

Association between vomiting and brief resolved unexplained events in infants: experience from a Tertiary Care Center

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Abstract

Background: Gastroesophageal reflux disease (GERD)-related vomiting is a frequent cause of Emergency Department (ED) visits in infants; however, its role in brief resolved unexplained events (BRUE) remains unclear. Distinguishing physiological reflux from GERD-induced BRUE is challenging because descriptions of vomiting are often vague. This study examined the association between vomiting and BRUE, identified potential risk factors, and assessed whether vomiting requires further clinical evaluation.

Methods: This retrospective cohort study evaluated 147 infants under 1 year of age who presented with vomiting at the Pediatric ED of our University Hospital between 2018 and 2019. The data included demographics, clinical symptoms, vomiting characteristics, and final diagnoses. In addition to the primary analysis, a secondary analysis was conducted specifically on infants diagnosed with BRUE based on clinical presentation.

Results: A total of 147 infants with vomiting were included in the study, with a mean age of 6.19 ± 3.15 months. The majority were boys (60%), 25 (17%) left without being seen, and 122 (83%) underwent a full evaluation. Vomiting was often accompanied by fever (23%), apnea (3%), color change (5%), and altered level of consciousness (4%). Most infants were discharged (59%); 23 (16%) were admitted to the Pediatric Medical Ward, and 12 (8%) required Pediatric Intensive Care Unit (PICU) admission. Among the 13 infants with BRUE (9%), 10 (77%) had comorbidities, 6 (46%) were admitted to the Pediatric Medical Ward, and 4 (31%) required PICU admission. The most common BRUE diagnoses were gastritis (31%), bronchopneumonia (23%), and sepsis (23%).

Conclusion: Infants with vomiting should be carefully assessed for BRUE, particularly in the presence of other significant symptoms. Accurate event description is crucial for diagnosis. Larger studies are needed to optimize management, improve outcomes, and reduce unnecessary hospital admissions.

Keywords

Apparent life-threatening events, brief resolved unexplained events, vomiting, gastroesophageal reflux disease, infants.

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Introduction

The classification of unexplained distress in infants has evolved significantly over time. Initially, infants experiencing sudden, worrying episodes were classified as having sudden infant death syndrome, which was later redefined as an apparent life-threatening event (ALTE), and now as brief resolved unexplained events (BRUE) [1]. The American Academy of Pediatrics introduced the term BRUE in 2016, replacing the broader term ALTE to improve diagnostic specificity and clinical management [2]. However, distinguishing BRUE from episodes indicative of serious pathology remains a challenge [3]. Unlike ALTE, BRUE is a diagnosis of exclusion, meaning that no readily identifiable cause is found after the event. BRUE is a transient, self-limiting episode occurring in infants under 1 year of age and is characterized by altered breathing, consciousness, muscle tone, and/or skin color [2]. Historically, ALTE was defined as a caregiver-reported event involving apnea, cyanosis, muscle tone changes, choking, or gagging [4]. The transition from ALTE to BRUE aimed to establish a more structured evaluation approach, focusing on high-risk cases while reducing unnecessary investigations [2]. The incidence of ALTE and BRUE varies significantly, ranging from 0.46 to 10 per 1,000 live births [5]. Although these events are typically self-limiting, they often result in Emergency Department (ED) visits and parental distress, contributing to the overall healthcare burden [6]. Most infants with BRUE experience a benign clinical course;

however, certain underlying conditions – including airway, cardiac, gastrointestinal, genetic, infectious, neurological, and traumatic causes – must be carefully evaluated [6]. The American Academy of Pediatrics guidelines classify BRUE into low- and high-risk groups to guide clinical decision-making. Infants are considered low risk if they meet all of the following criteria: age greater than 60 days but less than 1 year, gestational age of at least 32 weeks with a post-conceptual age of at least 45 weeks, first BRUE episode lasting less than 1 minute, no cardiopulmonary resuscitation performed by a trained provider, and no relevant medical history or abnormal physical examination findings [7]. High-risk BRUE cases require further assessment and monitoring, as they may be associated with conditions, such as arrhythmias, metabolic disorders, child abuse, or infections [7].

