Objective: A brief resolved unexplained event (BRUE) in infancy is a common reason for visiting the emergency department. However, little is known about the long-term outcomes of such an event. This study evaluates future mortality, morbidity, and/or developmental outcome after a BRUE.

Methods: A single-center retrospective study performed in 2009 to 2013 included 87 hospitalized infants (<1 year old) fitting the American Academy of Pediatrics' criteria of a lower-risk BRUE, with 2 exceptions: no time limit to duration of episode and no age limit of ≥60 days. Hospitalized infants were followed up for up to 5 years via a telephone questionnaire to assess mortality rates, developmental delay, neurological/cardiovascular morbidity, and future hospitalizations.

Results: Most infants (94%) who experienced a BRUE were hospitalized before 6 months of age. No cases of mortality occurred. In terms of developmental outcome, 1 child (1.15%) was diagnosed as having a global developmental delay and 12 (13.7%) with a language delay, similar to prevalence rates by age in the United States. Three children (3.4%) were diagnosed as having an autism spectrum disorder, with higher prevalence rates than the global average. Simple febrile and nonfebrile seizures were seen at a rate similar to the general population. None of the children developed cardiovascular disease. Rehospitalization occurred in 22% of cases: 90% for common acute pediatric causes and 10% for recurrent choking events secondary to gastroesophageal reflux disease.

Conclusions: Low-risk hospitalized infants younger than 1 year who experienced a BRUE seem to generally have an excellent prognosis.

Key Words: brief resolved unexplained episode (BRUE), infants, developmental outcome

A n episode described by a caretaker as a abrupt change in color or tone, loss of consciousness, altered responsiveness, or transient respiratory distress in an infant, usually younger than 1 year, is a frequent motive for visiting the emergency department. In the past, such an event might have been considered a low-risk "apparent life-threatening event" (ALTE). Most recently, the American Academy of Pediatrics (AAP) suggested modifying the definition of such an event as a brief resolved unexplained event (BRUE) defined as "an event occurring in an infant <1 year of age when the observer reports a sudden, brief and now resolved event described by a caretaker as an abrupt change in color or tone, loss of consciousness, altered responsiveness, or color or tone, loss of consciousness, altered responsiveness, or transient respiratory distress in an infant, usually younger than 1 year, is a frequent motive for visiting the emergency department.

Although a number of studies have investigated the short-term consequences of ALTE and subsequently the need for further workup and hospitalization, there is scant knowledge as to the long-term consequences after the discharge of an infant after a BRUE, differing from an ALTE, among other reasons, in that resuscitative or stimulatory measures are not performed and the episode is not considered "life-threatening."

The goal of this study was to evaluate the long-term outcome of children after a BRUE occurring in a lower-risk infant younger than 1 year, but yet severe enough that a clinician considered it necessary to hospitalize the infant. Long-term outcome included an assessment for future mortality/morbidity, developmental delay, or development of other cardiovascular/neurological deficits.

METHODS

This was a single-center retrospective study conducted at the Schneider Children's Medical Center of Israel, an urban, academic, pediatric tertiary-care center, handling >54,000 emergency department visits per year. Infants 1 year or younger hospitalized for an episode defined as a BRUE, from 2009 to 2013, were included in this study. Being that a BRUE is, as yet, not a codable diagnosis, patient records were searched for a chief complaint deemed by the authors as most likely to represent an episode of BRUE, namely, "respiratory distress,” “cyanosis,” “suspected choking,” “hypotonia episode,” or “altered level of consciousness.” Gastroesophageal reflux was not used as a search term because the presence of this condition is an exclusion factor for a BRUE. Patients were included if, upon further inspection of their hospitalization record, they fit the current clinical definition of a BRUE, where the episode was brief, and had rapidly resolved and if no qualifying explanation was given for the event (eg, gastroesophageal reflux, cough, fever, respiratory difficulties, and feeding difficulties).

Patients included in this study fit the “lower-risk” stratification, as per the AAP Clinical Practice Guidelines, with 2 exceptions: the length of the event was not limited to <1 minute, and there was no age limit of >60 days for inclusion. Because this was a retrospective study, it was not possible to accurately assess the duration of the episode as ≤1 minute. In addition, because this study was performed on hospitalized infants, most study participants were younger than 2 months, and thus, the age limit was not set. Patients were excluded if they had a history of significant prematurity (born at <32 gestational weeks) or diagnosed having one of the following: chronic heart disease, congenital neurological disease, or a chronic medical condition diagnosed before hospitalization for the BRUE episode.

