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Research Article

ETIOLOGY OF APPARENT LIFE-THREATENING EVENT IN INFANTS AT NATIONAL GUARD HEALTH AFFAIRS IN RIYADH, SAUDI ARABIA

Mohammad Khalaf Almutairi¹, Abdulmajeed Khaled Alkharji², Wael Abdullah Alhelal²,
Salman Ali Alqahtani², Meshal Mohammed Altalha²

¹Consultant, Pediatric emergency medicine department, Ministry of National Guard - Health
Affairs, KSA

²Medical Students, Faculty of Medicine, King Saud bin Abdulaziz for Health Sciences
University, KSA

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Abstract:

Background: An apparent life-threatening event (ALTE) is not a specific disorder. It is the sudden occurrence of certain alarming symptoms such as prolonged periods of no breathing (apnea), change in color or muscle tone, coughing, and gagging in children under 1 year of age. **Method and materials:** This is a retrospective cross-sectional study was conducted in King Abdullah Specialized Children Hospital in Riyadh. The study included 46 infants out of 1660 ED admissions that met the criteria from Feb2016- Feb2018, 63% males and 37% females and the majority 76.1% were 1-3 months. **Results:** Our study found that half of cases reported idiopathic causes followed by gastro-esophageal reflux disease (GERD) 19.6%, respiratory distress syndrome (RDS) 10.9%. Also, we found that there was significant relation between causes ALTE and smoking in parents ($p=0.04$). **Conclusion:** The study concluded that the most common causes of ALTEs were unknown.

Keywords: ALTE; Pediatrics; Saudi Arabia, Emergency

Corresponding author:

Mohammad Khalaf Almutairi,
Consultant, Pediatric emergency medicine department,
Ministry of National Guard - Health Affairs, KSA

QR code



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INTRODUCTION:

Apparent life-threatening event (ALTE) is a group of symptoms presenting in infants, that may frighten the caregiver, which is associated with physiological abnormalities that resolves in a short period, and usually before the arrival to the emergency department [1,2]. ALTE often presents with breathing difficulties for more than 20 seconds like apnea and/or irregular breathing, it could also be accompanied with cyanosis and pallor. Other than breathing difficulties, ALTE can present with changes in muscle tone, jerking movements, choking, gagging, and/or coughing [3,4]. Other terms for ALTE that have been used are near miss sudden infant death syndrome (SIDS) but was replaced recently due to the weak evidence of the association between ALTE and SIDS. Another term that the American Academy of Pediatrics recommend using is brief resolved unexplained events (BRUE) [1,5].

ALTE presentation in the Emergency Department was found to be around 0.5% to 6% of all visits to the ED, estimated at 2.4 in every 1000 live births [6,7,8]. In neonates, the incidence of ALTE was around 1.57 to 2.46 in every 1000 live births worldwide [9,10]. ALTE is responsible for 2.3% of children and infant hospitalization [11]. ALTE patients are 50% to 80% infants younger than three months old [1,12,13]. Episodes with known etiology comprise about half of all presentations. Gastrointestinal about 50% of the underlying cause of ALTE, neurologic 30%, respiratory problems 20%, cardiovascular 5%, metabolic and others are less than 5%. To be more precise, ALTE is not a disease it is a presentation of symptoms instead, therefore, a high attention and effort must be spent to identify the underlying cause, so during epidemiological studies, occasional ALTE is a consequence of gastroesophageal reflux disease, lower respiratory infections, and seizures [14,15,16]. In Saudi Arabia, a study connected vitamin D deficiency in early infancy to be associated with ALTE or recurrent ALTE secondary to severe hypocalcemia because of maternal infant vitamin D deficiency [17].