Vomiting is a common reason for ED visits in infants under 1 year of age, and one possible cause is the gastroesophageal response in this population [6]. Differentiating between physiological gastroesophageal reflux and gastroesophageal reflux disease (GERD) that can trigger BRUE remains difficult. Despite the adoption of new terminology, GERD continues to be considered a possible trigger of BRUE, although its contribution remains uncertain [8-12]. Gastroesophageal reflux is a physiological process in which gastric contents pass into the esophagus and commonly occurs in infants. Conversely, GERD is a pathological process that leads to clinical symptoms or complications [13]. GERD has often been implicated in BRUE, accounting for approximately 50% of cases, although its causal relation remains unclear [13-17]. Vomiting caused by GERD is often described vaguely by caregivers, complicating its role in BRUE etiology [2]. A study investigating infants diagnosed with BRUE identified GERD as an explanatory factor in 33% of cases; however, no significant associations were found with variables, such as gestational age, sex, or mode of delivery [1]. Nonetheless, low birth weight has been linked to GERD-related BRUE, emphasizing the need for targeted evaluation in this subgroup [18]. Although GERD has traditionally been associated with BRUE, emerging evidence suggests that factors, such as low birth weight and feeding-related issues, may be stronger predictors than GERD alone [1].

Given the high prevalence of vomiting in infants and its frequent association with GERD, further investigation is warranted to determine its role as a potential predictor of BRUE. However, only

a few studies have examined this association in detail. Therefore, this study aimed to examine the relation between vomiting and BRUE in infants presenting to the Pediatric ED, identify potential risk factors contributing to BRUE episodes, and assess whether vomiting should prompt further clinical investigation.

Methodology

This retrospective cohort study evaluated all infants under 1 year of age who presented with vomiting and associated symptoms at the Pediatric ED of King Abdul-Aziz University Hospital in Jeddah, Saudi Arabia, between January 2018 and December 2019. Ethical approval for this study was obtained from the Biomedical Ethics Committee of King Abdul-Aziz University (Reference No.: 278-20), and the study was conducted in accordance with the principles outlined in the Declaration of Helsinki. Considering the retrospective nature of the study, parental consent was not required.

Infants were included if vomiting was the primary reason for admission; those who presented solely with fever, shortness of breath, or other symptoms without vomiting were excluded. A total of 147 infants met the inclusion criteria, of whom 25 left without being seen, and the remaining 122 underwent a full evaluation, including history taking, clinical examination, hospital admission, investigation, and treatment.

Data collection included demographic information, such as age and sex, as well as clinical variables, including the number of vomiting episodes per day, projectile versus non-projectile vomiting, final diagnosis, and disposition. BRUE was diagnosed in accordance with the 2016 clinical practice guidelines [2]. In addition to the primary cohort analysis, a secondary analysis was conducted specifically on infants diagnosed with BRUE. Their medical records were reviewed for additional data, including presentation details, associated symptoms, such as fever, cough, diarrhea, head trauma, apnea, cyanosis, altered level of consciousness (ALOC), choking attacks, number of BRUE episodes, and seizures.

Data analysis was conducted using the IBM Statistical Package for the Social Sciences® version 22.0. Continuous variables are expressed as means and standard deviations, whereas categorical variables are summarized as frequencies and percentages. This analysis focused on describing the clinical characteristics, final diagnoses, and

outcomes of infants who presented with vomiting in the Pediatric ED. Secondary analysis was performed on infants diagnosed with BRUE to further evaluate their demographic characteristics, clinical presentation, vomiting frequency, choking episodes, and final disposition.

Results

In total, 147 infants were included in the study, all of whom presented with vomiting as the primary symptom in the Pediatric ED. The mean age of the infants was 6.19 ± 3.15 months, and the majority were girls ($n = 88$, 60%), with boys accounting for 40% ($n = 59$). Most infants were born at term ($n = 140$, 95%), whereas 7 (5%) were preterm (**Tab. 1**). Among the infants included, 25 (17%) left

Table 1. Clinical characteristics of the infants with vomiting at the Pediatric Emergency Department (ED) ($n = 147$).

