Pulmonary edema post-adenotonsillectomy in children

Elaf Ahmed, MBBS, *Nasser K. Almutairi*, MBBS.

ABSTRACT

تعتبر الوذمة الرئوية بعد اسْتِئْصالُ اللّوزَتين والغُدّانِيّات (pATPE) حالة مهددة للحياة تتطلب التدخل السريري الفوري. التشخيص المبكر والكشف عن علامات هذه الحالة أمر هام لعلاجها ونتائج المريض. الغرض من مقالة المراجعة هذه هو تقديم بيانات وبائية عن مدى انتشار pATPE، ومعالجة آليات تطورها، والأنواع، والمسببات، والفلسفيكولوجيا، وإدارة pATPE. وذلك لتقليل معدلات قبول وحدة العناية المركزة بعد العملية الجراحية من pATPE، واستعرضت هذه المراجعة كلا من طرق الاستفادة من التقييم السريري قبل الجراحة، وأدوات المراقبة الجراحية/بعد العملية الجراحية، والاحتياطات الإجرائية.

Post-adenotonsillectomy pulmonary edema (pATPE) is a life-threatening condition that necessitates immediate clinical intervention. The early diagnosis and detection of the signs of this condition is vital to its treatment and patient outcome. The purpose of this review article is to present epidemiological data on the prevalence of pATPE, and address the mechanisms of development, types, etiology, pathophysiology, and management of pATPE. In order to minimize postoperative intensive care unit admission rates of pATPE, utilization of preoperative clinical assessment, operative/postoperative monitoring tools, and procedural precautions are discussed.

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From the Department of Otorhinolaryngology, King Saud Medical City, Riyadh, Kingdom of Saudi Arabia.

Address correspondence and reprint request to: Dr. Elaf Ahmed, Department of Otorhinolaryngology, King Saud Medical City, Riyadh, Kingdom of Saudi Arabia. E-mail: dr.elaf1989@gmail.com ORCID ID: orcid.org/0000-0003-2940-1070

Sleep disordered breathing (SDB) is a spectrum of breathing disorders encompassing primary snoring at one end and obstructive sleep apnea syndrome (OSA) at the other end. While snoring is a primary symptom, OSA is a critical pathological condition that requires medical intervention.[1] Obstructive sleep apnea is a condition characterized by increased upper airway resistance to air flow and intermittent upper airway closure followed by subsequent hypoxemia, hypercapnia and an interrupted sleep. Polysomnography (PSG) is the gold standard for the diagnosis and assessment of the severity of OSA. In adults, continuous positive air pressure (CPAP) is the mainstay of treatment for OSA according to the mainstream of international societies;[2] while in children, adenotonsillectomy could be considered as first line treatment of OSA. According to Wiatrak et al,[3] children whose polysomnographic tests demonstrate an apnea-hypopnea index (AHI) >10/hours or significant oxygen desaturation <90% are candidates for surgical intervention. Prevalence of OSA among adults aged 30-70 years was estimated to be approximately 13% in males and 6% in females.[4] However, local studies of OSA in Saudi adults indicated that 33.3% of males and 39% of females are considered to be at high risk of OSA.[5,6] In pediatrics, one study reports a prevalence of OSA of approximately 4%,[7] while other studies estimate 1.2-5.7% of that population.[8,9] Generally, studies show an approximate 3-fold increase in behavior and neurocognitive abnormalities in children with sleep-disordered breathing.[10] The realization of neurocognitive and cardiopulmonary complications associated with recently treated OSA in children promoted awareness of OSA treatment in children.[11,12]

