A Systematic Review of the Probability of Asphyxia in Children Aged <2 Years with Unexplained Epistaxis

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Objective To determine the proportion of children aged <2 years who have been asphyxiated presenting with epistaxis in the absence of trauma or medical explanation and to identify the characteristics of the clinical presentation indicative of asphyxiation.

Study design An all-language systematic review was conducted by searching 10 databases from 1900 to 2015 and gray literature to identify high-quality studies that included children with epistaxis aged <2 years (alive or dead) with explicit confirmation of intentional or unintentional asphyxiation (upper airway obstruction). Studies of traumatic or pathological epistaxis were excluded. For each comparative study, the proportion of children presenting with epistaxis that were asphyxiated is reported with 95% CI.

Results Of 2706 studies identified, 100 underwent full review, resulting in 6 included studies representing 30 children with asphyxiation-related epistaxis and 74 children with non–asphyxiation-related epistaxis. The proportion of children presenting with epistaxis that had been asphyxiated, reported by 3 studies, was between 7% and 24%. Features associated with asphyxiation in live children included malaise, altered skin color, respiratory difficulty, and chest radiograph abnormalities. There were no explicit associated features described among those children who were dead on arrival.

Conclusion There is an association between epistaxis and asphyxiation in young children; however, epistaxis does not constitute a diagnosis of asphyxia in itself. In any infant presenting with unexplained epistaxis, a thorough investigation of etiology is always warranted, which must include active exploration of asphyxia as a possible explanation. *(J Pediatr 2016;168:178-84)*.

Although epistaxis is a frequent and often trivial finding in children, owing predominantly to trauma, congenital disorders, nasal mucosal abnormalities, and coagulation disorders, it is extremely rare in those aged <2 years, with an incidence of up to 31 per 10 000 children.[1-4] In a landmark study, epistaxis was observed in 37% of infants who were asphyxiated using covert surveillance.[5] Consequently, epistaxis has been described as a marker of asphyxiation in very young children.[6] The challenge is to distinguish between epistaxis from benign causes and epistaxis from asphyxiation.

In the US, more than 1.25 million children experience maltreatment annually.[7] Asphyxiation is a recognized form of fatal maltreatment. Although it is associated with high morbidity and mortality, asphyxiation may present with few or no external signs.[8] Child homicide is most frequent in infancy[9]; therefore, evaluating the likelihood of asphyxiation in young children, such as those presenting with epistaxis, is of paramount importance in identifying children at significant risk of further harm or death.[8] Whether asphyxiation has occurred intentionally or unintentionally, the challenge is to find clinical indicators that asphyxiation may be associated with the child's epistaxis.

The physiological mechanism underlying epistaxis in asphyxia is complex, which has led to controversy surrounding the use of epistaxis as an indicator of asphyxia.[3,10-12] The significance of epistaxis as an indicator of asphyxiation is particularly pertinent in a legal setting, as for example in a 2000 case in England, where the expert witnesses disagreed as to the relative significance of previous epistaxis as a possible indicator of repeated imposed asphyxiation.[13] The consequences of an incorrect decision either way has significant implications for the affected family.

Individual studies have aimed to define the relationship between epistaxis and asphyxiation, but given the rarity of the problem in infancy, they are necessarily small, with a high potential for bias. This systematic review aimed to address this situation by identifying associated features of epistaxis indicative of asphyxiation in children aged <2 years.

ALTE	Apparent life-threatening event
CPR	Cardiopulmonary resuscitation
SIDS	Sudden infant death syndrome

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Methods

An all-language search was conducted of published and gray literature across 10 databases from 1900 to 2015 (**Table I**; available at www.jpeds.com). The search strategy, developed in MEDLINE Ovid, consisted of 76 key words and Medical Subject Headings (**Table II**; available at www.jpeds.com). This was adapted for other databases. Supplementary "snowballing" techniques were used to augment search sensitivity including searching non-indexed journals, searching the references of all full-text articles, and correspondence with authors of included studies when necessary for clarification of clinical or social details.