Characteristic		Value
Age (months)		6.19 (± 3.15)
Sex	Male	59 (40%)
	Female	88 (60%)
Birth term status	Term	140 (95%)
	Preterm	7 (5%)
Symptoms	Vomiting and associated symptoms	147 (100%)
	Fever	30 (20%)
	Cough $\pm$ shortness of breath	15 (10%)
	Projectile vomiting	32 (22%)
	Choking attacks $\pm$ gagging	32 (22%)
	Apnea	4 (3%)
	Change in colour	7 (5%)
	ALOC	6 (4%)
Frequency of vomiting	1 time	12 (8%)
	2 times	22 (15%)
	3 times	15 (10%)
	4 or 5 times	40 (27%)
	> 5 times	33 (22%)
Final disposition	Home	87 (59%)
	Admitted to the PICU	12 (8%)
	Admitted to the Pediatric Medical Ward	23 (16%)
	LWBS	25 (17%)

Numeric data are presented as mean (SD) and categorical data are presented as number (%).

ALOC: altered level of consciousness; BRUE: brief resolved unexplained event; CPR: cardiopulmonary resuscitation; GERD: gastroesophageal reflux disease; LWBS: left without being seen; PICU: Pediatric Intensive Care Unit.

without being seen, whereas the remaining 122 (83%) underwent full clinical evaluation, which included history taking, physical examination, assignment to a hospital bed, investigations, and treatment. Vomiting was accompanied by other associated symptoms in many infants, with fever observed in 30 (20%) and cough or shortness of breath in 15 (10%). The frequency of vomiting varied as follows: 12 infants (8%) vomited once, 22 (15%) twice, 15 (10%) thrice, 40 (27%) 4 or 5 times, and 33 (22%) more than 5 times per day. Projectile vomiting was noted in 32 infants (22%), and choking or gagging episodes were reported in 32 infants (22%) (**Tab. 1**). Other symptoms included apnea in 4 infants (3%), color change in 7 (5%), and ALOC in 6 (4%). Disposition refers to the outcome or status of a patient after evaluation and treatment in a healthcare setting. Most infants in our study (n = 87; 59%) were discharged after clinical evaluation and supportive care. However, 23 infants (16%) were admitted to the Pediatric Medical Ward, and 12 (8%) required Pediatric Intensive Care Unit (PICU) admission because of severe presentations. Additionally, 25 infants (17%) were discharged from the ED without observation (**Tab. 1**). The final diagnoses of infants presenting with vomiting varied. The most common causes were gastroenteritis (n = 39, 27%) and gastritis (n = 22, 15%) (**Tab. 2**). GERD was diagnosed in 9 infants (6%), whereas other infectious conditions included viral upper respiratory tract infection in 8 infants (5%), bronchopneumonia in 3 (2%), and sepsis in 2 (1%). More severe cases included those with septic shock (n = 1, 1%), hypovolemic shock (n = 2, 1%), and aspiration pneumonia (n = 1, 1%) (**Tab. 2**). Neurological and metabolic causes were rare, with hypoglycemia, seizures, and meningitis occurring in 1-2% of cases. Head trauma was documented in 5 infants (3%), whereas intestinal obstruction was diagnosed in 4 (3%).

Among the 147 infants, 13 (9%) met the clinical criteria for BRUE based on caregiver-reported events and clinical assessment by senior pediatric emergency staff (**Tab. 2**). The mean age of these BRUE cases was 3.6 ± 3.1 months, with an almost equal distribution of boys (n = 6, 46%) and girls (n = 7, 54%). Of the 13 infants with BRUE, 4 (31%) were born preterm, and 10 (77%) had underlying comorbidities (**Tab. 3**). Symptoms varied, with fever present in 3 (23%) infants, cough or shortness of breath in 3 (23%), and choking attacks in 4 (31%). Vomiting frequency was diverse, with 7 infants (54%) vomiting 4 or 5

Table 2. Final diagnosis of infants who presented with vomiting at the pediatric Emergency Department (ED) (n = 147).