Adenotonsillectomy in pediatric patients has evolved from being a treatment of adenotonsillar hypertrophy and chronic pharyngitis to the management of sleep-disordered breathing.[13] According to the American Academy of Otolaryngology, Head and Neck Surgery (AAO-HNS), candidates for adenotonsillectomy in the past were patients with 3 or more infections of the tonsils and/or adenoids per year, or had cases of chronic tonsillitis which were unresponsive to

beta-lactamases.[14] Currently, however, adenotonsillar hypertrophy has been identified as the most commonly-recognized anatomic risk factor in pediatric OSA.[15] Therefore, adenotonsillectomy (AT) is now considered as the first-line treatment for OSA worldwide.[10,16] Adenotonsillectomy is proven to restore normal PSG in most OSA cases[17] and consequently improves the quality of life for those patients. Based on the need for cost optimization by third-party medical insurance providers, it became necessary to evaluate "the possibility of performing adenotonsillectomy on an out-patient basis. Such studies revealed "the suitability of performing this procedure with acceptable efficiency as long as good communication between the surgeon, anesthesiologist and the parents of the child is maintained.

Pulmonary edema (PE), although a rare complication of adenotonsillectomy,[18] is a life-threatening condition that necessitates immediate medical intervention. In the absence of comorbid pulmonary conditions, post-adenotonsillectomy pulmonary edema (pATPE) may be referred to as negative pressure pulmonary edema (NPPE). It is worth mentioning that NPPE can be classified into type I-NPPE and type II-NPPE.[19] Treatment options for pATPE are similar to those of PE and these include oxygen supplementation, restoration of optimal positive end-expiratory pressure (PEEP), and diuretics.

Cost-containment and reduction are among the major concerns of the health care systems in developing countries. The aim of this study is to perform a cost-benefit analysis of ICU admissions following adenotonsillectomy in OSA patients for fear of developing pulmonary edema. Is it really necessary to admit to the ICU all children with risk factors who underwent adenotonsillectomy to prevent this complication? Additionally, we aim to highlight the probable tools that can reduce rates of ICU admissions among such a cohort.

Etiology/pathophysiology. Post-adenotonsillectomy pulmonary edema may be considered as negative pressure pulmonary edema (NPPE) which has 2 major subclasses. The first is type I-NPPE which results from the forceful expiration against an acutely obstructed upper airway. The second is type II-NPPE which results from the surgical removal of a chronic upper airway obstruction, such as in an OSA patient who underwent adenotonsillectomy. This results in a sudden decrease in intrathoracic pressure precipitating transudation of fluid into the interstitial and alveolar spaces. Reasons for the development of type I-NPPE include accidental occlusion of an endotracheal tube while intubated,[20] croup and epiglottitis especially in children,[21] and laryngospasm due to post-extubation.[22] In addition, administration of muscle relaxants at the beginning of an inhalational induction of anesthesia can induce type I-NPPE due to the premature paralysis of glossal muscles before the diaphragm.[23] Generally, the symptoms of PE develop immediately, although sometimes the onset may be considerably delayed for a few hours in the postoperative period. Thus, close post-operative observation must be continued for an extended time in patients with risk factors for pATPE.[19]

A couple of widely accepted mechanisms have been published to demonstrate the development of pATPE. One mechanism suggests that chronic upper airway obstruction associated with OSA promotes an elevated level of auto positive end-expiratory pressure (auto-PEEP). Type II-NPPE develops upon sudden relief for chronic upper airway obstruction via adenotonsillectomy (sudden decrease in auto-PEEP), creating a negative intrathoracic pressure (-50 to -100 cmH$_2$O). Consequently, venous return to the heart is increased with subsequent elevation of ventricular end-diastolic volume. Thus, the left ventricular end-diastolic pressure is elevated leading to transudation of fluids in the lung interstitium and alveoli causing pulmonary edema.[24-26] On the other hand, type I-NPPE originates from negative intrathoracic pressure developed from forceful respiration against an acutely-obstructed upper airway. Furthermore, obstruction resulting in hypoxia in both types triggers a massive sympathetic discharge causing a blood shift from the systemic to the pulmonary circulation due to negative intrapulmonary pressure.[27] Another suggested mechanism states that the chronic mechanical stress developed from respiration against an obstructed upper airway may induce alterations in the alveolar epithelial and pulmonary microvascular membranes, resulting in increased pulmonary capillary permeability, and consequently, protein-rich PE.[25,28,29]