Most of infants presented with ALTE in Pediatrics Emergency Department or hospitalized, were below the age of 2 months and half of the patients showed normal findings upon physical examination [18,19]. There were some studies done that showed some predispositions for ALTE that included maternal smoking, male gender, gestational age, and very low birth weight. Another factor of ALTE and the most dangerous for the child was home abuse and neglect [1,20]. The aim of this study is to determine the etiology of apparent life threatening event and investigate the association between ALTE and

demographic association among infants in National Guard Health Affairs, King Abdulaziz Medical City in Riyadh.

MATERIALS AND METHODS:**Study Design**

A retrospective cross-sectional study was performed in 46 infants under the age of two years, admitted to the King Abdullah Specialist Children Hospital (KASCH) after an ALTE during the 24-months prior to Feb 2018. This study design is selected to identify if there is any connection between ALTE and underlying disease and to determine the incidence rate of ALTE in pediatric Emergency Department in KASCH.

KASCH Emergency Department has 4 units; resuscitation unit, acute care unit, triage unit, and urgent care unit. The number of beds in each unit is 11, 23, 6 and 16, respectively, with total of 56 beds. Approximately (10,500) pediatric patients per month presented to the ED and approximately 30 of whom are admitted to resuscitation unit with symptoms of ALTE, keeping in mind that other units will have patients with ALTE symptoms less severe or admitted a short while after the attack.

Sample Size

Study population will be pediatrics under the age of 2 years admitted to KASCH. The sample will be all patient with ALTE.

The estimated sample size is 384 confidence level is 95% and margin of error of 5% and the expected prevalence will be 50% for ALTE.

Sampling Technique

Non-probability consecutive sampling technique was chosen since patient population with ALTE is very small.

Data Collection

The data collection has been done through review of records of patient diagnosed with ALTE from the medical records department in KASCH by the co-authors and stored on a secure device. The language used for forms of data collection was English.

The data that has been collected from the records was MRN, demographic data, length of hospitalization, management and other medical conditions and the main outcome variable collected was the incidence rate of ALTE in the pediatric population of KASCH.

Statistical Analysis

The data were compiled, checked for completeness, and analysed using the Statistical Package for the

Social Science (SPSS), version 22 (IBM SPSS Statistics for Windows, IBM Corp., Armonk, NY). Qualitative variables were described by frequencies and percentages. Descriptive analysis involved Chi-squared test of association for categorical variables and Fisher's exact test and Student's *t*-test for continuous variables at 5% level of significance.

Ethical considerations

All ethical issues were taken into consideration, including the confidentiality and privacy of data as patient name will not be disclosed and MRN will only be kept as reference.

RESULTS:

Table 1: show the socio-demographic and ALTE related characteristics of the studied infants. The study includes 46 participants, 63% males and 37% female. The majority 76.1% were 1-3 months. Other diagnosis found in 47.8% of cases and 21.7% had risk factors of ALTE. Father's age was 30-40 years in 32.6% of cases. 19.6% of cases reported family history (chronic illness, surgeries). More than half 52.2% had 1-3 children in family and 82.6% do not

know the number of miscarriages, gestational age was ≥ 37 weeks in 67.4% of cases. The majority 93.5%, 97.8% and 89.1% had no travel history, family history of anemia and family history of atopy or asthma, respectively.

Table 2: show the percentage distribution of causes of admission due to ALTE. Our study reported; idiopathic by 50% followed by gastro-esophageal reflux disease (GERD) 19.6%, respiratory distress syndrome (RDS) 10.9%. Cardiac caused and dysmorphism reported by 6.5% for each of them. Neo natal sepsis and neurological disorder 4.3%. and only 2.2% for each of bronchopulmonary dysplasia (bpd), renal problem, glioblastoma multiform (gbm) +ve and hernia.

Table 3: show the relationship between causes ALTE and related risk factors among the studied infants. We found that there were no significant correlations between causes ALTE and age, gender, weight, gestational age, delivery methods, Apgar score and children were twins or triplet ($p > 0.05$) but, there were significant relation with smoking in parents ($p = 0.04$).

