criteria proposed by the Council of State and Territorial Epidemiologists [10]. Seizure disorder included epileptic conditions requiring anticonvulsant therapy and electroencephalography. Congenital heart diseases required medical or surgical treatment because of hemodynamic impact. Laryngomalacia was diagnosed by an otolaryngologist using flexible laryngoscopy. Inborn errors of metabolism were diagnosed through neonatal screening using chromatography.

Other factors studied were determined after a literature review. These were: age, sex, infant history (prematurity, abnormal perinatal history, frequent regurgitation, and recent illness), family history (a disease similar to the current episode in siblings or cousins, cardiac arrhythmias, and genetic disease), social history (exposure to tobacco smoke and living with an adult with mental illness), and suspected child abuse (family legal problems or changes in the account narrated by caregivers). The patients who were admitted or placed under observation or hospitalization were also recorded, as well as the proportion, whether admitted or not, who underwent complementary tests. These tests included complete blood count, serum electrolytes, liver and kidney function tests, venous blood gas analysis, serum ammonia, urinalysis, multiplex viral testing for respiratory infections, chest radiographs, electrocardiograms, cranial CT scans, and electroencephalography.

Any patient with a gestational age of less than 37 weeks was considered premature. Abnormal perinatal history included maternal conditions such as hypertension (chronic or pregnancy-associated) and gestational diabetes, in addition to neonatal conditions such as bronchopulmonary dysplasia, hyaline membrane disease, perinatal asphyxia, and transient tachypnea of the newborn. Infants with frequent regurgitation were considered to be those with the effortless return of previously swallowed food into the mouth, according to the Rome III criteria [11]. Benign disease was defined as a prior medical diagnosis, within the two weeks preceding the event, of an acute rapidly resolving or self-limited illness that should not lead to hospitalization or that could be physiological for the patient's age. Cardiac arrhythmias in the family were determined electrocardiographically by a cardiologist. Exposure to tobacco smoke was considered present when at least one caregiver had smoking habits. Family legal problems included divorce and disputes over child custody or child support.

Instruments and procedures for data collection

A form specifically designed to collect the variables of interest and to monitor the included patients was used as the data collection instrument in order to determine their characteristics and conditions during subsequent consultations. Data were collected from information obtained during the outpatient and emergency consultations of the patients included in the study. Their course was also monitored by telephone, during follow-up consultations, and through care provided in the emergency department.

The data collection instrument underwent expert judgment validation. The evaluation criteria consisted of determining coherence and relevance on a three-level scale: 1 = mild, 2 = moderate, 3 = strong. For this evaluation process, three expert judges collaborated: a neonatologist, a pediatrician, and a pediatric cardiologist, each with more than 10 years of experience; in addition, all were university faculty members and had research training. None belonged to the team of study authors, and their participation was voluntary. The expert judges showed substantial or almost perfect agreement in most of the calculated indices (Cohen's kappa coefficient ≥ 0.61).

The data collection form was used to make the pertinent records and structure the collected information, both from the visit to the emergency room and from the outpatient consultation, in addition to the information obtained through telephone follow-up to record the patient's clinical course.

During consultations in the emergency area or routine follow-up consultations, a pediatrician performed the patient's physical examination, and those eligible were included in the study. Data were collected on any diagnosis attributed to BRUE or identified during evaluation, whether at the initial visit or at any other visit within the 90 days following the event.

Data analysis

Descriptive analysis included means and standard deviation (SD) for quantitative variables and percentages for qualitative variables. The variables compared according to the outcomes of interest, recurrence and underlying disease, were studied through bivariate analysis, in which Pearson's chi-square test was used to compare qualitative data and the Mann-Whitney U test was used to compare quantitative data. A p value < 0.05 was considered significant. JASP software®, version 0.95.3, was used for the statistical analyses.

Ethical considerations

Before the beginning of the study, and again at its completion, approval was granted by the Institutional Bioethics Review Committee, responsible for the ethical oversight of the research, under No. A-00113p. An informed consent form was used to obtain the voluntary participation of the parents and legal guardians of all patients included in the study. Likewise, the confidentiality of the collected data and the anonymity of the patients included in the analysis, as well as that of their representatives, were guaranteed.

RESULTS

Between January 2021 and October 2025, a total of 13,267 patients were seen in the Emergency Department and Outpatient Clinic. A total of 178 infants with BRUE, according to the AAP criteria, were included in the study (1.3 %); of these, 16 neonates or infants had an underlying disease (9 %). There was a 33.1% recurrence rate of the event. The mean age was 179 days, with a standard deviation of 106 days. Of the participants, 11.2 % were neonates and the rest were infants. Males accounted for 46.1 %.