Epidemiology. Post-operative adenotonsillectomy complications may be classified into respiratory and non-respiratory complications. Respiratory complications include persistent oxygen desaturation, laryngospasms, bronchospasms, and pulmonary edema. Generally, post-operative respiratory complications are approaching 6.5% in children; while children less than 3 years old have a rate of 10%.[30] However, pATPE is a rare, life threatening complication that requires immediate intervention.[31-33]

In a study of 86 post-adenotonsillectomy children with a mean age of 5.3±2.2 years and without craniofacial anomalies or significant cardiopulmonary comorbidities, cases with apnea-hypopnea index (AHI) ≥40 showed significant statistical correlations with post-

operative respiratory complications.[34] Results of the study revealed 11.6% had respiratory complications, none of which was pulmonary edema. Kon-Tai et al[35] conducted a study of 610 children aged <18 years, mean age 7.2 ±3.3 years, with diverse comorbidities and risk factors. All underwent adenotonsillectomy for the treatment of OSA. Although the study reported complications related to oxygen saturation-related between 1.6% to 14.3% with varying severity, only 0.5% developed pneumonia. The Kon-Tai study revealed a low risk of major respiratory complications (laryngospasm, bronchospasm, pulmonary edema, pneumonia) following adenotonsillectomy in this population. Melissa et al[30] reported 6.4% as prevalence of post-adenotonsillectomy respiratory complications in a study that involved 2315 patients under 6 years. Of this population, 0.7% developed serious complications including atelectasis, infiltrate, and pulmonary edema. Sofia et al[36] documented a 0.45% prevalence of PE among a study cohort of 221 school-aged children. Nuntiger et al[37] also conducted a study involving 216 patients with an average age of 6.6 years and high proportions of comorbidities such as craniofacial abnormalities, obesity, and pulmonary hypertension. In this study, a 4.3% prevalence of post-operative PE after adenotonsillectomy was reported. Guinard referred to Type I-NPPE that develops due to laryngospasm after airway surgery as laryngospasm-induced pulmonary edema.[27] The Australian Incident Monitoring Study of 4000 incidents of laryngospasm during anesthesia showed that NPPE occurs in up to 4% of all incident reports of laryngospasm.[38] The previous high ratios could be attributed to the wide inclusion criteria of the study regarding comorbidities and type of surgical procedure.

Risk factors for development of pATPE. Development of pulmonary edema after adenotonsillectomy is life threatening condition; however, it is uncommon complication. Young age (<3 years) or the presence of some comorbid conditions such as asthma, history of prematurity and craniofacial malformations may increase the risk of developing PE in children undergoing adenotonsillectomy.[30]

Asthma is one of the risk factors for the development of PE after adenotonsillectomy, as it predisposes pulmonary capillary epithelium to disruption either directly due to high breathing workload, or indirectly by cytotoxic proteins derived from the migration of inflammatory cells. Regarding etiological mechanisms, a pathophysiological cascade due to any of these mechanisms leads to an extravasation of proteins from post-capillary venules into interstitial tissues resulting in the development of PE.[39-41]

Premature infants with respiratory distress syndrome (RDS) who were ventilated at birth commonly have a condition known as chronic lung disease (CLD) of prematurity. From a histological point of view, Hulsmann R. and Van Anker[42] stated that the evolution of CLD can be divided into an early inflammatory phase followed by a subacute and chronic fibroproliferative phase. An influx of inflammatory cells and increased levels of cytokines in alveolar sacs characterize the first phase, while the second phase is characterized by hyperplasia of type II pneumocytes, and interstitial and perialveolar fibrosis. Surviving patients show persistent lung function abnormalities. Therefore CLD is considered a risk factor for pATPE due to abnormalities of alveolar wall.