Inclusion criteria were age <2 completed years with epistaxis, encompassing live and fatal cases. Epistaxis was defined as any nasal bleeding, which included oronasal bleeding but not serosanguinous secretions in fatal cases. Asphyxiation included intentional and unintentional upper airway obstruction.[14,15] Included study designs were cross-sectional, cohort, and case series with at least 3 cases (**Table III**; available at www.jpeds.com). Exclusion criteria included traumatic epistaxis or medical conditions that predispose to epistaxis, oral bleeding, case reports, review articles, expert opinion, studies in which adult and child data could not be separated, methodologically flawed studies, studies that used the presence of epistaxis to confirm asphyxiation, and studies that addressed epistaxis only in the absence of asphyxiation.

Data were extracted under the following headings: ascertainment, study population, clinical characteristics/presentation, coexistent injuries, past or subsequent medical histories, sibling medical histories, confirmation of asphyxiation, exclusion of asphyxiation, and exclusion of trauma and organic disease (**Table IV**).

Studies were assessed for inclusion, reviewed, and critically appraised independently by 2 reviewers, and disagreements were resolved by third reviewer arbitration. Studies were evaluated using a standardized critical appraisal tool that included 10 domains (**Figure 1**; available at www.jpeds.com).[20,21] This review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.[22] A ranking of asphyxiation confirmation and exclusion was designed to minimize circularity, that is, to exclude studies that used the presence of epistaxis to confirm asphyxiation, and to exclude studies that did not adequately detail how asphyxiation was confirmed or excluded in a child with epistaxis (**Table V**). Only studies with an asphyxiation ranking between 1 and 3 were included. This required asphyxiation to be witnessed or admitted by the perpetrator, or to be determined by multiagency child protection groups, postmortem, sudden death investigations, or legal panels.

Data Analyses

We compared children who had adequate confirmation of asphyxia and epistaxis with children who had epistaxis but had not been asphyxiated (**Table V**). The proportion of children presenting with epistaxis who had been asphyxiated, along with the associated 95% CI, was calculated for each study. When 2 publications from the same study were identified, we approached the authors to identify duplicate cases, which were removed from the analysis to prevent double-counting. We calculated the proportion of children with epistaxis who had been asphyxiated, and also performed a descriptive analysis of the associated features of children with asphyxiation-related epistaxis.

Results

Out of the 2706 articles identified, 7 articles (6 studies) were included, representing 30 young children with asphyxiation-related epistaxis and 74 children with non–asphyxia-related epistaxis (**Table IV** and **Figure 2**; **Figure 2** available at www.jpeds.com).[2,4,5,16-19] Children with non–asphyxia-related epistaxis and concurrent upper respiratory tract infection that was not considered a definitive medical cause of epistaxis, as confirmed by the authors when necessary, were included.[4,19] Two publications from the same study were clarified with the authors to avoid duplication of cases for statistical analysis.[4,19]

Included studies were cross-sectional and case-series designs, largely recorded by covert surveillance, autopsy reports, death scene investigations, and medical records.[2,4,5,16-19]

There was no clear differential presentation of age between those with asphyxiation-related epistaxis and those with non–asphyxia-related epistaxis (**Table VI**; available at www.jpeds.com). Children with asphyxiation-related epistaxis (n = 30) were aged 30 to 684 days (1 child aged >1 year), and those with non–asphyxia-related epistaxis (n = 74) were aged 10 to 398 days (1 child aged >1 year). Age ranges were affected by the various studies' inclusion criteria (**Table IV**). Only 14 of 49 live children with epistaxis were recorded as undergoing clotting investigation.[2,4,5,16-19]

Of the 6 included studies,[2,4,5,16-19] 3 were comparative[2,4,17,19] (ie, included 2 groups of children, 1 group with epistaxis with asphyxia and 1 group with epistaxis without asphyxia), and thus provided estimates of the proportion of children presenting with epistaxis who had been asphyxiated, which was between 7% and 24% (**Table VII**). Krous et al reported a proportion of 16.7% (95% CI, 7%-36%), McIntosh et al reported a proportion of 24% (95% CI, 12%-43%), and Paranjothy et al reported a proportion of 7.1% (95% CI, 1%-32%).

Of the 30 children who were asphyxiated, 17 presented alive, aged 30 to 684 days (1 child aged >1 year), and 13 were dead on arrival, aged 32 to 324 days (**Table IV**). Reported mechanisms of asphyxiation included overlaying, positional, and mechanical asphyxiation with clothing, bedding, and hands.

The clinical presentation of the 17 live children who were asphyxiated was adequately described by 3 studies in 4 publications.[4,5,16,19] There was variability in the features described in these children (**Table IV**), with some presenting as pale,