Table 1: socio-demographic and ALTE related characteristics of the studied infants

Variables	No.	%
Gender		
Male	29	63.0
Female	17	37.0
Total	46	100.0
Age groups (in months)		
< 1 (neonate)	8	17.4
1-3	35	76.1
>3	3	6.5
Other diagnosis		
No or unknown	24	52.2
Yes	22	47.8
Risk factors		
No or unknown	36	78.3
Yes	10	21.7
Father's age		
Unknown	14	30.4
<20	1	2.2
20-30	5	10.9
30-40	15	32.6
40-50	9	19.6
>50	2	4.3
Living in Riyadh		
0	40	87.0
1	6	13.0
Family history (chronic illness, surgeries)		

No or unknown	37	80.4
Yes	9	19.6
Number of children in the family		
1-3	24	52.2
4-6	15	32.6
>6	1	2.2
No or unknown	6	13.0
Number of miscarriage		
No or unknown	38	82.6
One	6	13.0
Two	1	2.2
Time since last birth		
Unknown	21	45.7
<1	1	2.2
1-2	8	17.4
3-4	13	28.3
>4	3	6.5
Travel history		
No or unknown	43	93.5
Yes	3	6.5
Gestational age (weeks)		
Unknown	4	8.7
<37	11	23.9
≥37	31	67.4
Delivery method		
Unknown	1	2.2
SVD	34	73.9
CC	11	23.9
Complications		
No or unknown	39	84.8
Yes	7	15.2
Pre-eclampsia or eclampsia		
No or unknown	45	97.8
Yes	1	2.2
Placental issue		
No or unknown	44	95.7
Yes	2	4.3
Family history of anemia		
No or unknown	45	97.8
Yes	1	2.2
Family history of atopy or asthma		
No or unknown	41	89.1
Yes	5	10.9
Twins or triplet		
No or unknown	42	91.3
Yes	4	8.7
Length of stay in NICU (in days)		
One	20	43.5
Two	16	34.8
≥ three	10	21.7

Table 2: Percentage distribution of causes of admission due to ALTE

Causes of admission due to ALTE	No.	%
Idiopathic	23	50.0
Gastro-esophageal reflux disease (GERD)	9	19.6
Respiratory distress syndrome (RDS)	5	10.9
Cardiac	3	6.5
Dysmorphism	3	6.5
Neonatal sepsis	2	4.3
Neurological disorder	2	4.3
Bronchopulmonary dysplasia (bpd)	1	2.2
Renal problem	1	2.2
Glioblastoma multiforme (gbm) +ve	1	2.2
Hernia	1	2.2
Total	46	100

Table 3: relationship between causes ALTE and related risk factors among the studied infants

Variables	Responses	Causes of ALTE							Total (N=46)	P value
		GERD (n=9)	Cardiac (n=3)	Dysmorphism (n=3)	Hernia (n=1)	RDS (n=5)	Neurological (n=2)	Idiopathic (n=23)		
Age groups (in months)	< 1	2	1	1	0	0	0	4	8	0.348
		22.2%	33.3%	33.3%	.0%	.0%	.0%	17.4%	17.4%	
	1-3	5	1	2	1	5	2	19	35	
		55.6%	33.3%	66.7%	100%	100%	100%	82.6%	76.1%	
	>3	2	1	0	0	0	0	0	3	
		22.2%	33.3%	.0%	.0%	.0%	.0%	.0%	6.5%	
Gender	Male	6	2	1	1	2	2	15	29	0.657
		66.7%	66.7%	33.3%	100%	40.0%	100.0%	65.2%	63.0%	
	Female	3	1	2	0	3	0	8	17	
		33.3%	33.3%	66.7%	.0%	60.0%	.0%	34.8%	37.0%	
Weight (Grams)	No or unknown	1	0	0	0	1	0	6	8	0.206
		11.1%	.0%	.0%	.0%	20.0%	.0%	26.1%	17.4%	
	1000-2500	3	0	2	1	3	1	8	18	
		33.3%	.0%	66.7%	100%	60.0%	50.0%	34.8%	39.1%	
	2500-3500	5	2	1	0	1	1	9	19	
		55.6%	66.7%	33.3%	.0%	20.0%	50.0%	39.1%	41.3%	
	>3500	0	1	0	0	0	0	0	1	
		.0%	33.3%	.0%	.0%	.0%	.0%	.0%	2.2%	
Gestational Age (weeks)	Unknown	2	1	0	0	0	0	1	4	0.563
		22.2%	33.3%	.0%	.0%	.0%	.0%	4.3%	8.7%	
	26-36	2	1	2	0	1	0	5	11	
		22.2%	33.3%	66.7%	.0%	20.0%	.0%	21.7%	23.9%	
	37-40	5	1	1	1	4	2	17	31	
		55.6%	33.3%	33.3%	100%	80.0%	100%	73.9%	67.4%	
Delivery	Unknown	1	0	0	0	0	0	0	1	0.856