The most frequent BRUE criterion was altered muscle tone (47.8 %), followed by abnormal breathing, changes

in skin color, and altered level of consciousness. A total of 48.9 % were classified as high risk. The most frequent patient histories were prematurity (18.5 %), abnormal perinatal history (15.2 %), and frequent regurgitation (8.4 %). In 5.6 % of the cases, there was a family history of genetic disease. A total of 6.2% were exposed to tobacco smoke. The most frequently diagnosed underlying disease was gastroesophageal reflux (37.5 %). A total of 5.1 % were admitted, and complementary tests were performed in 57.9 % of the cases. The remaining characteristics of the study population are presented in Table 1.

Table 1. Characteristics of neonates and young infants with BRUE at a pediatric care medical center in Venezuela, 2021–2025

General characteristics	n = 178
	fi (%)
Demographics	
Age in days, mean (SD)	(179 ± 106 days)
Neonates	20 (11.2)
Infants	158 (88.8)
Younger than 60 days	42 (23.6)
Sex	
Male	82 (46.1)
Female	96 (53.9)
BRUE criteria[a]	
Abnormal breathing	78 (43.8)
Altered muscle tone	85 (47.8)
Changes in skin coloration	75 (42.1)
Altered level of consciousness	37 (20.8)
BRUE characteristics[a]	
Risk stratification	
Low risk	91 (51.1)
High risk	87 (48.9)
Event recurrence	59 (33.1)
Patient history	
Prematurity	33 (18.5)
Abnormal perinatal history	27 (15.2)
Frequent regurgitation	15 (8.4)
Recent benign illness	7 (3.9)
Family history	
Similar illness in siblings	9 (5.1)
Cardiac arrhythmias in family members	6 (3.4)
Genetic disease in the family	10 (5.6)
Social history	
Exposure to tobacco smoke	11 (6.2)
Living with an adult with mental illness	4 (2.2)
Suspected child abuse	
Family legal problems	4 (2.2)
Changes in the narrative	4 (2.2)
Underlying disease	16 (9.0)
Underlying diseases[b]	
Gastroesophageal reflux	6 (37.5)
Lower respiratory infection[c]	3 (18.8)
Seizure disorder	3 (18.8)
Inborn error of metabolism[d]	2 (12.5)
Congenital heart disease[e]	1 (6.2)
Laryngomalacia	1 (6.2)
Hospital admissions	9 (5.1)
Complementary tests	103 (57.9)
Mortality	0 (0)

Note. SD: standard deviation; [a] According to AAP criteria; [b] Based on 16 patients with underlying disease; [c] Bronchiolitis, pneumonia, and pertussis-like syndrome; [d] Phenylketonuria and galactosemia; [e] Ventricular septal defect and patent ductus arteriosus.

Table 2. Characteristics according to event recurrence in neonates and young infants with BRUE at a pediatric care medical center in Venezuela, 2021–2025

General characteristics	Recurrence		*p*-value[a]
	Absent n = 119	Present n = 59	
	fi (%)	fi (%)	
Demographics			
Age in days, mean (SD)	(182 ± 103 days)	(172 ± 114 days)	0.635
Neonates	12 (10.1)	8 (13.6)	0.490
Infants	107 (89.9)	51 (86.4)	
Younger than 60 days	23 (19.3)	19 (32.2)	0.057
Sex			
Male	51 (42.9)	31 (52.5)	0.222
Female	68 (57.1)	28 (47.5)	
BRUE criteria			
Abnormal breathing	49 (41.2)	29 (49.2)	0.313
Altered muscle tone	58 (48.7)	27 (45.8)	0.708
Changes in skin coloration	46 (38.7)	29 (49.2)	0.182
Altered level of consciousness	9 (7.8)	28 (47.5)	<0.001
BRUE risk stratification			
High risk	28 (23.5)	29 (49.2)	<0.001
Patient history			
Prematurity	19 (16.0)	14 (23.7)	0.210
Abnormal perinatal history	11 (9.2)	16 (27.1)	0.002
Frequent regurgitation	7 (5.9)	8 (13.6)	0.083
Recent benign illness	3 (2.5)	4 (6.8)	0.169
Family history			
Similar illness in siblings	5 (4.2)	4 (6.8)	0.460
Cardiac arrhythmias in family	6 (5.0)	0 (0)	0.079
Genetic disease in family	7 (5.9)	3 (5.1)	0.828
Social history			
Exposure to tobacco smoke	7 (5.9)	4 (6.8)	0.815
Living with an adult with mental illness	4 (3.4)	0 (0)	0.154
Suspected child abuse			
Family legal problems	2 (1.7)	2 (3.4)	0.469
Changes in narrative	3 (2.5)	1 (1.7)	0.726
Underlying disease	4 (3.4)	12 (20.3)	<0.001
Hospital admissions	7 (5.9)	2 (3.4)	0.475
Complementary tests	70 (58.8)	33 (55.9)	0.713