Data were collected from the patient's electronic medical records and included demographic and clinical details of the infant's hospitalization due to the BRUE event. A follow-up investigation was performed via a telephone questionnaire with the infant's caretaker after obtaining informed consent.
telephone questionnaire was conducted at a single time from 6 months after the event and up to 5 years after the initial hospitalization. The follow-up questionnaire was developed by the authors and consisted of 22 open-ended questions performed by a pediatrician (1 of the 2 study authors). By using the questionnaire, we were able to determine whether there had been further hospitalizations (for a BRUE and/or other causes) and/or if the child had developed a chronic disease, developmental delays/neurological deficits, and/or other medical conditions. The study was approved by our institution’s medical ethics committee.

RESULTS

During the 5-year period between 2009 and 2013, 150 patients hospitalized at the Schneider Children’s Medical Center of Israel were categorized as having experienced a BRUE. Thirty children were excluded from the study because of prematurity (gestational age of ≤32 weeks) or a chronic disease diagnosed before hospitalization. Of the 120 remaining children, 87 were available for follow-up via a telephone questionnaire. Of the 33 children unavailable for follow-up, the caregiver of one child refused to participate in the study, and the remaining children could not be reached.

Of the children remaining in the study, 35 (40.2%) were male and 52 (59.8%) were female. Preterm infants (33–36 gestational weeks) comprised 13.7% of the study participants (n = 12), of whom 25% were boys and 75% were girls. The ages of the infants at hospitalization are shown in Figure 1. Most of our patients were neonates: 84% were 2 months or younger. Overall, 94% were younger than 6 months. The chief complaint for which the patient sought care in the emergency department is shown in Table 1.

Median age at the time of the follow-up questionnaire was 42 months (ranging from 8 to 64 months; Table 2).

The results of the developmental consequences after a BRUE that required hospitalization are summarized in Table 3. Overall, of the 87 children in our study, 1 was diagnosed as having global developmental delay by professional neurological assessment. A verbal delay was reported in 12 children, 13.7% of the study population, comprising 9 boys and 3 girls. A verbal delay was diagnosed by a pediatric neurologist/developmental pediatrician and reported by the caretaker. Verbal delay was seen in 3 children 2 years or younger, in 2 children aged 3 years, in 2 children aged 4 and in 5 years, and in children aged 5 years. No child exhibited fine- or gross-motor delay, as assessed by a pediatric neurologist/developmental specialist and reported by the caregiver. Three children were diagnosed as having an autistic spectrum disorder (1 boy and 2 girls), representing 3.45% of the study population. Most children (81.6%) in our study developed normally. Seizures were recorded in 3 cases (3.45%)—simple febrile seizures in 2 children (2.3% of study population) and nonfebrile seizures in 1 child (1.15%). There were no reported cases of cardiovascular disease on follow-up.

After hospitalization for a BRUE, 22% of the patients experienced recurrent hospitalization (a total of 19 hospitalizations), ranging from 1 month to 5 years after hospitalization for a BRUE. The causes for most of the hospitalizations included common pediatric ailments, that is, diarrhea, upper respiratory infections, bronchiolitis, urinary tract infections, and breath-holding spells. There was a single case of aseptic meningitis, without any neurological consequences. Two children were rehospitalized because of choking events; in both cases, the etiology of the choking events was gastroesophageal reflux.