Method	wn	11.1%	.0%	.0%	.0%	.0%	.0%	.0%	2.2%	
	SVD	6	3	2	1	3	2	17	34	
		66.7%	100%	66.7%	100%	60.0%	100%	73.9%	73.9%	
	C.S	2	0	1	0	2	0	6	11	
		22.2%	.0%	33.3%	.0%	40.0%	.0%	26.1%	23.9%	
Apgar score	Unkno wn	1	0	0	0	0	0	9	10	0.401
		11.1%	.0%	.0%	.0%	.0%	.0%	39.1%	21.7%	
	6	1	0	0	0	1	1	2	5	
		11.1%	.0%	.0%	.0%	20.0%	50.0%	8.7%	10.9%	
	7	0	0	0	0	1	0	1	2	
		.0%	.0%	.0%	.0%	20.0%	.0%	4.3%	4.3%	
	8	1	0	1	1	0	0	4	7	
		11.1%	.0%	33.3%	100%	.0%	.0%	17.4%	15.2%	
	9	6	3	2	0	2	1	6	20	
		66.7%	100%	66.7%	.0%	40.0%	50.0%	26.1%	43.5%	
	10	0	0	0	0	1	0	1	2	
		.0%	.0%	.0%	.0%	20.0%	.0%	4.3%	4.3%	
Twins or triplet	No or unkno wn	8	2	3	1	5	2	21	42	0.756
		88.9%	66.7%	100.0%	100%	100%	100%	91.3%	91.3%	
	Yes	1	1	0	0	0	0	2	4	
		11.1%	33.3%	.0%	.0%	.0%	.0%	8.7%	8.7%	
Smoking in parents	No or unkno wn	9	3	3	1	4	0	18	38	0.040
		100%	100%	100.0%	100%	80.0%	.0%	78.3%	82.6%	
	Yes	0	0	0	0	1	2	5	8	
		.0%	.0%	.0%	.0%	20.0%	100.0%	21.7%	17.4%	

DISCUSSION:

Apparent life-threatening event (ALTE) is a major cause of neonatal emergency visits [21]. Apparent life-threatening event (ALTE), as defined by National Institutes of Health (NIH), is "an episode that is frightening to the observer and that is characterized by some combination of apnea (central or occasionally obstructive), color change (usually cyanotic or pallid but occasionally erythematous or plethoric), marked change in muscle tone (usually marked limpness), choking, or gagging [22]. In some cases, the observer fears that the infant has died [23]. It is associated with a 0%–7.6% mortality rate [24]. ALTEs occur predominantly in infancy at a mean age of 1–3 months [25], and equally between boys and girls [26]. Infants with an ALTE are often asymptomatic at hospital and there is no standard workup protocol for ALTE. Therefore, a detailed initial history and physical examination are important to determine the extent of the medical evaluation and treatment. This is a retrospective cross-sectional study was conducted among 46 infants with ALTE. The study aims to determine the etiology of Apparent Life-Threatening Event and demographic association in infants in National Guard Health Affairs, King Abdul-Aziz Medical City in Riyadh, KSA.