Note. SD: standard deviation. [a] Pearson's chi-square test for qualitative data and Mann-Whitney U test for quantitative data.

Altered level of consciousness (7.8 % vs. 47.5 %; $p < 0.001$), high-risk BRUE (23.5 % vs. 49.2 %; $p < 0.001$), abnormal perinatal history (9.2 % vs. 27.1 %; $p = 0.002$), and the subsequent diagnosis of underlying disease (3.4 % vs. 20.3 %; $p < 0.001$) showed a significantly higher proportion in the neonates and younger infants who presented recurrence of the event (see Table 2).

Table 3 shows that age younger than 60 days (19. % vs. 62.5 %; $p < 0.001$), high-risk BRUE (45.7 % vs. 81.3 %; $p = 0.007$), recurrence of the event (29.0 % vs. 75.0%; $p < 0.001$), prematurity (16.7 % vs. 37.5 %; $p = 0.041$), and frequent regurgitation (6.2 % vs. 31.3 %; $p < 0.001$) showed a significantly higher proportion among neonates and young infants who developed an underlying disease.

DISCUSSION

Despite the introduction of the BRUE definition in 2016, there are still few published regional data

Table 3. Characteristics according to underlying disease in neonates and young infants with BRUE at a pediatric care medical center in Venezuela, 2021-2025

General characteristics	Underlying disease		*p*-value[a]
	Absent n = 162	Present n = 16	
	fi (%)	fi (%)	
Demographics			
Age in days, mean (SD)	(186 ± 104 days)	(101 ± 98 days)	0.005
Neonates	17 (10.5)	3 (18.8)	0.320
Infants	145 (89.5)	13 (81.2)	
Younger than 60 days	32 (19.8)	10 (62.5)	< 0.001
Sex			
Male	73 (45.0)	9 (56.2)	0.392
Female	89 (55.0)	7 (43.8)	
BRUE criteria			
Abnormal breathing	71 (43.8)	7 (43.8)	0.995
Altered muscle tone	75 (46.3)	10 (62.5)	0.216
Changes in skin coloration	65 (40.1)	10 (62.5)	0.084
Altered level of consciousness	33 (20.4)	4 (25.0)	0.663
BRUE risk stratification			
High risk	74 (45.7)	13 (81.3)	0.007
Event recurrence	47 (29.0)	12 (75.0)	<0.001
Patient history			
Prematurity	27 (16.7)	6 (37.5)	0.041
Abnormal perinatal history	22 (13.6)	5 (31.3)	0.060
Frequent regurgitation[b]	10 (6.2)	5 (31.3)	<0.001
Recent benign illness	5 (3.1)	2 (12.5)	0.065
Family history			
Similar illness in siblings	8 (4.9)	1 (6.3)	0.819
Cardiac arrhythmias in family	5 (3.1)	1 (6.3)	0.504
Genetic disease in family	9 (5.6)	1 (6.3)	0.908
Social history			
Exposure to tobacco smoke	10 (6.2)	1 (6.3)	0.990
Living with an adult with mental illness	4 (2.5)	0 (0)	
Suspected child abuse			
Family legal problems	4 (2.5)	0 (0)	0.525
Changes in narrative	4 (2.5)	0 (1.7)	
Hospital admissions	8 (4.9)	1 (6.3)	0.819
Complementary tests	95 (58.6)	8 (50.0)	0.504

Note. SD: standard deviation; [a] Pearson's chi-square test for qualitative data and Mann-Whitney U test for quantitative data; [b] 4 of 6 patients (66.7 %) with GER presented frequent regurgitation; additionally, frequent regurgitation occurred in 10 of 162 patients without underlying disease and in 1 of 2 with inborn error of metabolism.

on its epidemiology. In this study, the incidence of BRUE was 1.3 % of the total visits to the emergency room or outpatient clinic, with a similar proportion in both sexes, which is consistent with the reviewed literature [4,6,12]; however, the proportion of high-risk BRUE (48.9 %) was lower than that described in other studies, which report a range between 87 % and 93.8 % using the same diagnostic criteria.