Alida et al[43] reported that 95% of infants with Down syndrome who were referred for PSG had OSA, out of which 75% had severe OSA, which qualified them as candidates for adenotonsillectomy. Bronchial asthma, Down syndrome, and other craniofacial conditions may precipitate high auto-PEEP, which upon sudden relief via adenotonsillectomy result in the development of pATPE.[44]

Management. As a subtype of pulmonary edema, pATPE is usually self-limited and easily corrected.[45] Supportive therapy in these patients begins with close observation in an ICU or step-down unit that has high surveillance. Strategies for correction of pATPE include maintenance of airway via intubation. If the airway is obstructed due to the patient biting down on the endotracheal tube, a dose of succinylcholine (0.1-0.2 mg/kg) may be given to relax the jaw muscles.[19] Invasive or non-invasive supplemental oxygen to restore appropriate PEEP via continuous positive airway pressure (CPAP) or bi-level positive airway pressure (BPAP) should be provided. Generally, diuretics may be administered to correct fluid accumulation in lung interstitial spaces and alveoli, unless the patient is hypovolemic. In severe cases of pATPE, mechanical ventilation may be required. It is worth mentioning that non-invasive respiratory support via CPAP or BPAP decreases the work of breathing, improves alveolar gas exchange, reduces left ventricular preload and afterload, increases cardiac output and improves hemodynamics.[19] Evidence suggests that noninvasive respiratory support may be an effective strategy to reduce intubation rates,[46,47] as well as ICU and hospital lengths of stay[46] in postoperative patients.[19]

Perioperative measures to minimize the probability of pATPE and ICU admission rates. Generally,

adenotonsillectomy is an out-patient procedure; the patient may be discharged on the same day after procedure regardless the surgical technique utilized. However, in some situations it is recommended to hospitalize patient for few hours to a few days based on clinical evaluation and the presence of comorbid conditions.[30] Specifically, children at risk for upper airway obstruction or respiratory compromise following tonsil and adenoid surgery such as those under the age of 3, or who have comorbidities like neurological problems, congenital heart disease, prematurity, Down syndrome or craniofacial abnormalities are candidates for post-adenotonsillectomy admission. It has been found that 80% of pulmonary edema occurs within minutes after relief of upper airway obstruction.[48]

Edema ranges from mild to severe depending on the degree of obstruction and pulmonary capillary injury.[45] Cost reduction is a worldwide trend in the health care system. This current work involves a cost/benefit assessment of OSA patients who underwent adenotonsillectomy and were admitted to the ICU as a precaution for the possibility of developing pulmonary edema. Patient variation and waste associated with the delivery of care is a major factor that contributes to the escalation of healthcare costs. In order to minimize ICU admission rates, it is necessary to analyze the root causes leading to ICU admissions. In this context, the optimum management of healthcare resources requires, first of all, the assessment of the cluster of patients with OSA who require in-patient admission. Secondly, it is

Table 1 - Summary of the Articles which were Reviewed.