Final diagnosis	N (%)
Viral URTI	8 (5%)
Otitis media	2 (1%)
Urinary tract infection	3 (2%)
Sepsis	2 (1%)
Septic shock	1 (1%)
Hypovolemic shock	2 (1%)
Bronchopneumonia	3 (2%)
Aspiration pneumonia	1 (1%)
Hypoglycemia	1 (1%)
Gastritis	22 (15%)
Gastroenteritis	39 (27%)
GERD	9 (6%)
Intestinal obstruction	4 (3%)
Infant colic	1 (1%)
Head trauma	5 (3%)
Shunt obstruction	1 (1%)
Meningitis	3 (2%)
Seizures	2 (1%)
BRUE	13 (9%)
LWBS	25 (17%)

BRUE: brief resolved unexplained events; GERD: gastro-esophageal reflux disease; LWBS: left without being seen; URTI: upper respiratory tract infection.

times per day and 3 infants (23%) vomiting more than 5 times per day. Apnea was documented in 4 infants (31%), whereas 7 (54%) experienced color changes and 7 (54%) experienced ALOC (**Tab. 3**). No patients required cardiopulmonary resuscitation, and the mean duration of hospital admission for infants with BRUE was 10.2 ± 5.4 days. Regarding final disposition, most cases required hospitalization. Six infants (46%) were admitted to the Pediatric Medical Ward, whereas 4 (31%) required PICU admission because of the severity of their presentations. Only 3 infants (23%) were discharged after 4 hours of observation in the ED, all diagnosed with gastritis requiring minimal intervention (**Tab. 3**).

The final diagnoses of BRUE cases revealed a mix of conditions, with gastritis being the most common (n = 4, 31%), followed by bronchopneumonia (n = 3, 23%) and sepsis (n = 3, 23%). Less frequent diagnoses included bronchiolitis, septic shock, and gastroenteritis (each: n = 1 [8%]) (**Tab. 4**). Notably, 2 BRUE cases were initially diagnosed as bronchopneumonia and gastritis but were later identified as GERD upon follow-up.

Table 3. Comprehensive clinical characteristics and final outcomes of 13 infants diagnosed with brief resolved unexplained events (BRUE).

Characteristic		Value
Age (months)		3.6 ($\pm$ 3.1)
Sex	Male	6 (46%)
	Female	7 (54%)
Birth term status	Term	9 (69%)
	Premature	4 (31%)
Comorbidities	No	3 (23%)
	Yes	10 (77%)
Symptoms	Febrile	3 (23%)
	Cough $\pm$ shortness of breath	3 (23%)
	Choking attacks $\pm$ gagging	4 (31%)
	Apnea	4 (31%)
	Change in color	7 (54%)
	ALOC	7 (54%)
Frequency of vomiting	1 time	1 (8%)
	2 times	1 (8%)
	3 times	1 (8%)
	4 or 5 times	7 (54%)
	> 5 times	3 (23%)
Number of choking attacks	0	10 (77%)
	1	1 (8%)
	2	1 (8%)
	3	1 (8%)
CPR needed		0 (0%)
Admission days		10.2 ($\pm$ 5.4)
Final disposition	Home 4 hours after ER observation	3 (23%)
	Admitted to the PICU	4 (31%)
	Admitted to the Pediatric Medical Ward	6 (46%)

Numeric data are presented as mean (SD) and categoric data are presented as number (percentage).

ALOC: altered level of consciousness; CPR: cardiopulmonary resuscitation; ER: Emergency Room; PICU: Pediatric Intensive Care Unit.

Table 4. Final diagnosis of patients who presented with brief resolved unexplained events (BRUE) during emergency (n = 13).

Final diagnoses of BRUE cases	N (%)
Bronchopneumonia	3 (23%)
Bronchiolitis	1 (8%)
Sepsis	3 (23%)
Septic shock	1 (8%)
Gastritis	4 (31%)
Gastroenteritis	1 (8%)

BRUE: brief resolved unexplained events.