It is important to note that there were no cases of mortality during our short- and long-term follow-up. Furthermore, no cases

![FIGURE 1. Number of infants hospitalized for a BRUE by age, in months. BRUE indicates brief resolved unexplained event.](image)

| Infants Hospitalized for BRUE, per age (in months) |
|----------------------------------|
| AGE (IN MONTHS) | NUMBER HOSPITALIZED |
| 1 or less | 62 |
| 2 | 13 |
| 3 | 7 |
| 4 | 1 |
| 5 | 1 |
| 6 | 0 |
| 7 | 0 |
| 8 | 3 |
| 9 or more | 2 |

![TABLE 1. Chief Complaint Upon Presentation to the Emergency Department](image)

| Infants Presented With | n (%) |
|------------------------|-------|
| Cyanosis or pallor     | 28 (32) |
| Absent, decreased, or irregular breathing | 46 (53) |
| Sudden marked changes in tone | 6 (7) |
| Altered responsiveness | 7 (9) |

![TABLE 2. Number of Children Per Age (in Months) at Follow-Up Telephone Questionnaire](image)

| Age (in Months) | <12 | 12–23 | 24–35 | 36–47 | 48–59 | >60 |
|----------------|-----|-------|-------|-------|-------|-----|
| n             | 1   | 13    | 20    | 21    | 30    | 2   |
| %             | 1   | 15    | 23    | 24    | 35    | 2   |
Developmental Consequences in 87 Children After a BRUE During Infancy

| Global Developmental Delay | Verbal Delay | Autism Spectrum Disorders | Motor Developmental Delay | Normal Development |
|----------------------------|-------------|--------------------------|--------------------------|--------------------|
| n                          | 1           | 12                       | 3                        | 0                  | 71                 |
| % (95% CI)*                | 1.15 (0.03–4.20) | 13.8 (7.34–21.74) | 3.45 (0.07–8.15) | 0 (0–4.15) | 81.6 (71.86–88.98) |

*Fisher exact 95% confidence interval.
BRUE indicates brief resolved unexplained event.

were found where a BRUE was the first sign of chronic heart or lung disease.

**DISCUSSION**

The present study describes the long-term follow-up of young low-risk infants hospitalized due to a BRUE. During the 5-year study period, BRUE-related hospitalizations comprised 1.2% of all hospitalizations of infants 1 year or younger in a pediatric department, this being less than the 2% noted in previous ALTE studies.5,6 In our study, most of the participants were young infants: 94% were younger than 6 months, in congruence with previous ALTE studies,5 which is possibly due to the fact that infants in the younger age groups were more likely to be hospitalized than older infants.

In terms of neurological consequences, a previous study noted that 4.9% of infants hospitalized for ALTE had adverse neurological outcomes, including chronic epilepsy and a developmental delay.7 In our study population, 2.3% had experienced febrile seizures and 1.15% nonfebrile seizures. This is quite similar to the prevalence for febrile and nonfebrile seizures, respectively, in the general population.2 Furthermore, the prevalence of a global developmental delay in our study was 1%, near the global prevalence rate, ranging from 1% to 3% of the total population.15

In terms of verbal development in the United States, it is estimated that 10% to 15% of those younger than 2 years and 4% to 5% of those younger than 3 years are diagnosed as having verbal delay,14 and approximately 6% to 8% of school children are diagnosed with language impairments.15 In our study, 3 patients (3.4%) at age 2 years and 2 (2.3%) patients at age 3 years were diagnosed as having verbal delay. Similarly, 5 patients (5.7%) at age 5 years had a specific language impairment, similar to that found in the general population, but had outgrown the impairment when they reached school age. As in other studies,15 a male preponderance was noted in our study as well (9/12 cases).

It is also worth noting that in our study, there was a relatively large percentage (3.4%) of patients subsequently diagnosed as having an autism spectrum disorder as opposed to the global average of 1.3%.16 Given the relatively small number of participants in our study, future investigations should be performed to confirm this relationship. Moreover, the true global prevalence of this disorder remains quite dubious.

We found that a BRUE, even one considered severe enough to lead to hospitalization upon evaluation in the emergency department by a trained clinician, is not an ominous sign predicting the future development of severe neurological deficits, developmental delay, or other chronic diseases. Moreover, these findings are true even when the hospitalized infants did not completely fulfill the lower-risk stratification of the AAP’s Clinical Practice Guidelines requiring that a BRUE episode be of a short duration (<1 minute) and does not appear in neonates (infants >60 days old). As such, it is important to note that our findings are in contrast to the bleak long-term consequences reported after ALTE including death in 1.1% of patients after discharge,10 chronic epilepsy in 3.6%,7 motor delay, severe learning disabilities in 7.1%,13 and minor developmental delay in up to 29%.17