Author's name	References	Type of study	Year	No. of patients	Results
David Kasle	34	Case Series	2016	86	Eighty-six patients (mean age 5.3 ± 2.2 years) were included. There was a statistically significant (p=0.03) relationship between an apnea-hypopnea index ≥40 (AHI40) and post-operative respiratory complications. Apnea-hypopnea index 40 also had the greatest magnitude of association with postoperative respiratory complications (OR = 5.313). An AHI ≥25 (AHI25) was marginally significant (p=0.067). No significant difference in outcome occurrence was found when analyzing rates of complication in patients with BMI above and below 18 (p=0.20) or oxygen (O_2) nadir above and below 80% (p=0.09). The AHI ranged from 0 to 112.2, and no postoperative respiratory complications were identified in children with an AHI less than 10.
Nuntigar Sonsuwan	37	Retrospective	2014	216	There were 216 patients who underwent adenotonsillectomy due to airway obstruction during the study period. Five patients were excluded due to incomplete data. Of those included, 129 patients (61.1%) were male with mean age of 6.6 (SD 3.2) years. Four significant factors associated with the development of post-operative pulmonary edema after the adenotonsillectomy were procedure, age, obesity, and pulmonary hypertension.
Peppard et al	4	Cohort study	2013	1520	The prevalence estimates of moderate to severe sleep-disordered breathing (AHI, measured as events/hour, ≥15) are 10% (95% confidence interval [CI]: 7, 12) among 30-49 year-old men; 17% (95% CI: 15, 21) among 50-70 year-old men; 3% (95% CI: 2, 4) among 30-49 year-old women; and 9% (95% CI: 7, 11) among 50-70 year-old women. These estimated prevalence rates represent substantial increases over the last 2 decades (relative increases of between 14% and 55% depending on the subgroup).
BaHammam et al	6	Cross-sectional study	2008	578	Five hundred and seventy-eight middle-aged Saudi males with a mean age of 45.02 ± 9.3 year were surveyed in this study. Snoring was present in 52.3%, and breathing pauses more than once per week was noticed in 11.3%. Based on the Berlin questionnaire stratification for risk of obstructive sleep apnea syndrome (OSA), 33.3% were considered as high risk patients for OSA. The occurrence of daytime tiredness more than once/week was reported by 35.5%. The prevalence of snoring and risk for OSA is similar to that reported in the US.
Bixler et al	9	Phase I cross sectional study	2009	5740	Each child was assessed with a full polysomnogram and completed a history/physical examination including an electrocardiogram, otolaryngology examination, and pulmonary evaluation. The prevalence of moderate sleep disordered breathing (SDB) (apnea-hypopnea index ≥5) was 1.2%. The independent risk factors included nasal abnormalities and minority associated only with mild (1 <AHI <5) SDB and snoring and waist circumference associated with all levels of SDB. Tonsil size, based on visual inspection, was not an independent risk factor.
		Phase II clinical study		7000	
Thomas et al	33	Case report	1999	1	The rapidity of onset of negative pressure pulmonary edema may lead to death if the disease is not recognized thus it must be emphasized that this disease can occur in any patient especially in patients with obstructive process of upper airway.

important to highlight the tools and precautions that can reduce rates of ICU admission even among such a risky group (**Table 1**).

Preoperative clinical assessment. A pre-operative clinical assessment of patients could dramatically help rule out children with comorbid risk factors, generally decreasing the rate of post-operative ICU admissions. It is important to mention the controversial criteria of the American Academy of Otolaryngology (AAO) and American Academy of Pediatrics (AAP) which recommend overnight monitoring of all OSA patients with AHI ≥10 (by the AAO) and AHI ≥24 (by the AAP) following an adenotonsillectomy. As discussed in the next section, simple monitoring of pulse oximetry could empirically help solve such controversies surrounding the potential development of PE. Specifically, the next few paragraphs will focus on children who do have risk factors for development of pATPE.

Operative/postoperative monitoring tools. With prompt diagnosis and intervention, most pATPE patients can be treated without complications. Since PE develops in a matter of minutes after adenotonsillectomy, simply monitoring the oxygen saturation in the operating room and post-anesthesia care unit using pulse oximetry usually identifies patients at risk and in need of in-patient hospitalization rather than ICU admission. This is because signs and symptoms in most cases are subtle.[45] On the other hand, in the absence of pulse oximetry, in-patient admission of patients with OSA could be limited to patients who have risk factors for the development of pATPE. Such patients include children younger than 3 years old, patients with severe OSA, those with comorbid conditions including asthma, obesity, cardiac involvement (right ventricular hypertrophy), Down syndrome, history of prematurity, craniofacial abnormalities, neuromuscular diseases, chronic lung disease, and sickle cell disease.[49-55]