Discussion

Vomiting and spitting in infants can be distressing for parents and caregivers, particularly when accompanied by concurrent infections or respiratory compromise. We retrospectively reviewed 147 infants who presented to the Pediatric ED with vomiting. Our findings highlighted that vomiting was frequently associated with other symptoms, including apnea, color change, gagging, choking, and respiratory distress (**Tab. 1**). The relation between ALTE or BRUE and GERD has been extensively studied; however, multiple studies have failed to establish a direct causal link [11]. This finding emphasizes the need for a more thorough review of the criteria used to assess vomiting in infants retrospectively. In our study, all the patients with a final diagnosis of GERD (9 out of 147 patients) exhibited mixed presentations of gastrointestinal and respiratory symptoms, which aligns with the known extraesophageal manifestations of GERD that can lead to respiratory compromise. Given the potential overlap in presentations, accurately distinguishing between GERD-related symptoms and those associated with BRUE is crucial for appropriate management. Infants with vomiting require a careful history, which should include intake and weight gain, followed by a complete examination, as well as infection screening tests if any red flags appear during presentation, while escalating imaging if required. We still have limited access to 24-hour pH-metry, which is the gold-standard diagnostic modality that helps rule out non-physiological gastroesophageal reflux.

The prevalence of BRUE varies across different studies, with European reports estimating a frequency between 0.6 and 5 per 1,000 live births, and another study reporting an incidence of 2.46 per 1,000 live births [12]. In our cohort, BRUE was identified in 13 of 147 infants who presented with vomiting, with 10 of these infants being $\leq$ 3 months old and 4 being preterm (**Tab. 3**). Additionally, comorbidities were identified in 10 of the 13 infants, including congenital heart disease, structural kidney abnormalities, and brain anomalies, with 2 infants having a history of complications during their Neonatal Intensive Care Unit stay. These findings emphasize the need for clinicians to carefully evaluate infants presenting with vomiting, especially those with underlying medical conditions, to rule out serious pathologies that may contribute to their symptoms. The revised BRUE criteria now include irregular breathing as

a consideration, acknowledging that hypoxemia during feeding can occur in young infants because of immature swallowing coordination. This further complicates the evaluation of vomiting in infants, as GERD can lead to airway obstruction, laryngeal spasm, and aspiration, making it a potential but not definitive contributor to BRUE [19-21].

One of the key advancements in BRUE classification has been the validation of risk stratification models, such as the study by Colombo et al., which classified infants with ALTE into no BRUE, low-risk BRUE, and high-risk BRUE categories over a 10-year follow-up period [22]. This study helped refine the diagnostic approach and ensure appropriate follow-up of infants at risk of recurrence or secondary diagnoses. In our study, only 2 patients diagnosed with BRUE were later referred to the Pediatric Gastroenterology Department for GERD evaluation, reinforcing that GERD may not be a primary factor in BRUE. This supports the importance of applying BRUE diagnostic criteria based on clinical history and examination, while ensuring that secondary diagnoses are made when symptoms persist, such as cough or shortness of breath. Infants with persistent symptoms require further evaluation beyond BRUE, as highlighted in a Swiss Tertiary Hospital study of 65 infants diagnosed with ALTE/BRUE. This study found that only 15% of cases met low-risk BRUE criteria, indicating that most infants underwent extensive investigations with no clear underlying cause [18]. These findings highlight the importance of reducing unnecessary hospital admissions and focusing on essential diagnostic testing through appropriate risk stratification.

Recent research has also explored GERD and oropharyngeal dysphagia as potential risk factors for recurrent BRUE episodes and hospital readmissions. This emphasizes that more efforts are needed to explore BRUE presentations mimicking GERD. A multicenter retrospective study of 17,500 infants found that 34% were diagnosed with GERD and 2% had oropharyngeal dysphagia [23]. Infants diagnosed with GERD had a significantly higher risk of repeat hospital visits than those with oropharyngeal dysphagia ($p < 0.001$). Despite the frequent prescription of acid suppression therapy in 12% of cases (increasing to 26% in some hospitals), no evidence supports its effectiveness in reducing hospital readmissions. These findings suggest that feeding difficulties, rather than GERD, may play a more significant role in BRUE pathophysiology. The overuse of acid suppression therapy without

proven benefits raises concerns regarding the need for alternative management strategies, such as feeding modifications and parental education, to reduce unnecessary interventions.