This could be explained by a higher mean age in the study population and a lower proportion of patients younger than 60 days compared with what has been reported in previous studies [5], taking into account that high-risk BRUE is more frequent at younger ages. In this regard, it is important to clarify that, of the 87 patients meeting high-risk criteria, 42 were younger than 60 days, of whom 5 were

premature, 39 presented recurrences, and 6 had an event lasting more than 1 minute. Of the 91 patients with BRUE who met low-risk criteria, all were older than 60 days; of these, 10 were premature at ≥ 32 weeks, and all had a single event lasting less than 1 minute and without cardiopulmonary resuscitation maneuvers.

In this context, one study has suggested that the AAP high-risk criteria for BRUE result in substantial overclassification of infants within the high-risk group, possibly due to the inclusion of factors such as age younger than 2 months and recurrence of the event; in view of this discrepancy, the authors developed new BRUE classification and prediction rules, which were derived from a large U.S. cohort and showed better discrimination; however, these rules have not been validated in an external cohort [8].

As for the overall recurrence rate of 33.1 %, it was higher than that described in the literature, where reported ranges vary between 10.8% and 17.6 % [6,13,14]. This finding may possibly be due to the fact that the risk of recurrence is higher when age is younger than 60 days, there is an abnormal perinatal history, or criteria for high-risk BRUE are present. In this study, the latter two factors showed a significantly higher proportion in the group that presented recurrence of the event.

The AAP provided evaluation and management recommendations for patients with BRUE at low risk of recurrence [7]. It also recommended not performing diagnostic tests in patients with low-risk BRUE, and weakly recommended obtaining an electrocardiogram and a pertussis test in low-risk patients [7,15]. Nevertheless, in this study it was found that nearly 60% of patients underwent some type of complementary testing. In addition, these tests were performed similarly regardless of risk stratification, which is not consistent with AAP recommendations. In this regard, it is important to emphasize that laboratory tests and imaging studies had a very low yield for diagnosing underlying diseases, contributing to the diagnosis of disease in 1.5 % of cases [16].

It is important to highlight that, possibly due both to the pediatrician's concern about diagnosing a serious underlying condition and to the anxiety of the caregivers and family members of the patient with BRUE, there is a perceived need to perform whatever tests are considered pertinent, as well as general evaluations for systemic infections, neurological diseases, or metabolic diseases, regardless of the patient's risk stratification and AAP recommendations. For many of these tests, the probability of a positive result is very low, and the probability of a contributory result is even lower. It is important for the physician to use the AAP recommendations as a guide, which would also facilitate explaining the patient's condition and prognosis to caregivers and family members, while maximizing productivity, efficiency in evaluation and follow-up, and communication between physician and family. Likewise, there were no deaths attributable to BRUE during follow-up or to the diagnosed underlying diseases; this finding was similar to that of other studies, in which mortality has been reported to be very low or absent [17].

A large cohort of 3,283 infants with BRUE reported that 4.6 % had a serious underlying diagnosis, with seizures requiring antiepileptic medication (1.3 %), airway abnormalities requiring surgery (0.6 %), and GER disease and dysphagia requiring tube feeding (0.5 %). In addition, 14.3 % had a recurrent event, and only one death was recorded [18]. Another study reported 31% with GER, this being the most frequent cause, followed by 19% with acute respiratory infections and 9% with neurological causes [12].

These data are therefore similar to those reported in this study, where the most frequently diagnosed underlying disease was gastroesophageal reflux (37.5 %), followed by lower respiratory infection, seizures, and inborn error of metabolism. Thus, GER, respiratory infections, and seizures may be common conditions to evaluate in infants with BRUE. It is important to emphasize that a broad and standard approach to testing and treatment for all patients with a BRUE/ALTE is not reasonable, and more recent publications suggest a stepwise approach, prioritizing the identification of conditions whose delayed diagnosis or treatment could affect outcomes [19].

Regarding the BRUE criteria, altered muscle tone was the most frequent criterion in this study, which differs from other reports, where the most frequent presenting symptoms were apnea or respiratory pause in 85 % of cases, followed by cyanosis in 70 % [12]. Other studies have reported that abnormal respiratory pattern is the most common manifestation, followed by altered muscle tone, in addition to prematurity in 14.6 % of patients with BRUE and 30.7 % with abnormal medical history [14], findings similar to those reported in this study.