Our study had several limitations. First, it is a retrospective study, limiting some of the data available for analysis. Second, the diagnosis of a “BRUE” is not a codable diagnosis, and therefore, a search was made for symptoms at admission that best fit the criteria of a BRUE, which might have led to a potential loss of patients who would have otherwise been enrolled in the study. Third, approximately 25% of the patients in our study were lost to follow-up. Fourth, data regarding a developmental delay or medical condition, although diagnosed by a clinician, were gathered via parental report, comprising a possible reporting bias. Lastly, the period from discharge for a BRUE hospitalization to the follow-up telephone questionnaire varied. Most children (61%) were followed up until the age of 3 years or more (Table 2). However, it is possible that the participating children might not have developed any adverse events during the study period but rather at a later age.

In conclusion, our study suggests that hospitalized infants younger than <1 year who experienced a BRUE seem to have a generally excellent prognosis, no different from the general pediatric population. Further prospective studies of a larger pediatric population of children visiting the emergency department are warranted.

**ACKNOWLEDGMENT**

The authors thank Mrs Phyllis Curchack Kornspan for her editorial services.

**REFERENCES**

1. Tieder JS, Bonkowski JL, Etzel RA, et al. Brief resolved unexplained events (formerly apparent life-threatening events) and evaluation of low-risk infants. *Pediatrics*. 2016;137:e20160590.
2. Tieder JS, Altman RL, Bonkowski JL, et al. Management of apparent life-threatening events in infants: a systematic review. *J Pediatr*. 2013;163:94–99.
3. Kaji AH, Claudius I, Santillanes G, et al. Apparent life-threatening event: multicenter prospective cohort study to develop a clinical decision rule for admission to the hospital. *Ann Emerg Med*. 2013;61:379–387.
4. Mittal MK, Sun G, Barren JM. A clinical decision rule to identify infants with apparent life-threatening event who can be safely discharged from the emergency department. *Pediatr Emerg Care*. 2012;28:599–605.
5. McGovern MC, Smith MB. Causes of apparent life threatening events: a systematic review. *Arch Dis Child*. 2004;89:1043–1044.
6. Kiechl-Kohlendorfer U, Hof D, Peglow UP, et al. Epidemiology of apparent life-threatening events. *Arch Dis Child*. 2005;90:297–300.

7. Bonkowsky JL, Guenther E, Filloux FM, et al. Death, child abuse and adverse neurological outcomes of infants after an apparent life-threatening event. *Pediatrics*. 2008;122:125–131.

8. Hoki R, Bonkowsky JL, Minich LL, et al. Cardiac testing and outcomes in infants after an apparent life-threatening event. *Arch Dis Child*. 2012;97:1034–1038.

9. Claudius I, Keen T. Do all infant with apparent life threatening events need to be admitted? *Pediatrics*. 2007;119:679–683.

10. Kant S, Fisher JR, Nelson DG, et al. Mortality after discharge in clinically stable infants admitted with a first-time apparent life-threatening event. *Am J Emerg Med*. 2013;31:730–733.

11. DiMario FJ Jr. Apparent life-threatening events: so what happens next? *Pediatrics*. 2008;122:190–191.

12. Hauser WA. The prevalence and incidence of convulsive disorders in children. *Epilepsia*. 1994;35:1–6.

13. Shevell M, Ashwal S, Donley D, et al. Practice parameter: evaluation of the child with global developmental delay: report of the Quality Standards Subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Society. *Neurology*. 2003;60:367–380.

14. Stein MT, Parker S, Coplan J, et al. Expressive language delay in a toddler. *J Dev Behav Pediatr*. 2001;22:S99–S103.

15. Tomblin JB, Records NL, Buckwalter P, et al. Prevalence of specific language impairment in kindergarten children. *J Speech Lang Hear Res*. 1997;40:1245–1260.

16. Autism and Developmental Disabilities Monitoring Network Surveillance Year 2008 Principal Investigators, Centers for Disease Control and Prevention. Prevalence of autism spectrum disorders—Autism and Developmental Disabilities Monitoring Network, 14 sites, United States, 2008. *MMWR Surveill Summ*. 2012;61:1–19.

17. Milioti S, Einspiel C. The long-term outcome of infantile apparent life-threatening event (ALTE): a follow-up study until mid-puberty. *Neuropediatrics*. 2005;36:1–5.