In conclusion, a combination of pulse oximetry monitoring and clinical evaluation of patients can effectively identify cases in need of in-patient monitoring. Since the management of pATPE ranges from simple oxygen supplementation, application of noninvasive positive airway pressure up to diuretic therapy, advent of inexpensive portable versions of pulse oximeters allow close patient monitoring for pATPE development in sub-ICU level care units, stepping up and down to ICU or normal ward care according to case progression. Primarily, patients with risk factors may be admitted to sub-ICU level care units provided there are no signs of oxygen desaturation and other vital signs. Such simple surveillance could dramatically reduce the cost of healthcare services. Intensive care unit admissions should be limited to cases that require multiple-organ support or advanced respiratory support such as severe PE in which pulmonary venous pressure exceeds 30 mm Hg[56] and which requires invasive mechanical ventilation/CPAP/BPAP via trans-laryngeal tracheal or tracheostomy.

Procedural "Surgical-anesthetical" precautions. Several surgical techniques have been developed over the years, but the core principles remain unchanged. The achievement of successful surgery starts with induction of anesthesia, patient positioning for oral intubation, and the surgical dissection technique. Extracapsular techniques include sharp dissection, monopolar electrocautery, bipolar cautery and harmonic scalpel, while intracapsular techniques include microdebrider, bipolar radiofrequency ablation, or carbon dioxide laser.[57]

Mechanical stimulation of the endotracheal tube during extubation often results in laryngospasm which may induce type I-NPPE. Therefore, patient intubation should be carried out either under deep anesthesia or after muscle relaxant administration to lower the incidence of laryngospasms. Redundant controversies exist among anesthesiologists regarding which technique of tracheal extubation (awake versus anesthetized), is better at reducing the incidence of laryngospasms.[58] With regards to this, Lee recommended extubation while the lungs are inflated by positive pressure.[59] There is a close association between the type of surgery performed and the occurrence of laryngospasm. Tonsillectomy and adenoidectomy are associated with the highest incidence of laryngospasm (21-26%).[58,60] However, induction of anesthesia in pediatrics either intravenously or by inhalation, using suitable anesthetic drugs is a controversial topic that should be addressed on a case by case basis. Intravenous anesthesia was found to be associated with a lower incidence of laryngospasm than inhalational anesthesia.[61] Despite extensive debate regarding the avoidance of laryngospasm, several strategies have been suggested to lower the incidence of laryngospasm. Koc et al[62] reported that topical lignocaine 2% at a dose of 4 mg/kg sprayed on the glottis, or 2% intravenous lignocaine given at 1 mg/kg five minutes before extubation are fairly effective in preventing laryngospasm following adenotonsillectomy. According to Gulhas et al,[63] 15 mg/kg magnesium sulfate in 30 ml 0.9% NaCl administered over 20 minutes after tracheal intubation has also been suggested to reduce the incidence of laryngospasm post-adenotonsillectomy. Intravenous administration of 0.25-0.5 mg/kg propofol prior to extubation has also been shown to be effective.[58]

Some anesthesiologists indicated that inhalation of 5% carbon dioxide could prevent laryngospasm, since respiratory drive to exhale the carbon dioxide overrides the laryngospasm reflex.

In conclusion, pATPE is a rare but life-threatening complication that requires immediate intervention. Young age (<3 years) or the presence of some comorbid conditions such as asthma, history of prematurity, craniofacial malformations, Down syndrome and severe OSA may increase the risk of developing PE in children undergoing adenotonsillectomy. With prompt diagnosis and intervention, most pATPE patients can be treated without incident. Since PE develops in a matter of minutes after adenotonsillectomy, simply monitoring oxygen saturation using pulse oximetry in the operating room and in the post-anesthesia care unit usually identifies patients at risk and in need of in-patient hospitalization rather than ICU admission.

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