Another important aspect to consider in the evaluation of patients with BRUE is the suspicion of

child abuse. In this study, family legal problems and changes in the relatives' accounts of the patient's event were reported; these aspects, in themselves, are not diagnostic criteria for child maltreatment or abuse, but they do constitute elements that require closer monitoring in that patient, given the suspicion that family dynamics may not be favorable. Child maltreatment may be subtle in these cases and requires a high level of suspicion. Doswell et al. [20] found physical examination findings related to trauma, and 0.3 % of the infants were diagnosed with physical abuse at the initial BRUE encounter. Of these, 57.1 % were high risk and 57.1% had a diagnosis of GER at discharge from their initial encounter.

Regarding the bivariate analyses, recurrence of the event was significantly associated with altered level of consciousness, high-risk BRUE, abnormal perinatal history, and the development of an underlying disease. Likewise, underlying disease was significantly associated with age younger than 60 days, high-risk BRUE, recurrence of the event, prematurity, and frequent regurgitation.

In the literature, one factor associated with recurrence is the presence of cyanosis, as described in a recent multicenter study [4]; this finding differs from the result of the present study, in which the BRUE characteristic associated with recurrence was altered level of consciousness. Although altered level of consciousness is difficult to define and characterize, both for the family or caregivers and for the physician's interpretation of the event, it is reasonable to consider that a decreased level of consciousness could indicate a clinical problem [21] or, in this case, a greater risk of recurrence, beyond the mechanisms involved in the alteration of consciousness. A history of previous BRUE episodes, which constitutes one of the high-risk BRUE criteria, has been associated with underlying diagnoses and recurrence of events [22]. It has also been described that the presence of at least one of the AAP high-risk criteria may increase the likelihood of event recurrence [18].

Most of the diseases diagnosed in low-risk BRUE are related to feeding problems and gastrointestinal diseases [6]. Regurgitation, especially in the context of GER, may cause apnea and hypoxia due to laryngospasm and aspiration, being the most frequent cause of ALTE/BRUE [23]. GER may be present in 32.8 % of infants diagnosed with ALTE [24] and in 24% of infants with BRUE [25], a proportion similar to the frequency of GER cases found in this study. However, frequent regurgitation was not present only in GER cases; it also occurred in infants without underlying disease and in infants with inborn errors of metabolism. Thus, regurgitation was associated with the development of an underlying disease in patients with BRUE, regardless of whether or not it was related to GER.

Recurrence was associated with the subsequent development of an underlying disease; this finding is similar to that described in the literature. The factors most frequently associated with underlying disease are age younger than 60 days, prematurity, abnormal medical history, changes in skin coloration or abnormal breathing, multiple events, and high-risk BRUE [4,6,14]. This is why the presence of event recurrence should alert the physician to the existence of an underlying condition that must be investigated.

This study had important limitations. Follow-up for each patient lasted 90 days after the event, which may have generated follow-up bias, since recurrences could have occurred after that period or an underlying disease might have been diagnosed later. It is also possible that the BRUE presentation and the diagnosis subsequently identified were unrelated in some patients and that the association between the diagnosis made and the BRUE event was overestimated in the absence of a causal link. This uncertainty represents an important challenge for BRUE research in general. This observation, together with the study design itself, did not allow for multivariable analysis. In addition, it should be taken into account that some caregivers who observe BRUE in their children or relatives do not seek medical care. Finally, despite having a sample with good statistical precision, it is possible that the study did not have sufficient power to detect other underlying diseases, considering that the sample size was small compared with multicenter studies.

Conclusions

BRUE had an incidence of 1.3 % of emergency visits; in addition, 9 % of patients developed an underlying disease, one-third had recurrence, and half were classified as high risk. A total of 5.1% were hospitalized, and no deaths were recorded. Likewise, the relevant history to be evaluated during the clinical history and the assessment of the index event may include prematurity, abnormal perinatal history, and frequent regurgitation, as well as each BRUE criterion. The most frequently diagnosed underlying diseases may be gastroesophageal reflux, respiratory

infections, and seizure disorders. The rate of admissions and hospitalizations may be low, but the performance of complementary tests that may not be necessary is striking, despite the recommendations on management and risk stratification provided by the AAP.

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Authorship contribution

ONR: conceptualization, formal analysis, methodology, software, supervision, review, editing, and final review of the manuscript.

MFC, TPC, DLS, FLC, RM, YY, TLR, SBT, JMV: data curation, investigation, resources, visualization, writing, drafting, and final review of the manuscript.

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