Further evidence of BRUE risk factors was provided in a study of 255 BRUE cases, in which 45 infants experienced recurrence, and 23 were diagnosed with severe conditions, primarily apnea or central hypoventilation [3]. Premature birth and prolonged fasting were identified as significant predictors of severe pathology, reinforcing the need for individualized risk assessment. Although BRUE is typically considered benign and self-limiting, clinicians must remain vigilant when ruling out life-threatening conditions and secondary diagnoses that require intervention. This aligns with our study's findings, where most BRUE cases required hospital admission, including 6 infants admitted to the Pediatric Medical Ward and 4 who required PICU admission. Only 3 infants were discharged after 4 hours of observation in the ED, all of whom had gastritis and required minimal intervention. This suggests that, while many BRUE cases resolve spontaneously, some infants present with more complex symptoms, necessitating further evaluation and monitoring.

The diversity of final diagnoses in our study further supports the need for careful assessment of infants presenting with vomiting. Conditions ranged from gastrointestinal disorders – such as gastroenteritis (27%) and gastritis (15%) – to respiratory infections, including viral upper respiratory tract infections (5%) and bronchopneumonia (2%) (**Tab. 2**). Neurological and metabolic causes, including seizures, hypoglycemia, and meningitis, are less common but still account for a small proportion of cases. The broad spectrum of underlying conditions highlights the importance of a thorough diagnostic approach in infants with vomiting, as multiple underlying causes can present with overlapping symptoms.

Future research should focus on refining risk-stratification tools to better differentiate between benign BRUE cases and those requiring further investigation. Prospective studies are needed to explore the role of GERD, feeding difficulties, and other factors contributing to BRUE. The effectiveness of acid suppression therapy has not been widely validated nor consistently evaluated. Alternative management strategies, including feeding interventions and parental guidance, should be further explored as potential approaches to reduce hospital readmissions and improve patient

outcomes. Ultimately, although BRUE remains a challenging diagnosis, applying standardized diagnostic criteria, ensuring appropriate risk stratification, and investigating secondary causes will improve clinical decision-making and optimize care for affected infants. These recommendations help clinicians reach an optimal conclusion to distinguish critically straightforward cases from those with secondary causes.

Limitations

This study had several limitations. The retrospective design and small sample size may have limited the generalizability of the findings. Additionally, this study focused only on BRUE cases that presented to the ED and excluded potential cases from Outpatient Clinics. Furthermore, emphasizing vomiting as the primary presenting symptom may have limited the comprehensive evaluation of other potential causes and factors contributing to BRUE. Although the findings were clinically significant, statistical analysis using the Chi-square test showed no significant associations ($\chi^2 = 3.51 \times 10^{-31}$, $p = 1.0$), suggesting that observed trends may have occurred by chance. Larger prospective studies are needed to validate these findings and explore additional risk factors.

Conclusions

Our findings emphasize the importance of thoroughly evaluating infants presenting with vomiting for possible BRUE, particularly those with associated symptoms, such as apnea, color changes, or choking. Accurate event descriptions and post-event assessments are crucial for appropriate diagnosis and management. Given the ongoing uncertainty surrounding the role of GERD in BRUE, prospective studies are needed to identify the causative factors and refine risk stratification. Further research should explore the impact of gastrointestinal symptoms, optimize discharge criteria, and assess alternative management strategies to improve outcomes and reduce unnecessary hospital admissions. Lastly, frequent pediatric emergency visits with complaints affecting growth require further evaluation by pediatric gastroenterologists in Tertiary Centers.

Declaration of interest

The Author declares that there is no conflict of interest.

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