The estimated frequency of apparent life-threatening events among healthy term infants widely varies (0.5–6% of all newborns), reflecting figures derived from older retrospective reviews of hospital records [27]. A systematic review reported that apparent life-threatening events accounted for 0.6–0.8% of all emergency department visits among children younger than 1 year, was noted in 2.27% of hospitalized children, and had an incidence of 0.6 cases per 1,000 live-born infants [28]. A prospective population-based study of apparent life-threatening events conducted in Austria reported an incidence of 2.46 cases per 1,000 live births. [9]. A population based infant cohort in Italy suggesting a cumulative incidence of 4.1 per 1,000 live births in the study area [29].

There are several potentially dangerous or treatable conditions associated with ALTEs. The causes of ALTE are categorized into problems that are: gastrointestinal (50%), neurological (30%), respiratory (20%), cardiovascular (5%), metabolic and endocrine (2%–5%), or others such as child abuse. Up to 50% of ALTEs are idiopathic, where the cause cannot be diagnosed. Regardless of the cause of an ALTE, all infants with an ALTE should require hospitalization and continuous cardiorespiratory monitoring and evaluation for at least 24 hours [30]. Our study reported that the causes of ALTEs were

idiopathic in 50% of cases followed by gastro-esophageal reflux disease (GERD) 19.6%, respiratory distress syndrome (RDS) 10.9%. cardiac caused and dysmorphism reported by 6.5% for each of them. Neonatal sepsis and neurological disorder 4.3%. and only 2.2% for each of bronchopulmonary dysplasia. Similar to our results another study conducted among 275 infants reported; the most common causes were idiopathic (32%) followed by gastro-esophageal reflux (GER) in (22%), bronchiolitis in (21%), multiple diagnoses (12%) and only 4% for neurological problems [22]. Also, Ariagno RL et al [31] found that more than half of cases 51% reported unknown causes of ALTEs. Another study reported idiopathic causes in 42% of infants followed by gastro-esophageal reflux 26% [32]. In contrast to our results, another study conducted among 23 infants found that the most common established etiology was lower respiratory tract infections (39.1%) followed by intracranial and extra cranial hemorrhages (13.0%), and central nervous system infections (8.6%) but, the cause remained unknown in 8.7% of cases [33]. Another study conducted among 65 infants reported; causes of ALTEs were esophageal reflux (26%), unknown cause (23%), pertussis (9%), seizures (9%), urinary tract infection (8%), factitious illness (3%). Other causes reported; hypocalcaemia, brain tumor, atrial tachycardia, persistent ductus arteriosus and opioid related apnea [2]. Another study reported; pneumonia or bronchiolitis (12%), seizure (8%), sepsis (7%), intracranial hemorrhage (3%), bacterial meningitis (2%), dehydration (2%), and severe anemia (2%) [3].

Regarding to the relationship between causes ALTE and related risk factors among the studied infants. We found that there were no significant correlations between causes ALTE and age, gender, weight, gestational age, delivery methods, Apgar score and children were twins or triplet ($p > 0.05$) but, there were significant relation with smoking in parents ($p = 0.04$). Another study found that the prone sleeping position, smoking during pregnancy, low gestational age, profuse night sweating, and family history of infant death showed a moderate relation to the risk of overall ALTE, but only smoking maintained significance in the multivariate risk model [9].

CONCLUSION

This study concluded that the most common cause of apparent life-threatening event was idiopathic by 50% followed by gastro-esophageal reflux disease (GERD), this results were similar to a lot of previous studies. Also, we found that there were no significant correlations between causes ALTE and age, gender,

weight, gestational age, delivery methods but, there were significant relation with smoking in parents.

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